

ANNUAL REPORT

2016-2017



Department of Biotechnology
Ministry of Science & Technology
Government of India

Annual Report 2016-17 Committee

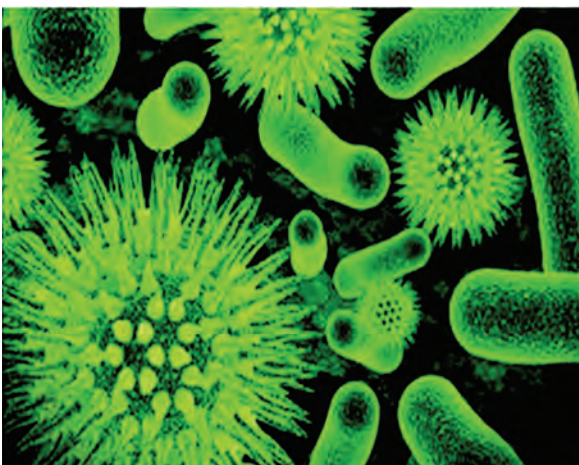
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NATIONAL INSTITUTE OF IMMUNOLOGY
 NATIONAL CENTRE FOR CELL SCIENCE
 CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS
 NATIONAL BRAIN RESEARCH CENTRE
 INSTITUTE OF LIFE SCIENCES
 REGIONAL CENTRE FOR BIOTECHNOLOGY
 NATIONAL INSTITUTE OF BIOMEDICAL GENOMICS
 INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE
 MEDICINE
 NATIONAL AGRI-FOOD BIOTECHNOLOGY INSTITUTE
 CENTER OF INNOVATIVE AND APPLIED BIOPROCESSING
 NATIONAL INSTITUTE OF ANIMAL BIOTECHNOLOGY
 TRANSLATIONAL HEALTH SCIENCE AND TECHNOLOGY
 INSTITUTE
 NATIONAL INSTITUTE OF PLANT GENOME RESEARCH
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01 OVERVIEW

Department of Biotechnology (DBT) under the Ministry of Science and Technology, over the past 30 years, has given a new impetus to developments in modern biology and biotechnology. The Department has provided continue support to facilities the journey from a nascent sector to a sunrise industry. There have been significant achievements in the growth and application of biotechnology in the areas of agriculture, healthcare, animal sciences, environment and industry. Today, India is among the top 12 biotech destinations in the world and ranks third in the Asia-Pacific region. India has the second-highest number of US Food and Drug Administration (USFDA)–approved plants, after the USA and is the largest producer of recombinant Hepatitis B vaccine.

RCB Bill, 2016

The Parliament passed The Regional Centre for Biotechnology Bill, 2016. The Bill establishes Regional Centre for Biotechnology, an institution of education, training and research, under the auspices of United Nations Educational, Scientific and Cultural Organization (UNESCO) in the National Capital Region and declares it as an institution of national importance. The Gazette of India notification has been issued.

Implementation of announcements made in the National Biotechnology Development Strategy

The National Biotechnology Development Strategy of the Department of Biotechnology was announced in December, 2015.

The Department has over the year worked towards implementation of key recommendations in collaboration and partnership with Other Ministries, Departments, State Governments and international agencies towards achieving the goals of:

- Making India ready to meet the challenge of achieving US\$100bn by 2025
- Launching Four Major Missions – Healthcare, Food and Nutrition, Clean Energy and Education
- Creating a Technology Development and Translation network across the country with global partnership-5 new clusters, 40 Biotech incubators, 150 TTOs, 20 Bioconnectcentres
- Strategic and focussed investment in building the Human Capital by creating a Life Sciences and Biotechnology Education Council

BIOTECHNOLOGY RESEARCH AND DEVELOPMENT

The Department supports research programmes in basic, translational and specialized areas of biotechnology. All proposals are received in the Department through the online portal

e-ProMIS and of subject to fair, uniform and transparent screening-cum-selection process comprising an internal screening, peer review by experts and Task Forces/Expert Committees. During the last year a total of 2918 proposals was received

and 243 sanctioned till January, 2017. The R&D supported programmes have contributed not only to knowledge generation but also new technologies and product.

Some major achievements are:

RESEARCH & DEVELOPMENT

Funding in **Basic Research** is to develop scientific theories for better understanding or prediction of natural or other events. It is for exploiting new knowledge to enhance-and where possible, transform-future capabilities. A number of research programs were supported during the period.

Noteworthy achievements of some of the projects supported are Functional characterization of sugar- and auxin-regulated DUF581 domain containing genes encoding expressed proteins of unknown functions in model plant system has led to the identification of a novel class of plant-specific zinc finger proteins, studies on chromatin remodeling for activation of systemic acquired resistance in Arabidopsis has revealed an epigenetic regulator that modulates both flowering and SAR, research work being carried out by scientists at Delhi University and IIT Delhi on development of potent small molecule inhibitors against dopamine beta-hydroxylase to combat cardiovascular diseases has led to the discovery of five small molecules as potent anti-hypertensive etc.

In the **Agriculture and Allied areas** DBT has supported projects for managing various biotic and abiotic stresses and improving yield and quality traits of the existing crops, which has been a priority for the country. These research projects are supported and implemented in networks, centre of excellence as well as individual investigator driven projects. During the period 65, research publication and 4 new IP were generated.

- Proof of concept of transgenic rice lines and advanced generation transgenic chickpea lines with high

root growth have been developed

- Rust and Late Leaf Spot, resistant backcross lines of groundnut developed which gave ~15% higher yield than the recurrent parent.
- Twenty soybean homozygous lines with Phytophthora and powdery mildew resistance were developed through molecular markers.

In the Animal Biotechnology area, during this period, projects on basic and applied aspects of animal reproduction, molecular characterization of indigenous livestock breeds, animal nutrition, utilization of animal byproducts and development of transgenics were actively pursued in Animal Biotechnology. Animal cartilage of caprine origin was successfully used for implantation in microtia and rhinoplasty of human patient. The Network Program on Brucellosis has successfully completed the first phase. A repository was established for storing and cataloguing different Brucella species. A novel penside diagnostic, lateral flow assay kit, indirect ELISA kit against Brucella species and a hand held ELISA reader have been developed. Other major achievements include more than 50 research publications, 10 patent applications filed, 08 technologies developed and 04 commercialized.

Aquaculture and Marine Biotechnology programme is being implemented to support projects for development of useful products and process from marine resources and also for enhancement of aquaculture production and productivity with the adoption of biotechnology tools and techniques. The innovation supported expected to benefit the aquatic and marine sectors and help the scientific and research community in pursuing research priorities giving emphasis on various aspects of Aquaculture & Marine Biotechnology. 14 patents have been filed for product/process development and 07 technologies have been successfully transferred to Industry for commercialization.

Projects supported under **Environmental Biotechnology** led to development of microbial technologies for waste management & environmental improvement, environment friendly treatment processes for industrial effluent, bioremediation/ biodegradation of xenobiotic pollutants, environmental genomics and metagenomics research for waste management & pollutant mitigation, conservation of viable habitat and restoration of degraded habitats using the bio-restoration technologies. Initiatives have also been taken to start R&D projects on river cleaning. Development of a green technology for improvement of paper quality and to minimize the generation of genotoxic effluents has been carried out at NIT, Durgapur. A proof of concept has been developed to provide the paper pulp mills an economic feasible strategy involving direct application of *Planococcus* sp. and *Pseudomonas* fluorescence whole cells in pre-bleaching of pulp.

In **Energy Biosciences area**, recognizing the need for alternate energy and Clean Energy the Department has been promoting R&D for Biofuel technology development. Many leads have been achieved from the research since last 5 years with potential translational value in field. During last year various new initiatives were taken to address the challenges associated with Clean Energy development. The First 2G Ethanol Technology was demonstrated at 10 t / day scale and transferred to two oil marketing companies for setting up commercial plants. The Department was also coordinating activities for Mission Innovation.

Nano-biotechnology Task Force addresses various issues in health, agriculture and environment. Research outcomes arising out of the projects are evaluated for translational potential and support is extended for development of an application of the knowledge with translational values. An ideation system has been created to enhance the innovative potential of the proposals through setting up dynamic and interactive website/supporting

programs for idea generation. The total no. of patents filed during the period are 05 and 57 research publications.

Support in **Genome Engineering technologies** and their applications was provided in the emerging areas of genome analysis and engineering technologies and to foster innovations to make such technologies affordable and available for basic and applied research in life sciences. Department has supported various projects in the identified areas of Bioengineering and gave special emphasis to generate research initiatives on organ development and assisted technologies using bioengineering methodologies.

In the area of **Medical Biotechnology** programme are supported for vaccines, drugs, therapeutics, infections and non-infections diseases.

Under the umbrella programme of **Bio-design and Bio-engineering** development of indigenous affordable medical technologies and med tech innovations led centres/programmes were implemented at School of International bio-design centred at AIIMS and IIT Delhi; Centre for Bio-design and in-vitro Diagnostics at Translational Health Science & Technology (THSTI), Faridabad. Two technologies namely Patient Transfer Sheet and ostomy Management Appliance were licensed and two technologies i.e. Fecal Incontinence Device and Neonatal Resuscitation Device-NeoBreathe were commercialized during the year.

Under the aegis of Human Genetics and Genome Analysis programme, a network project for diagnosis and management of celiac disease has been implemented.

In order to address various issues and concerns related to infectious diseases, DBT has constituted a Task Force (TF) on Infectious Disease Biology to focus on research and development and capacity building for the purpose of suggesting novel and topical areas for R&D and developing partnerships and collaborative programs.

20 new R & D projects were supported in the areas of complications in pregnancy such as preeclampsia, IUGR, recurrent miscarriages, effect of maternal nutritional status on pregnancy outcome, development of neonatal immune system.

DBT-ICMR Collaborative Efforts on HIV/AIDS and Microbicides have been launched. A new multi country collaborative initiative, co-ordinated by Canadian institute of Health Research and WHO, to establish a Healthy Life Trajectories initiative (HeLTi) based on developmental origin of health and diseases

Under the inter-institutional program on Pre-Term birth (PTB), Lab, Ultrasound facility & site infrastructure at Gurgaon Civil Hospital has been set up to collect bio-specimens, USG images & clinical data from the participants.

Stem Cells and Regenerative Medicine has been identified as one of the thrust areas under biomedical research of the Department to promote basic, early and late translational research and formulation of regulatory framework for stem cell research in India. During the years 2015-2017, a number of projects have been implemented on various aspects of embryonic, adult and induced pluripotent stem cells. The Department implemented a programme titled 'Accelerating the application of stem cell technology in human disease (ASHD)' as Indo-Japan collaborative programme with four participating institutions from India, namely: in Stem, Bangalore; NCBS, Bangalore; NIMHANS Bangalore; CSCR, CMC Vellore; & CiRA, Kyoto University, Japan as international partner.

Research and Development endeavours have been continued in food biotechnology and nutrition Biology. A pilot scale demonstration facility with a production capacity of 100 kg/day iron fortified rice premix has been established at IIT Kharagpur. (ii) A state of art whole body potassium counter to accurately estimate the body cell mass (lean body mass) has been built. (iii) five types of hypo

immunogenic products, namely hypo immunogenic muffins, hypo immunogenic bread, hypo immunogenic biscuits, hypo immunogenic chapatti and hypo immunogenic spinach pasta were developed.

Glue Grant Scheme was initiated aiming to link Basic, Clinical and Public Health Research Departments in an inter-institutional linkage(s) leading to long-term partnership programs to bridge the gap between laboratory/field research and its application to clinical and policy outcomes with a potential for translational research and technological innovation and capacity building efforts.

Promotion and use of biotechnological processes and tools for the benefit of the disadvantaged section of the society comprising women, rural population and SC/STs continued to create platform for self-employment generation among the target population by diffusion of proven and field-tested technologies through demonstration, training and extension activities.

The Review Committee on Genetic Manipulation (RCGM) functioning from the Department of Biotechnology; and the Genetic Engineering Appraisal Committee (GEAC) in the Ministry of Environment, Forest and Climate Change, has been established for evaluation, approval and monitoring of safety aspects associated with handling of recombinant DNA (rDNA) products in healthcare and agricultural sectors leading to their commercial/ environmental release.

Biotechnology Patent Facilitating Cell (BPFC) strengthened to provide administrative and financial support to biologists and biotechnologists in filing of patent applications in Indian Patent Office (IPO), United States Patent and Trademark Office (USPTO) and other countries and creation of awareness and understanding relating to Intellectual Property Rights (IPR) among the scientific community.

During the period, the RCGM evaluated more than 1050 applications in its 12 meetings in the areas of agriculture, healthcare and industrial products. 26 applications for conduct of event selection trials (ESTs)/ Biosafety Research Level 1 (BRL1) trials in confined conditions for seven transgenic crops under development viz. cotton, corn, rice, chickpea, pigeonpea, brinjal, and okra were also considered from public/private organizations for generation of biosafety data.

In the pharmaceutical sector, 44 rDNA products were permitted for conducting pre-clinical toxicity studies by private/public institutions & companies.

The International collaboration for DBT has become nimble and flexible setting the priorities in alignment with the most challenging of the country. Innovative joint programmes have been worked out. The Department has active collaborations with Canada, Denmark, Finland, Germany, Netherlands, Spain, Sweden, UK, US and EU as well as on Non Governmental organisations such as Grand Challenges, Canada, Bill and Melinda Gates Foundation, Wellcome Trust, PrakashLab, Stanford University, Nobel Media AB of the Nobel Foundation and EMBO.

In a recent Vibrant Gujarat, DBT played a proactive role with Nobel laureates during January 9-10, 2017 with participation by Scientists and entrepreneurs and by sharing the experiences in science led innovations that underpins with human welfare.

HUMAN RESOURCE DEVELOPMENT PROGRAMMES

The Department is continuing implementation of integrated Human Resource Development (HRD) Programme in Biotechnology comprising of post graduate teaching programme, short term training courses for upgradation of skills of mid-career scientists and faculty engaged in teaching and R&D, industrial training of students fellowship for doctoral and post-doctoral research training in frontier areas of life sciences. Under HRD scheme,

Department is generating critical mass of trained and skilled manpower required for overall development of Biotechnology in the country.

Two new PG programs viz., M. Tech. Pharma Biotechnology at Institute of Chemical Technology, Mumbai and M. Tech. Computational Biology at Indraprastha Institute of Information Technology, New Delhi have been supported.

Department is working towards for revision and reframing of model course curriculum of Post-graduate teaching programmes in Biotechnology. A web based dynamic portal PROMPT (Review of Mechanism & Protocols of Teaching) has been developed for effectively capturing feedback of postgraduate students admitted under DBT supported teaching programmes in universities about quality of teaching programme.

Star College Scheme is a unique scheme initiated by the Department with an aim to nurture excellence in science education at Under Graduate level. The Star college scheme was chosen to be the first starting place to explore a pilot programme to bring Foldscape to the scientific community. Currently 85 colleges are being supported.

The DBT-JRF programme is being supported by Department of Biotechnology since 2004 with an objective to provide opportunities for pursuing Ph.D. in biotechnology. During 2016-17, 6825 applications were received, 5865 students appeared for the online exam. Merit list of 300 students in category -I and 112 students in Category-II was announced.

Department initiated DBT Research Associateship programme in 2001 for providing post-doctoral exposure in frontier areas of research in Biotechnology in premier institutes engaged in major biotechnological research activities in India. During 2015-2016 & current year a total of 148 students have been selected in this fellowship.

The **Ramalingaswami Re-entry Fellowship** was conceived with the idea of encouraging Indian

scientists working outside the country (Indian Nationals), and who would like to come back home and pursue their research interests in life sciences and biotechnology and other related areas. 202 candidates have joined so far.

CENTRES OF EXCELLENCE (COEs) IN BIOTECHNOLOGY

The CoE supported under various programme areas are providing a flexible model of long-term support for highly innovative research, both basic and translational to create high quality state-of-art facilities for R&D and promote quality publications and intellectual property. The specific goal is to enhance the innovative ability of the institutions and investigators with well-developed multi-disciplinary research programme in specific areas of biotechnology. The research supported in various disciplines of life science and biotechnology.

During the year, six new “Centres of Excellence (including one Phase II)”, two new “Long-term R&D Project” and five proposals have been funded in “Programme Support (including one Phase II)”

BIOTECH FACILITIES

The major facilities created are next generation DNA sequencing, Proteomics, Platform for agriculture and veterinary science, Animal Resource Facility at Faridabad, Biocluster and Facilities for educational, teaching and training purpose. In addition, extension of the availability of synchrotron beamline facility at Grenoble carried out for the science community. Furthermore, the existing repositories and depositories have been strengthened.

A National Mouse Research Resource (NaMoR) was established at NCBS Bangalore to expand the existing facility and provide SPF space in a new building on the shared cluster campus. This will help to create a facility in which targeted strains using RNAi, lentiviruses, Zinc Finger Nucleases and TALENs can be generated.

AUTONOMOUS INSTITUTIONS

The Department has established a number of autonomous institutions for basic, applied and translational research in the field of Life Sciences and Biotechnology. These institutes are encouraging basic, applied and translational research in the field of Life Sciences and Biotechnology.

National Institute of Immunology (NII), Delhi continued expansion of scientific programmes in a multi-investigators driven mode to address challenging questions in biology for improvement of healthcare. It also promotes state-of-art teaching and training facilities in advanced biological sciences using an interdisciplinary approach so as to inculcate the highest level of aptitude and ability in the country's skilled manpower pool.

National Centre for Cell Science (NCCS), Pune has taken new initiatives in nurturing young scientific talent and research scholars into its PhD programme with the University and dealing with cutting-edge research areas in structural biology, stem cell biology, deciphering the role of RNA in biological control processes and the cellular and molecular basis of memory.

Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad is well equipped with world class state-of-the-art instrumentation and computing infrastructure to facilitate working in frontier areas of research in Life Sciences. It provides services for agricultural and processed food products for testing purity of samples of agricultural commodity using DNA markers that can distinguish different Basmati varieties and also traits identification and validation. The major areas of research in the institute centered around Cell Signalling, Transcription, Structural Biology, Computational Biology and Bioinformatics, Immunology, Genetics and Molecular Pathogenesis. Institute is taking a lead for establishment of Plant DNA Fingerprinting research facility recently.

Institute of Life Sciences (ILS), Bhubaneswar is giving focus on infectious disease biology, gene function and regulation and translational research. It has state of the art infrastructural facilities for cutting-edge multidisciplinary research in frontier areas of life science research.

National Brain Research Centre (NBRC), Manesar is pursuing interdisciplinary research and teaching on epilepsy and brain mapping. The focus of the institute is on generation of skilled manpower in brain research that would help India to achieve an international leadership in this frontier area of science.

National Institute of Plant Genome Research (NIPGR), Delhi is focusing research on understanding of the structure, expression and function of genes along with arrangement of genes on plant genomes and manipulation of plant genes / genomes to breed improved varieties of food and industrial crops for high yields and of better quality products. The institute is making attempts to translate some of the technologies developed through basic research activities for their application in agriculture.

Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram working on research programme on chronic disease biology, tropical disease biology and disease biotechnology.

Institute of Bio-resources and Sustainable Development (IBSD), Imphal is involved in conservation and sustainable utilization of bio-resources for the socio-economic development of the North Eastern region. The institute has taken initiatives in collaborations with other institutions/ organizations/ universities nationally and internationally relevant to the bio-resources for sharing and sustainable exploitation.

Center of Innovative and Applied Bio-processing (CIAB), Mohali is giving focus on secondary agriculture and catalyzing research, innovations and knowledge translation for production of secondary

agricultural bio-products. The institute is currently involved in processing of agri-farm and food-industry spare biomass through chemical, biological and biotechnological approaches and engaged in transmitting knowledge and leads of bio-resources for productive processing and value additive primary and secondary agriculture bio-products for edible and non-edible usage.

National Institute of Biomedical Genomics (NIBMG), Kalyani is engaged in accelerating genomics for health and disease and discovering genomic evidence that underpins disease and health-related traits. The Institute is pursuing projects on discovery of biological and environmental correlations of pre-term birth and study natural histories of diseases and health-related traits.

Regional Centre for Biotechnology (RCB), Faridabad is providing world class education, training and conduct innovative research at the interface of multiple disciplines to create high quality human resource in disciplinary and interdisciplinary areas of biotechnology in a globally competitive research milieu.

Translational Health Science and Technology Institute (THSTI), Faridabad is working on integrated approach in the field of medicine, science, engineering and technology into translational knowledge and making biomedical innovations accessible to public health. The institute plays a pivotal role in NCR Biotech Science Clusters and targeting at specializing in translational research and related endeavours.

National Institute of Animal Biotechnology (NIAB), Hyderabad has taken initiatives on infectious diseases: Brucellosis, Theileriosis, Babesiosis, Newcastle disease virus (NDV), Leptospirosis, Toxoplasmosis, Mastitis, Peste des petits ruminants virus (PPR) and Foot and Mouth Disease (FMD) and development of new tools for diagnosing and preventing the diseases.

Institute for Stem Cell Science and Regenerative Medicine (InStem), Bangalore has successfully attracted outstanding investigators, who have initiated theme driven programmes. A key focus is given to support young investigators through a fellowship program in stem cell research and applications.

National Agri Food Biotechnology Centre (NABI), Mohali engaged in research programmes and technologies for the biotech cluster at Mohali to make Indian agriculture & food industry more innovation driven, remunerative and sustainable. It is providing sustainable and meaningful answers towards quality nutrition and provides multiple biotechnological and inventive products in agriculture and food sector.

International Centre for Genetic Engineering and Biotechnology (ICGEB) is functioning under the Administrative control of Department of Biotechnology, Ministry of Science & Technology. The institute's mission to bring excellence in genetic engineering with collaborative partnership of scientists from all over the world. The center is engaged in conducting training programs on discovery of new drugs against malaria and microRNAs in plant development and stress management. The broad research areas are malaria, virology, immunology, recombinant gene products, structural and computational biology, plant molecular biology, insect resistance, plant transformation and synthetic biology and bio-fuels.

Institute on Ocean Biology (Neel): The Department has taken bold initiatives on the establishment of the state-of-art institute Neel: Institute of Ocean Biology. This has been a major lead in national programme of marine sciences and also promotion of India's Ocean biology research and biotechnology globally. Neel will have laboratories in a hub-and-spoke model, with the hub in Goa and spokes from the Andaman to Lakshadweep, covering coastal India from Odisha, Andhra Pradesh to Gujarat. The

institute will be set up with in partnership with Ministry of Earth Sciences and with the technical collaboration of CNRS, UPMC and French Marine Research Labs.

The Department is strengthening research in biotechnology through the establishment of autonomous institutes and its clusters to have access to the state-of-the-art experimental animal facility and the platform technology center.

UNESCO's center for biotech

is promoting training and research for generating interdisciplinary human resource through world-class research, training and education facility and creating innovative opportunities by integrating science, engineering and medicine through breakthrough research relevance to India.

Apart from institutional set up of DBT **Biotech Science Clusters** are also supported by DBT for multi scale basic and applied research in Biological Sciences. The cluster partnering institutes are: Institute for Stem Cell Science and Regenerative Medicine (inStem), National Centre for Biological Sciences (NCBS), Centre for Cellular and Molecular Platforms (C-CAMP), and Institute of Bioinformatics and Applied Biotechnology (IBAB), Bangalore. The clusters are engaged in establishment of innovative institutional model for cutting-edge scientific research, where existing centres of excellence are used for the development of new centres with challenging new mandates.

NCR Biotech Science Cluster is established by involving five autonomous institutes of DBT (NII, NIPGR, NBRC, THSTI and RCB). The cluster is supporting discovery driven research in biology and developments of novel technologies and facilitation of public-private partnerships through biotech business incubators and parks. It creates network with the potential constituent institutions to bring synergistic ecosystem for accelerating discoveries.

PROMOTION OF BIOTECHNOLOGY IN NORTH-EASTERN REGION (NER) OF INDIA

The North East Region (NER), of India is a treasure house of exceptional natural beauty, floral and faunal biodiversity and abundant mineral, water and forest resources. It has been identified as one of the biodiversity hotspots of the world. Rich bio-resources spread across NER's diverse ecosystems and nurtured by indigenous communities, provide ample opportunities for furthering economic development of the region. To address the developments in North East Government of India has made unprecedented commitment to allocate 10% of its total budget for the development of NER. Accordingly, the Department of Biotechnology has earmarked 10% of its total annual budget towards biotechnology-backed development activities in the North Eastern Region of India. Towards this commitment, DBT established the North Eastern Region-Biotechnology Programme Management Cell (NER-BPMC) in 2009-10, functioning through Biotech Consortium India Limited (BCIL), for implementation and monitoring of biotechnology programmes in the NER. Apart from continuing the ongoing projects in North-East in various areas of life sciences and biotechnology, during the year, 30 Scientists/Faculty have been selected for bringing advancement in the Biotechnology and Life Science related activities in various institutions of research and higher learning in the NER under "DBT-NER Visiting Research Professorship (VRP) Scheme".

PUBLIC SECTOR UNDERTAKINGS

The department has promoted new industry-academia interface and stimulating strategic research and innovation capabilities of the Indian biotech industry, particularly start-ups and SME's, for creation of affordable products addressing the needs of the largest section of society. As an interface agency Biotechnology Industry Research Assistance Council (**BIRAC**) has been set up to foster

innovation and entrepreneurship, promote affordable innovation in key social sectors, empowerment of start-ups & small and medium enterprises, contribute through partners for capability enhancement and diffusion of innovation, enable commercialization of discovery and ensure global competitiveness of Indian enterprises. BIRAC has initiated partnerships with several national and global partners to collaborate and deliver the salient features of its mandate. **Biotech Ignition Grant (BIG) Scheme** under BIRAC is encouraging scheme for the young investigators for entrepreneurial and managerial development of SME's in biotechnology through Incubators. Over 500 start ups, Entrepreneurs and biotech industries have been supported so far.

The Department of Biotechnology is also having two **PSUs** namely Bharat Immunologicals and Biologicals Corporation Limited (**BIBCOL**) and Indian Vaccines Corporation Limited (**IVCOL**). BIBCOL is a leading biotechnology company based in Uttar Pradesh India, currently manufactures and produces a range of pharmaceutical products such as Oral Polio Vaccines (OPV Vaccine), zinc tablet & Diarrheal management kit etc. Its mission is to save the lives of millions of children from avoidable disability, through polio vaccination. Another Indian Company IVCOL, Gurgaon, is engaged in various research & development programmes and manufacturing of viral vaccines.

In consonance with the call of Hon'ble Prime Minister, the Department of Biotechnology (DBT) alongwith its 15 Autonomous Bodies and 2 PSUs decided to launch "Swachh Bharat Abhiyan" from its campuses in different parts of India from 2nd October, 2014. Also DBT geared up its employees to launch "Swachh Bharat Mission" from 25th September, 2015 to 31st October, 2015 and 18th December, 2015 to 27th December, 2015 with a 'Cleanliness drive' on the concept of Mahatma Gandhi's vision, "sanitation is more important than Independence".

ADMINISTRATION AND FINANCE

Administration is responsible for providing a good and ambient working atmosphere for the in-house scientists, officers and staff. Logistic supports were provided for organizing various Task force & Expert Committee meetings. The department housed part of the Scientific and Administrative activities in Block 3 has now been allotted to the officers & staff for efficient and speedy disposal of the official work. The Department has gone for e-office premium version through NICS implemented in various

programme division have been given training on e-office application through NIC.

Early this year, the Department announced the institution of a named annual lecture in the honor of founder-secretary Late Dr S. Ramachandran . The Dr. S. Ramachandran Lecture will be delivered each year by an eminent person, from India or abroad. The first Dr S Ramachandran Memorial lecture was organized by the Department of Biotechnology on 9th Sep, 2016 in memory of the founder-secretary Late Dr S. Ramachandran. The lecture was delivered by Dr Manju Sharma, former DBT Secretary.



02 HUMAN RESOURCE DEVELOPMENT PROGRAMME

DBT initiated an integrated Human Resource Development programme HRD way back in 1985 to cater to the needs of trained manpower for teaching, R&D and manufacturing. HRD programme comprises of post graduate teaching programmes, short term training courses for upgradation of skills of mid-career scientists and UG & PG teacher, overseas training and industrial training of students etc. The Department has taken special steps to improve hands on training for undergraduate science students and faculty improvement programmes by providing support to selected colleges under 'Star College Scheme. The support has strengthened physical infrastructure in laboratories, library, teaching aids, and promoted networking of different science departments as well as neighboring institutes for exchange of knowledge and sharing infrastructure and manpower resources.

Teaching Programmes:

Ongoing Postgraduate teaching programmes (M.Sc./ M.Tech./M.VSc.): The post graduate teaching programmes were initiated by DBT in 1985 in six universities in close collaboration with University Grants Commission. These programmes were conceived as collaborative, inter-departmental, inter Institutional programmes and initiated on the basis of core strength in the area in terms of faculty expertise, infrastructural facilities, R&D grants on competitive funding basis, nearby institutions engaged in biotechnology R&D. These programmes played a catalytic role and inspired other institutes to initiate these programmes on their own. Liberal grants were provided for

establishment of specialized laboratory infrastructure, equipment, recurring grants for consumables, studentship, books and journals, travel, visiting faculty, contingency, thesis grant for in-house dissertation etc. In-house dissertation to give research exposure to PG students has been made mandatory and Department is providing thesis grant of Rs. 50,000/- per student to ensure intensive practical training. Keeping in mind the demand for trained manpower, these programmes have been expanded in general biotechnology as well as area specific expansion in medical, agricultural, marine, veterinary, industrial biotechnology, computational biology to cover 63 universities. To ensure admission of quality students, selection is made through All India common entrance test conducted by JNU, JEE or JAM joint entrance test conducted by IIT and all India test conducted by other universities. Students of DBT supported programmes have consistently performed well at the national level competitive exams for research fellowships conducted by CSIR, UGC, DBT, DAE, and ICMR.

Course Curriculum Revision for Post-Graduate teaching Programmes in Biotechnology: Model course curricula are developed by Department of Biotechnology through a consultative process to maintain uniformity and to ensure standard of quality education in area of biotechnology. During the year, Department implemented the project for revision and reframing of model course curriculum of Post-graduate teaching Programmes in Biotechnology for incorporation of modern trends and latest developments. Several brainstorming

sessions of experts groups have been conducted for achieving balance between foundation courses and recent developments in the biotechnology.

Online Feedback System: Department of Biotechnology has developed a web based dynamic portal PROMPT (Review of Mechanism & Protocols of Teaching) for effectively capturing feedback of postgraduate students admitted under DBT supported teaching programmes in universities about quality of teaching programme. Feedback is being collected at end of every semester for eliciting information about learning experience from students across all DBT supported universities and institutions on Theoretical Courses, Practical Courses, Dissertation, Academic Activities and Departmental/Institutional Facilities to gain critical insights about the ongoing teaching programmes for further improvement of quality of teaching and learning under DBT support.

Skill Development Program in Biotechnology: The Department has initiated new skill development programme to provide high quality hands on training in tools and techniques in Medical Biotechnology, Agricultural Biotechnology and Computational Biology for jobs in industries, hospitals, medical colleges, R&D laboratories, diagnostic laboratories.

Fellowship Programmes:

DBT Junior Research Fellowship (DBT- JRF) Programme: Department is providing fellowships to biotechnology students for pursuing doctoral research in universities and / or research institutions in the country. The programme is being coordinated by BCIL, New Delhi. The program has contributed in building human resource capital and institutional capacity in life science sector and nurtured excellence in basic and applied research in biotechnology. Guidelines for DBT-JRF have been finalised. Students are selected through online Biotechnology Eligibility Test (BET) conducted at 49 centres. Students are selected under two Categories namely.

Category I: The programme has provision to select top 275 JRF's each year in this Category. Candidate selected under this category are eligible to avail fellowship under DBT-JRF at any university/institute in India once they are registered for PhD.

Category II: Next 100 students in merit list are selected and these students are eligible to join any DBT sponsored project after following selection process of host institute. They can avail fellowship equivalent to NET/GATE qualification from the project funds. There is no binding on institutions to select project personnel from category II. The programme is very popular which is evident from the fact that during the year, 6825 applications were received, 5865 students appeared for the online exam. Merit list of 300 students in category -I and 112 students in Category-II was announced in 2016-17.

DBT Research Associateship (DBT- RA) Programme: Department of Biotechnology is providing fellowship for post-doctoral research in frontier areas of Biotechnology and life sciences at premier institutions in India. This program is being coordinated by IISc, Bangalore. The fellowship is initially awarded for a period of two years and support can be extended for 1-2 years based on review of progress. The objective of DBT-RA program is to train and nurture young scientists and generate critical mass of manpower in modern areas of biology and biotechnology and build a robust postdoctoral base in India. DBT-RA programme is very popular among the researchers as is evident from increase in number of applicants in last five years (Fig. 1).

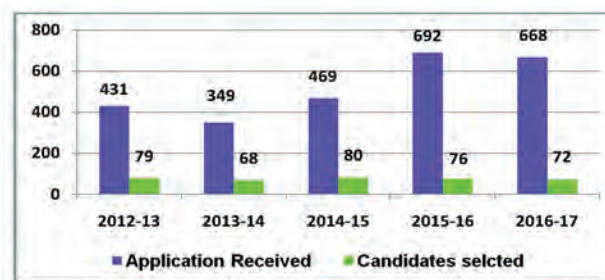


Figure 1 : No. of applicants vs. selected under DBT-RA programme in last five years
Figure 1 : No. of applicants vs. selected under DBI-RA programme in last five years

Training Programmes

Short Term Training Programme for Mid-career Scientists and UG & PG Teachers: Department is supporting short term training programmes for upgrading skills of mid-career scientists from R & D institutions and UG & PG faculty from universities and colleges involved in teaching in multidisciplinary areas of biotechnology and life sciences. These specialized training courses are organized in colleges, universities and premier research institutions for duration of 2-4 weeks for 15-20 participants. During the year, 36 proposals were received out of which 24 were recommended for financial support by expert committee.

Biotech Industrial Training Programme: Department of Biotechnology is supporting Biotech Industrial Training Programme (BITP) for providing hands-on training for six months to fresh B.E./B.Tech./M.Sc./M.Tech. students in biotechnology. The programme is being implemented through Biotech Consortium India Ltd., New Delhi. BITP provides industry-specific training to Biotech students for skill development and enhancing their job opportunities in biotech industries. Around 125 companies are involved in imparting training. The programme is mutually beneficial for students and companies as students get first-hand experience of industry environment and expectations and industries can select the prospective candidates for suitable employment. This programme has completed 28 years and is very popular among biotech students as is evident from number of applications received in last five years (Fig 2).

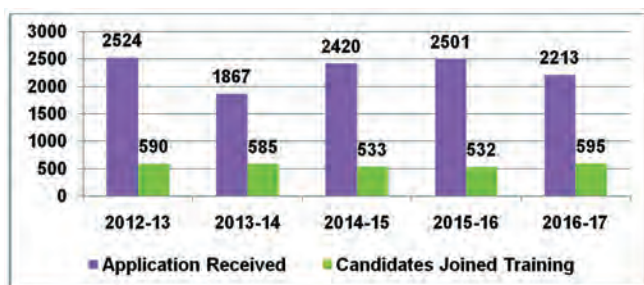


Figure 2: Number of applicants and candidates selected for six months industrial training in last five years

Star College Scheme

Star College Scheme was conceived by the Department in the year 2008 with an aim to nurture excellence in undergraduate science education at across the country, the primary focus was to strengthen the under-graduate science departments by providing academic and physical infrastructure to the colleges, imparting hands-on training to UG students, promoting faculty improvement programme, networking with neighboring colleges and institutions, providing better library facilities, motivating students towards research and even encouraging out-reach activities for teachers, students from neighboring schools & colleges.

There are currently 101 ongoing Colleges and support to 10 colleges has been discontinued on successful completion of one tenure after review during 2015-16. Participating departments in 19 colleges have been accorded Star Status. The Star College programme has led to revival of interest in science stream as evidenced by increase in number of applicants. Initially, it was observed that colleges applied only for biology based science departments/courses but with wider publicity and outreach, the Department has seen a significant increase in inclusion of Mathematics, Statistics and Computer Science departments from several applicant colleges. Colleges have been able to considerably enhance quality of practical training in terms of conducting number of experiments that could not be performed earlier due to non-availability of equipments or expensive chemicals. The optimized research environment has encouraged students to opt for minor projects along with the regular class room teaching. Several teaching aids and laboratory manuals in form of e-resources and SOPs developed by the participating colleges have been evaluated by expert committees and project has been assigned to Sri Venkateswara College, Delhi University and Ramnarain Ruia College, Mumbai for preparation of Lab-Manuals

and SOPs covering innovative experiments conducted by different colleges. This will help in compilation of the protocols in a uniform format for individual subjects and publication and access on DBT website by all participating colleges and other also.

Department in collaboration with British Council is supporting teachers training programme on multi-level workshop on research based pedagogical tools to improve undergraduate science education in indian colleges and universities for undergraduate science teachers on research based learning. 3 levels of training programmes will be organized. Selected teachers from level 1 training will be given advanced training in level 2 who will then conduct regional workshops for teachers. The Department organized level 1 Teachers' Training workshop at IISER, Mohali and Tezpur in Jan, 2017. This is aimed to equip around 1000 undergraduate science teachers with expertise required to empower students with the problem-solving skills that form a part of scientific methodology, such as meticulous observation, analytical ability, critical thinking, and reasoning. Considering the need to impart quality education for such a large population as ours, it is important to develop less expensive, at the same time, highly interactive pedagogical tools to communicate the fundamental principles of science.

Sri Venkateswara college organized International Conference and Outreach Program on Environment and Ecology: Sustainability and Challenges under the Aegis of Star College Scheme on 4-6th Jan 2017 with the objective of promoting awareness about the ecological and environmental changes, to bring together scientists, stake holders from field of environmental management, policy makers such as environmentalists, government officers, young adults and school children at a common platform. Eco-Quiz, Rendezvous with Nature-Photography event, Poster making, Young Innovative

Environmentalist Award/Green school award, Best of waste and Health Camp were organized where more than 4000 students, teachers of 13 public and government schools in Delhi NCR were covered during this outreach program. DBT supported the 2nd National Conference on "Understanding the Challenges and Mechanisms of Complex Diseases:UMCCD-2017" on 24-25th January 2017 at Shaheed Rajguru College of Applied Sciences for Women, University of Delhi, one of the Star Colleges under outreach activities.

Programmes for North Eastern States (NER)

In 2010, Department has made special provision in the existing HRD scheme for providing the support to students/ candidates from the North Eastern Region of country.

DBT-RA for North East: The Department initiated DBT-RA programme in 2010 for students with domicile of North-East or those who have studied for past 3 years in university/ institute in North Eastern states. The Programme is being coordinated by Indian Institute of Science, Bengaluru. During the year, total 65 applications were received, 31 applicants appeared for interview and 15 candidates have been awarded of DBT-RA.

DBT-BITP NER: Department is offering industrial training to fresh B.Tech /M.Sc./M.Tech students of biotechnology from North Eastern States for a period of 6 months. The programme is being implemented through Biotech Consortium India Ltd., New Delhi. There is a provision for placement of 100 candidates in industries for training under BITP-NER. During the year, total 153 applications were received, 89 candidates appeared for interview and 80 candidates have been selected for training. Programme has been well-conceived by Biotechnology students from NE region as evident from increase in no. of applicants in last 3 years (Fig. 3)

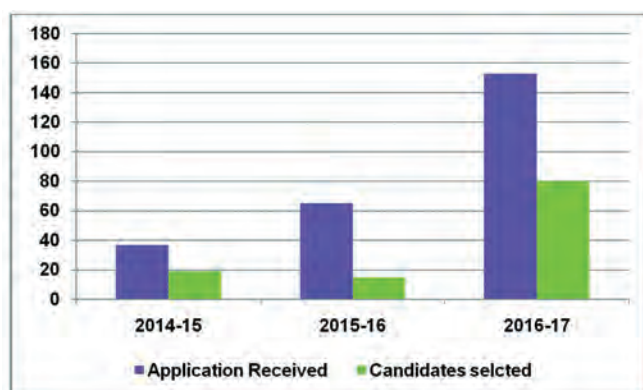


Figure 3: Applicants vs. Selected Candidates for DBT-BITP NER

DBT FELLOWSHIPS FOR STUDENTS AND RESEARCH FELLOWS

Ramalingaswami Re-entry Fellowship: The main objective of the fellowship is to bring back Indian Scientists who are working in overseas laboratories to the home country who wish to pursue their research interests. The objectives of the scheme is to improve India's human resource capacity in life sciences and biotechnology research – both in terms of development, translation and diffusion by means of attracting scientists (Indian nationals) settled abroad. During the last nine years 1121 applications were received and out of these 346 were offered fellowship 211 have already taken up positions in Indian Laboratories. 141 fellows have already been absorbed as permanent faculty. Based on the current data available, it is quite apparent that people want to relocate themselves to Indian Institutes/National R&D laboratories as these institutes are now providing excellent research facilities to do high quality research. Each year 50 fellowships are awarded.

Wellcome Trust/DBT India Alliance (India Alliance): The Wellcome Trust/DBT India Alliance (India Alliance) was established in 2008 as a public charitable trust with a total commitment of Rs. 1296 crores (£ 160 Million) for ten years with equal funding by its two partners, the Wellcome Trust, UK and The Department of Biotechnology (DBT), Ministry of Science and Technology, Government

of India.

Major initiatives in the programme offered fellowships at three different career levels – Early Career Fellowship (ECF), Intermediate Fellowship (IF) and Senior Fellowship (SF). These fellowships are offered under two different streams -Basic Biomedical Research Fellowships and Clinical and Public Health Fellowships. Besides these, India Alliance also offers the Margdarshi Fellowship, which is awarded to global science leaders, to set up Centers of Excellence at an Indian institution of their choice. The Research Training Fellowship (RTF) is for clinicians to train in research under the guidance of basic / clinical / public health researchers. This is for 2 years and is offered to Indian nationals only.

Science Communication and Public Engagement are the two other important initiatives of India Alliance that aim to train young researchers in the practice and communication of science, and provide better appreciation of biomedical sciences to the common public, respectively.

From its inception till November 2016, India Alliance has awarded 254 Fellowships at 79 institutions across India. Of these, 26 Fellows have completed their tenure, 150 are currently active and 43 Fellowships are yet to be activated. The distribution of Fellowships is as follows:

Fellowship Scheme	Awards*
Early Career Fellowships	68
Intermediate Fellowships	136
Senior Fellowships	34
Margdarshi Fellowships	5
Research Training Fellowships	11
Total Awards Recommended	254

*Each Fellowship Scheme includes both basic research and clinical and public health research awards.

In 2016-17, a total of 11 ECFs (basic research), 25 SIF (7 Senior and 18 Intermediate Fellowships – basic research), 15 Clinical and Public Health Fellowships (all categories) and 1 Margdarshi Fellowship were awarded.

Public Engagement and Outreach: As part of public engagement and outreach, India Alliance has taken up many initiatives, which include, public lecture series, health awareness programmes, Art and Science projects, Science communication workshop, supporting national scientific meetings and workshops, and a bimonthly newsletter. During 2016-17, the “Voices for Health” Series brought together health researchers, social scientists, doctors, journalists, health workers, local organizations, government, scientists, and the public to discuss important health problems in the country.

Research Publications: Between 2010 and November 2016, there are around 336 peer reviewed academic publications associated with India Alliance funding. Over 85% of these publications are primary research articles. Fellows supported by India Alliance are publishing in highly respected international journals, with increasing citation.

Patents obtained / applied: A total of 14 patents have been filed / obtained by Fellows as an outcome of India Alliance funding during 2014-2016. In the current year, six patents were filed / obtained by India Alliance Fellows.

Bilateral / multilateral agreements with other agencies: IA has a Memorandum of Understanding (MOU) with European Molecular Biology Organization (EMBO) to jointly fund upto three interdisciplinary meetings per year in India. These meetings would address discovery and innovation through an interdisciplinary approach, with the speakers and participants discussing important global challenges in the context of life sciences.

Tata Innovation Fellowship: The Department initiated the scheme in 2006 to reward the scientists

engaged in innovation and in the pursuit of path breaking solutions to major challenges, interdisciplinary work and an emphasis on translational research in life sciences, agriculture, biomedical science and related areas of biotechnology. The awardees are provided a fellowship of Rs. 25,000/- per month in addition to regular salary and contingency grant of Rs. 6 lakhs per annum. The duration of the fellowship is initially for three years which can be extended further by two years on a fresh appraisal. During the current year, five scientists have been awarded Tata Innovation Fellowship in the areas of Medical Biotechnology, Agricultural Biotechnology and Environmental Biotechnology. Altogether, 47 scientists have been awarded the fellowship since its inception.

DBT SCHOLARSHIPS AND AWARDS

Biotech Product, Process Development and Commercialization Award: These Awards are given in recognition of outstanding contributions of scientists / innovators / entrepreneurs/ Indian institutions & companies both in public as well as private sector for a new process, product development and commercialization of a technology or a product in the areas of biotechnology and biological sciences including agriculture, biomedical and environmental sciences. Up to five awards are given every year. Each award carries a cash amount of Rs 2.00 lakh along with a citation and trophy. Rs 5.00 lakh would be given if the product is commercialized and has much higher impact of utilization in the country. The awardees should be a citizen of India or an Indian institution or an Indian company actively involved in the development of biotechnology processes, products and commercialization of technologies or product based on indigenous research. For the year 2016, out of 22 nominations received, three teams were selected for two awards of Rs 2.00 lakh each.

National Women Bio-scientist Awards: The National Women Bio-scientist Awards are given

every year under two categories. These are (i) National Women Bio-scientist Award (Senior Category) (One) – awarded to senior woman biologist for life time contributions, who has done excellent research work in the country and has applied the results for the benefit of students and society, and (ii) National Women Bio-scientist Awards (Young Category) (Two) – given for outstanding contributions of women scientists below 45 years' of age in basic and applied research in the areas of biosciences and biotechnology including agricultural, biomedical and environmental sciences with potential for application/ product and technology development. Contribution made during last 5 years, is the main consideration. The Award for the National Women Bioscientist (Senior Category) carries a cash prize of Rs 5.00 lakh with citation and a gold medal. The Award for National Women Bioscientist (Young Category) carries a cash prize of Rs 1.00 lakh with citation and a gold medal and Research Grant of Rs 5.00 lakh per annum for a period of 5 years. For the year 2015, out of 9 nominations under Senior Category, one Awardee was selected and out of 24 nominations under Young Category, 2 Awardees were selected. The National Women Bio-scientist Award for the year 2016 is under process.

National Bioscience Awards for Career Development: National Bioscience Awards for Career Development are awarded in recognition of outstanding contributions of young scientists below 45 years of age in basic and applied research in the areas of biosciences and biotechnology including agricultural, biomedical and environmental sciences with potential for application/product and technology development. Each Award carries a cash prize of Rs 2.00 lakh, a citation and trophy along with project research grant of Rs 15.00 lakh for a period of 03 years. For the year 2015, out of 52 nominations received, 10 Awardees were selected for the Award. The National Bioscience Awards for Career Development for the year 2016 is under process.

DBT Biology Scholarship: BT Biology Scholarships are awarded to students from the combined merit list of Biology/ Biotechnology at Higher Secondary/ Intermediate/ 10+2 level each year to encourage students to pursue studies in biological sciences after 10+2 level. The amount of scholarship is ' 20,000/- per student selected for the purpose and a maximum upto 100 students are selected for this scholarship each year. The Award carries a medal and a certificate of merit.

The Innovative Young Biotechnologist Award: The Innovative Young Biotechnologist Award (IYBA), initiated in 2005, is a career-oriented prize to identify and nurture outstanding young scientists with innovative ideas and desire of pursuing research in biotechnology. The prize is for those below 35 years of age subject to certain relaxations in cases of women, OBC, SC/ST. This includes scientists without regular employment also. The applications through an open advertisement and selection are done after comprehensive review by an empowered committee of reputed scientists.

In the last five year, DBT has awarded 80 young scientists as per the break up below:

Sl. No.	Year	No. of Scientists Awarded
1	2011	16
2	2012	15
3	2013	20
4	2014	14
5	2015	15
6.	Total	80

RGYI- Rapid Grant for Young Investigators: Rapid Grant for Young Investigators fosters creative research in various fields of biotechnology (Medical, Agriculture, Animal Biotech, Environment and Industry etc.) to enhance early career development of young investigators below 40 years of age. The programme aims to provide first grant to establish the lab and initiate research in the frontier areas of biotechnology. The RGYI scheme is under

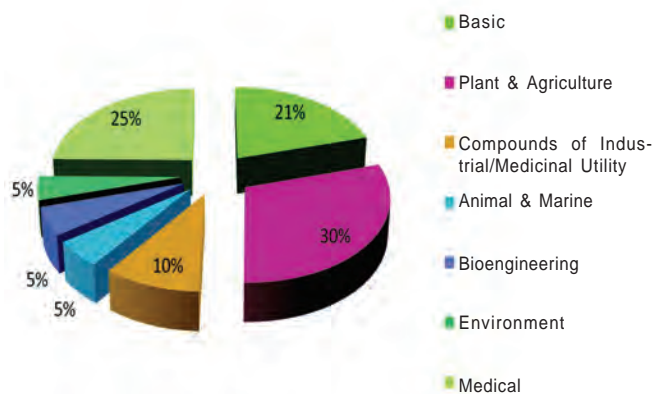
implementation since 2005-2006 and over the years there has been overwhelming response to this scheme as more than 3000 proposals have been received and about 600 projects recommended (based on their merit) and implemented so far. In past twelve months continued efforts have been made to support ongoing projects implemented in various areas of Biotechnology. Thus RGYI provided start-up grants to young investigators across the country working in different settings such as central government funded institutions, State Government funded University departments, scientists at DSIR approved private institutions etc.

RESEARCH OPPORTUNITIES FOR WOMEN SCIENTISTS

Biotechnology Career Advancement and Re-orientation Programme (BIOCARE) for Women Scientists: Scheme for the women scientists - Biotechnology Career Advancement and Re-orientation (BIOCARE) Programme was initiated in the year 2011. The first call for applications was announced by the Department in January, 2011. 3 calls have been announced so far and 214 (113 Employed and 101 Unemployed) women Scientists have been supported under the Bio-CARE scheme. The 4th call for proposals was announced in January, 2016. A total of 1027 applications were received. An extensive process of evaluation of these applications through area wise panels of Experts was followed and 109 applicants were selected. Funds are being released to the selected applicants. Few achievements of the scheme are as below:

- Total no. of publications - 90
- Total no. of patents Filed – 4
- Employment generation – 11 women scientists got permanent job after getting the BIOCARE project.

% of supported proposals



Area-wise distribution of projects

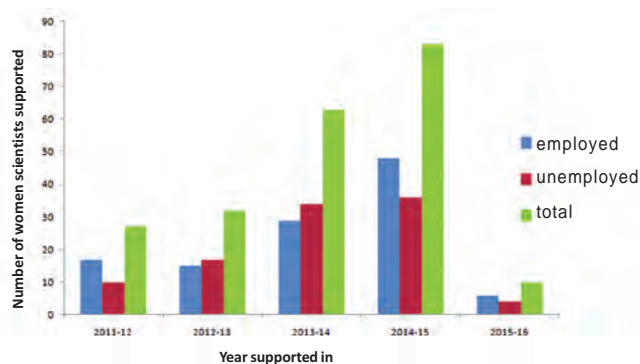


Figure 2. Details of Women Scientists Supported-Employed/Unemployed

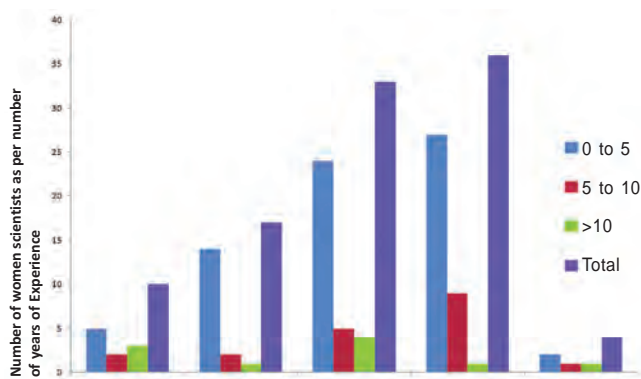


Figure3. Experience wise details of the unemployed scientists

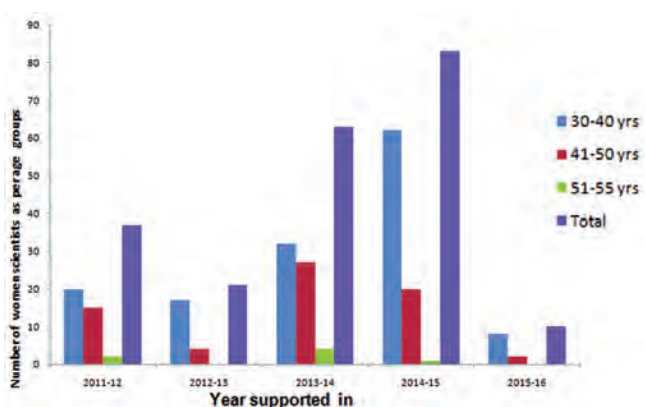


Figure 4. Age wise details of women scientists supported

MEETING SUPPORT & BIOTECHNOLOGY POPULARIZATION PROGRAMME

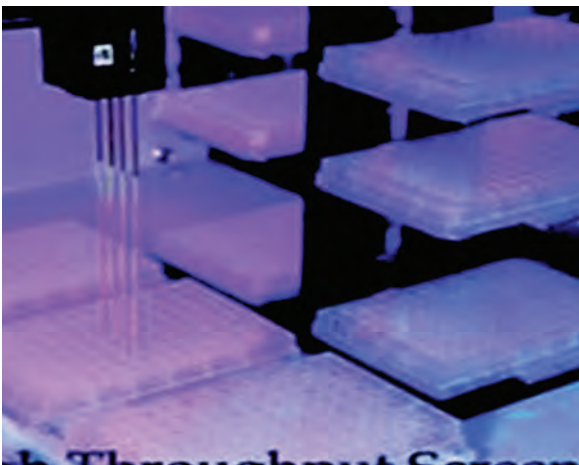
DBT-CTEP Programme: To popularize Biotechnology activities in India, Department of Biotechnology (DBT), Government of India provides financial assistance towards organizing Conference/Seminar/Symposium/Workshop and Travel support to the researchers for presenting their papers in the conferences which are being organized outside the country. It also extends support for organizing DBT stalls in Exhibitions held within the country as well as outside the country. Financial supports are also provided for organizing Popular Lectures. The collective term for these four activities is CTEP (Conference, Travel, Exhibition and Popular

Lectures). The collective term for these four activities is CTEP (Conference, Travel, Exhibition and Popular Lectures).

Moving forward, DBT has introduced a web portal i.e. Online Submission and Monitoring System (OSMoSys) which would act as a single window for the submission, processing and settlement of grants that would not only ease the assistance process but also provide timely deliverables.

Monthly Expert Committee on Popularization & Promotion of Biotechnology (ECPPB) takes place at DBT for considering the proposals for the above mentioned programme. 9 ECPPB meetings have been held till date in the year 2016-17 and details of the same is as below:

Sl. No.	Schemes	Total No. of Proposals/ applications received	Total no. of Proposals Recommended
1	Conference/ Seminars	352	152
2	Travel Support	950	459
3	Exhibition	19	09
4	Popular Lecture	11	08
5	Total	1332	628



03

BIOTECH FACILITIES, TECHNOLOGY PLATFORMS & RESEARCH RESOURCES

Biotech Facilities:

The programme is to promote, upgrade and establish new biotech facilities/infrastructure viz. animal house; gene banks; repositories for microbes, plants, model organisms and infectious organisms; towards augmentation of research activities of scientific community at regional, National and International level. Furthermore, to promote growth of life science and biotechnology in the university system and linking research to education at every opportunity through creation/reengineering/remodeling/up-gradation of life science departments in central/state universities. The outcome of the research activities supported for strengthening the research infrastructure in Universities and Institutions are as follows:

A DBT-BM14 program coordination unit (DBT-BM14-PCU) at Regional centre for Biotechnology, Faridabad for providing access to Indian Scientific community to synchrotron X-ray beam line (BM14) in Grenoble, France completed in 2016 and continues to have access for Indian scientific community, a new agreement will be signed between European Molecular Biology Laboratory (EMBL), Germany and Regional centre for Biotechnology (RCB), Faridabad for availability of better beamlines is in progress. During last year, the beam time was shared as 24% to EMBL, 36% to India and 40% to ESRF. However the actual share of ESRF, EMBL and India was 30%, 20% and 50% respectively. A total of 84 days were available for Indian users at the beamline in the past year. During last year, 45 new proposals have been processed. The total number of crystals shipped is 2370 and

the total number of data sets collected was 800 including 82 SAD/MAD dataset. A total of 19 scientists from India visited the ESRF beamline to collect diffraction data. A total of 39 peer reviewed publications came out of this support.

A project on 'Maintenance of Repository for Filarial Parasites & Reagents (MVR Reddy, Sevagram, MH)' was supported for re-innovation of Repository for Filarial parasites & reagents. The filarial repository upgradation would be completed soon. Filarial serum bank has the collection and storage of about 1368 bancroftian filarial sera of different patient groups (i.e., microfilaraemia, acute, chronic and occult filarial cases & endemic normals) from different endemic zones (viz., Maharashtra, Karnataka, Raipur, Calicut, Mangalore, Bhubhaneshwar & Rourkela) and as well from non-endemic normal individuals. A rapid diagnostic kit for filarial IgG4 antibody using filarial recombinant WbL2 antigen which has been developed in collaboration with Ubio Biotechnology pvt. Ltd., Kerala, has been tested with randomly collected 629 human sera samples from the two endemic areas where MDA has been implemented. About 21.85% (144) of the sera samples were found to be positive for the presence of filarial IgG4 antibody. Results of the WbL2 rapid test indicated that this test can detect more number of actively infected cases and will be quite useful tool to monitor the effect of MDA in the elimination program. Two new filarial vaccine candidates *B. malayi* abundant larval transcript 2 (rBmALT-2) & *W. bancrofti* glutathione-s-transferase (rWbGST) have been identified. Five publications and one Indian patent have been filed. The transfer of the technology developed under the project is under discussion.

A new Electron Microscopy Facility at Department of Pathology, Govind Ballabh Pant Institute of Postgraduate Medical Education and Research, New Delhi is under establishment stage to meet out the research requirement of the medical institute as well as to improve the patient diagnoses in Delhi Government Hospitals.

DBT launched a scheme i.e. DBT-Boost to University Interdisciplinary Departments of Life Sciences for Education and Research (DBT-BUILDER) for advanced education and research for the up gradation/reengineering/remodeling/ creation of Life Science departments in central and state universities. The objective of this scheme is to promote Interdisciplinary research and technology development at university level. Till now, the total numbers of universities received support under this programme are 24. In General, the Programme resulted in training of SRF(39), JRF(86), Ph.D. (48), RA(15), M.Sc. Students (570), UG students(180), Technical Assistant (10), Faculty (5) and publications of Research articles (107). In Central University of Jharkhand, teaching and research facilities have been established right from the beginning as it is a new university.

Personnel trained under Biotech facility and DBT-BUILDER Programme in 2016

S. No.	Item	SC/ST	OBC	GEN
1.	Assistant Professor	-	-	11
2	Research Associate (RA)	-	-	19
3.	Ph.D.	17	8	62
4.	Senior Research Fellow (SRF)	2	4	54
5.	Junior Research Fellow (JRF)	34	35	93
6.	Master of Science (M.Sc.)	158	279	220
7.	Under Graduate (UG)	18	100	434
8.	Technical Assistant (TA)	-	-	15
9.	Lab Technician	4	-	-
10.	Multi-skilled Assistant	-	1	-
	Total=	233	426	908

In Madurai Kamaraj University, Tamilnadu, an integrated M.Sc.- Ph.D. programme in Genomics was initiated in 2011-12 is now changed to M.Sc. Genomics from 2015-16 onwards. As a result of integrated programme, one student has been awarded the Ph.D. degree. Biology Main Building, Animal House Building up gradation of the laboratory facilities, computer lab facility, higher-end equipments facility etc. were completed. 92 Students passed the M.Sc. Genomics Programme and more than 300 publications came out during 5 yr support.

In Patna University, Bihar, Central Instrumentation facility has been established. In addition, two state of the art laboratories and an animal house was strengthened to improve the research and teaching environment in the University for Biotechnology.

In Kuvempu University, Karnataka, the existing plant tissue culture laboratory, microbial mycology laboratory are upgraded and Construction of central instrumentation laboratory has been completed. The facilities are recently inaugurated. As a result of support, 240 M.Sc. Students are benefitted and 10 JRF students are under training.

In M.D. University, Rohtak, Haryana, a novel immuno-PCR method was developed, which has advantages of both ELISA and PCR, for an early diagnosis of both pulmonary and extra-pulmonary TB patients. The translation of this test requires validation in large number of patients. Multiplex RT-PCR Assay for Detection and Typing of Dengue and Chikungunya viruses in clinical samples is underway.

In Pondicherry University, animal cell culture facility has been developed in this project, training of many students and several publications has been achieved. A group engaged in bioprospecting of biomolecules of natural and synthetic origin lead to identification of 12 lead molecules such as astaxanthins as antiaging molecules, piperin as antifertility molecule, acylhomoserine, Sesamin as anticancer drug and novel bacteriocins as antimicrobial molecules.

In Anna University, six high end equipments, instruments for upgrading the teaching facility and a cluster computer facility have been installed. These facilities are open to users of other institutions. Flow Cytometry has been installed and training to 30 research scholars imparted. High-end bioprocess facility has been established and utilized for workshop with hands-on training for 10 research scholars from other institutions. The space of about 1750 sq. ft. for establishing the proteomic facility has been prepared. Construction of Single Chain Fragment variable (ScFv) antibody and improving its affinity by evolutionary method & screening by ribosome display technique for the diagnosis of filariasis is underway. Mangosteen rind extract found effective against breast cancer cell lines. EtOH caused an increase in cell proliferation, which is induced by the ROS-linked inflammatory response in breast cancer.

A SRM-DBT Partnership Platform for Contemporary Research, Services and Skill Development in Advanced Life Science Technologies has been established in SRM University, Tamilnadu. GLP enabled facilities are established for providing service as well as for skill development. A PG diploma course with focus on technical skill development in association with Biotech industries is approved by Board of Studies and Academic Council and the course will begin in June 2017.

A National Facility for Gene Function in Health and Disease is established at IISER, Pune in association with University of Alabama, Alabama, USA. The building required to establish the facility is complete. The import of several transgenic lines (eg. mouse lines used for optogenetics) from Jackson lab and various other collaborators are under process. Multiple Drosophila and zebra fish strains are already being maintained in the facility. A workshop in June 2016 on Genome engineering in model organisms along with NCCS and Centre for Transgenic & Genetically Engineered Models (TGEMS), University of Alabama.

DBT-IISC PARTNERSHIP PROGRAMME

Indian Institute of Science (IISc.), Bangalore has immensely contributed in stimulating Indian academic Life-science sector; therefore, DBT supported a 'DBT-Partnership Programme for advanced research in Biological Sciences and Bioengineering' at IISc. With major objectives to supplement the already available resources for making the IISc research intensive with added interdisciplinary nature and among top institutions of the world through extensive national and international collaborations. During last year, 50 Ph.D. students & 28 Research Scientists received training, 10 patents filed and two technologies are in development.

Under the Partnership Programme, a number of facilities like Bioimaging, Surface Plasmon Resonance, Gas Chromatograph-Mass spectrometry facility, Bioplex Facility, X-ray Facility, Computational Cluster Facility, Biosafety (BSL-3) Facility, Live Animal Imaging Facility, Central Animal facility and Bioengineering Facility has been supported.

Flow Cytometry Facility caters to 11 different departments which include biological sciences as well as the Engineering units, NMR and chemical sciences. The Facility hosted a two day international symposium.

With Gas Chromatography-Mass Spectrometry facility, 1878 internal and 146 external samples are analyzed. Two peer reviewed articles published from this facility. Surface Plasmon Resonance facility has resulted in publication of 12 scientific articles. Mass spectrometry facility, a service facility, has resulted in publication of 8 scientific articles.

With X-ray facility, 114 biomolecular crystals have been tested and 67 datasets have been collected. IISc solved twenty two 3-D structures and 4 structures are solved by external users. Facility has resulted in publication of 5 quality scientific articles. Computational cluster Facility and Phytotron facility has resulted in good publication.

BSL-3 laboratory facility is mainly used by researchers of Division of Biological sciences and one day BSL3 workshop on “Bio-risk preparedness in laboratory setting” was organized in collaboration with National Institute of Virology, Pune. This facility also provides services for conducting animal training, training, Health Check-up, Teaching and open day programmes of IISc.

Central Animal Facility supplied 7732 animals. A total of 26 project proposals on animals were approved by the Institution Animal Ethics Committee (IAEC) and a total of 4353 animals were approved. A total of 39 papers were published by using animals from the Central Animal Facility.

Bioengineering Facility is used by multiple departments of the institution. AFM installed is used for used for imaging of DNA, bacteria, biofilms, nanoparticles, nanofibers, polymers and to find the mechanical properties these samples (Fig). Facility has resulted in publication of 2 quality scientific articles.

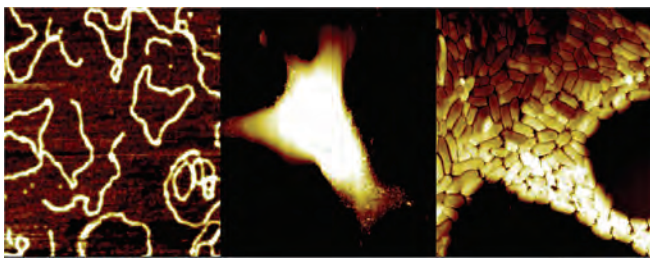


Figure: AFM images of DNA, MCF7 cell and wild-type *S. typhimurium* cells (From left)

PLATFORMS & RESEARCH RESOURCES

Centre for Cellular and Molecular Platforms (C-Camp)

Centre for Cellular and Molecular Platforms (C-CAMP) was instituted in June 2009 with the unique mandate of enabling cutting-edge research by making available state-of-the-art technologies and providing training on these platforms. The C-CAMP facilitates Bioscience Research and Entrepreneurship by providing Research, Development, Training and Services in state-of-the-

art Technology Platforms. C-CAMP is now a major Platform Technology, Industry-Interaction, Innovation and Incubator unit.

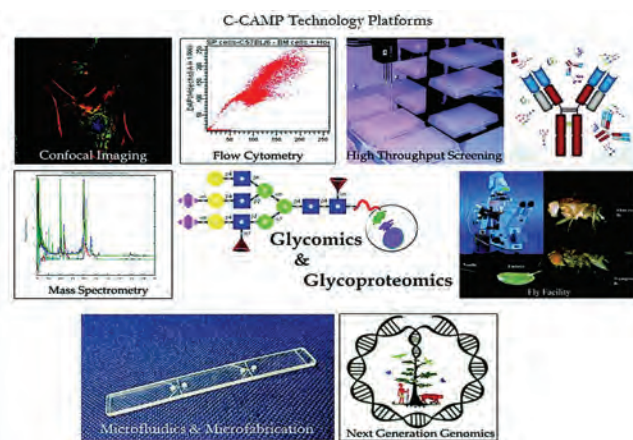
C-CAMP has established high-end technologies via research/technology-based collaborations within and outside the Bangalore Life Sciences Cluster comprising of NCBS, inStem, C-CAMP; made available these technologies and expertise to researchers in academia and industry, and provided technology training to generate a pool of technology experts capable of developing and ameliorating C-CAMP platform technologies.

As a part C-CAMP's mandate of promoting entrepreneurship and innovation, C-CAMP has created and fostered an entrepreneur-friendly culture in and around Academic/Research environment through its involvement in Seed Funding Schemes for Startups, Entrepreneur Mentorship program and Bio-Incubation facility. The mainstay in Promoting entrepreneurship among scientists is by developing strategic interactions with the biotechnology industry to develop and disseminate new technology.

By achieving the above objectives C-CAMP contributes significantly towards enhancing the biotechnology research output, innovation and entrepreneurship in India.

Activities and Achievements:

A. Technology Platforms : Till date, C-CAMP has made significant contribution within the larger realm of Life Sciences research in India by establishing and managing 10 High-End Technology Platforms, namely: Imaging and Flow Cytometry Facility; High Throughput Screening and High Content Screening Facility; Biologics Characterization Facility; 4) Proteomics Facility; Glycomics and Glycoproteomics Facility; Metabolomics Facility; Drosophila Facility; Microfluidics & Microfabrication Facility; Next Generation Genomics Facility; Electron Microscopy Facility



Two additional facilities, namely, Lipidomics and Mouse Genome Engineering Facilities have been conceptualized and have begun the outreach during 2016-17.

This year, till date, C-CAMP has organized 7 hands-on training programmes, viz., 21-23rd Basic Flow Cytometry Course and the Bangalore Mass Spectrometry course, imparting hands-on training to nearly 100 researchers from across the country. 23rd Basic Flow Cytometry Course is scheduled for Mar 28-31, 2017.

The facilities have been used by more than 200 institutions (academia and industry) and have trained over 1200 researchers in different technologies. 1800+ Projects on High-End Technologies have been taken up at C-CAMP resulting over 75 papers being published. Further, 27 technologies are available for Licensing through C-CAMP.

B. Innovation & Entrepreneurship: As a part of the mandate of promoting innovation and entrepreneurship, C-CAMP has, through its various activities supported very early stage ideas to validation studies for commercialization. The activities undertaken are (a) C-CAMP has partnered with BIRAC, DBT to help with the Biotechnology Ignition Grant (BIG) scheme grant that funds start-up companies and individual scientific entrepreneurs to establish proof-of-concept and

transform these innovative ideas into viable competitive products and enterprises. C-CAMP has also received approval from the MoMSME for support to innovators under the incubator scheme (b) Bio-incubation: C-CAMP also provides some of these start-ups access to functional laboratory along with high-end technology platforms, through its bio-incubator. C-CAMP has also established a set-up for med tech prototype generation with basic designing, electronics and fabrication capabilities; (c) Mentorship Programme: Through C-CAMP's Entrepreneur Mentorship program, C-CAMP not only funds but also nurtures these start-ups with scientific and business mentorship; (d) Discovery to Innovation Accelerator: C-CAMP has also started the Discovery Innovation Accelerator program which focuses on making early stage discoveries from academic laboratories to make them "industry ready" and to takes them closer to the market through a possible license or spin-off.

In addition, C-CAMP Start-ups have hired over 30 employees; raised over 40 crores of follow on funding; filed over 5 patents and commercialized 6 innovative products.

Till date C-CAMP has supported over 70 start-ups/spin-offs through funding, incubation and mentorship, of which 24 have been Resident start-ups.

The overall impact of C-CAMP's efforts in promotion of Innovation and Entrepreneurship is summarized in the figure below.



C-CAMP's Efforts to nurture Start-ups



National Mouse Research Resource (NaMoR) NCBS, Bangalore:

The National Mouse Research Resource (NaMoR) established at NCBS, Bangalore is fully functional with a new rodent Specific Pathogen Free (SPF) animal care facility and dedicated animal care services allowing breeding and expansion of standard and genetically modified animals for Indian research laboratories. It has also developed a Mouse Genome Engineering Facility (MGEF) to generate novel genetically modified animals using TALENs, CRISPR/CAS and the latest mouse transgenic technologies. It is now offering services such as rodent strain cryopreservation, cryo recovery and *in vitro* fertilization to both internal and external users. NaMoR has also initiated training and workshops on mouse embryology, genetic manipulation, and husbandry of transgenic/disease animal models.

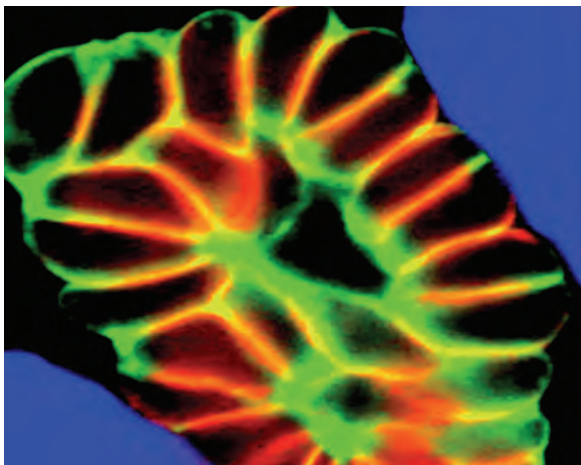
Centre for Neurodevelopment Synaptopathies (CNS) inStem, Bangalore:

The Centre for Neurodevelopmental Synaptopathies (CNS) established at inStem, Bangalore, aims to understand neurobiology of autism spectrum disorders (ASD) and intellectual disability (ID) including neurodevelopment, synaptic function and plasticity, human stem cells and cognition-behavior, with an intent to deliver in the following fields: i) human stem cell based disease modeling and drug

discovery, (ii) rodent systems for structural/functional imaging and correlative human relevant behavioral/physiological measures (iii) next generation transgenic rodent models to interrogate circuits and rescue phenotypes (iv) Capacity building and next generation faculty of translational neuroscientists.

The scientists at CNS have successfully established 9 new rat models of ASD/IDs, for simultaneous comparative assessment at the behavioral, electrophysiological and biochemical levels in a standardized, platform based approach, which is termed as the "pipeline". These include rat models for Fragile X Syndrome (FXS), Syngap 1-related non syndromic intellectual disability (Syngap), PTEN mutation, Rett Syndrome (MeCP2), Neuroligin 3 (NLgn-3), Neurexin 1 (Nrxn-1), Contactin associated protein like-2 (Cntnap2), Cyclin-dependent protein kinase like-5 (Cdkl-5) and NMDA receptor 2A (NR2A).

Using these transgenic rat models, the Centre is trying to address whether genetically heterogeneous disorders share common synaptic neuropathology, as well as whether the common synaptic patho-physiology that arises from shared "developmental" mechanisms could be a therapeutic target throughout the lifespan of the animal. For instance, do rare, highly penetrant forms of ID with co-occurring ASD share a common time-course of cellular circuit-level defects? A detailed characterization of post- and pre-synaptic defects in the amygdala of new rat models of FXS revealed deficits in activity-dependent synaptic plasticity in the amygdala. Further, a study on the rescue of deficits, using oral treatment with lovastatin, in the developmental acquisition of associative memory has also been undertaken. These results are also of therapeutic significance because lovastatin, which reduces the amount of cholesterol made by the liver, is already approved for use in humans.



04

RESEARCH AND DEVELOPMENT

AGRICULTURE BIOTECHNOLOGY

The Department has continued supporting projects in agriculture biotechnology during the year 2015-16. The salient achievements are given below:

A. PULSES

Chickpea: A project was carried out on genetic enhancement of chickpea pertinent to seed size/weight trait and yield through epigenomics, transcriptomics and molecular breeding studies. The whole genome, methylome and transcriptome sequence of diverse contrasting low and high seed weight chickpea accessions were decoded at a high-resolution scale. Maximum number >2300 genes at S7 development stage of high seed weight chickpea accession were preferentially expressed as compared to their low grain weight accessions. About 765 known and 1500 novel tentative microRNAs were scanned from seven different seed development stages of low and high seed weight chickpea accessions. Diverse integrated genomic strategies were developed by using the high-throughput marker genotyping and yield trait-related field-phenotyping information generated from numerous natural germplasm accessions (association panel) and 12 different mapping populations of chickpea. This approach delineated functionally relevant molecular tags (12 genes, six QTLs/eQTLs) and 10 natural allelic variants/haplotypes regulating seed size/weight in rice and chickpea. Two potential major QTLs/genes regulating seed weight and seed number were introgressed into promising Indian varieties through

marker-assisted breeding for improving chickpea yield. (figure 1)

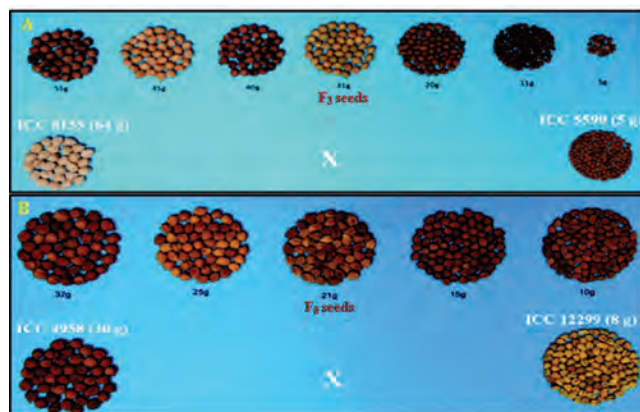


Figure.1 Chick Pea: Phenotypic variation for seed size/100-seed weight observed in a representative set of individuals derived from two advanced generation intra-specific mapping populations [A: (ICC 8155 × ICC 5590) and B: (ICC 4958 × ICC 12299)].

Functional genomics approach and complete chickpea genome has been sequenced at NIPGR. Significant efforts were made to utilize sequencing data through a sequel programme to explore transcriptome dynamics of chickpea development for candidate gene discovery and defining regulatory elements/modules, functional genomics of stress tolerance in chickpea and functional genomics of chickpea seed development and nutrition.

Molecular characterization of variation in root system architecture among selected Indica rice varieties and chick pea was carried out to enhance the yield of these two important crops. New genes potentially involved in root development, abiotic stress response, nutrient acquisition, phosphate utilization and nodulation have been identified in rice and chickpea and their modes

of action were demonstrated in model plant. Proof of concept of transgenic rice lines and advanced generation transgenic chickpea lines with high root growth have been developed. An advance generation chickpea mapping population developed by crossing two parents with contrasting root structure for mapping genes for root length produced some potential mapping individuals with high root growth. (fig-2)



Figure 2: Roots of control and transgenic chickpea lines expressing CKX gene in root.

At University of Calcutta, studies on understanding the molecular principles that predisposed plants to Root-Nodule. Symbiosis was carried out and a method of artificial nodulation was devised that was 6-8 fold more efficient than rhizobia induced nodulation and the same has been submitted for patenting.

Mungbean: Virus resistance: Mapping population from inter-specific cross between *V. radiata* and *V. mungo* for yellow mosaic disease resistance was developed along with whole genome sequence data of *V. radiata* (ML 267) and *V. mungo* (Mash 114).

Lentil: Drought tolerance: Genetics and molecular tagging of drought tolerance genes was undertaken in lentil and transcriptional profiles of drought tolerant and drought sensitive genotypes was generated. A new phenotyping technique was

developed and validated for drought stress tolerance under field conditions. Additionally the dataset for two genotypes of lentil (drought tolerant) was deposited in the SRA (Sequence read archive) repository with SRA IDSRR3105360. New breeding line 'PDL-1' for drought tolerance is under consideration for registration in NBPGR, New Delhi.

Yield enhancement studies were carried out to harness favourable QTL of wild and exotic germplasm for contributing traits in lentil using advanced backcross QTL analysis. The development of advanced backcrossing population is in progress. More than 539 SSR markers were tested for yield and 75 polymorphic markers were identified from them. Approx. 1600 intron spanning markers were developed as new markers in lentil and identified 24 polymorphic from a set 84 markers.

Cluster bean (Guar): Expression analysis of Galactomannan biosynthesis pathway genes in cluster Bean (*Cyamopsistetragonoloba* L) through Transcriptome sequencing was undertaken. Partial Sequencing and Characterization of enzymes involved in galactomannan biosynthesis pathway was elucidated. The Transcriptome data of two elite Indian Guar (*Cyamopsistetragonoloba*L) varieties, namely, HG365 and HG870 at different developmental stages of pod/seed formation has been submitted to NCBI.

Rice Bean: Insect resistance studies taken up for protease inhibitors to control insect pests on crops. The project on characterization of protease inhibitor and isolation of gene encoding protease inhibitors from rice bean (*Vigna umbellate*) describes the analysis of a protease inhibitor from a new plant source – rice bean. The protease inhibitor has been purified and its properties studied.

B. OILSEEDS

Indian Mustard: at PAU Ludhiana in COE studies on germplasm, enhancement for crop architecture and defensive traits in *Brassica juncea* L. Czern and Coss,

90 determinate *B. juncea* genotypes were developed. This is through backcross transfer of gene for determinacy to select high yielding genotypes of mustard. Determinate (CMS) x Indeterminate (FR) hybrids are ready for large scale evaluation.

At Delhi University genome sequencing and mapping studies carried out. A total of 5715 GBS markers were placed on the *B. nigra* framework map and this is the first high-density linkage map of *B. nigra*. The map is now used for mapping white rust resistance and also for accurate arrangement of scaffolds on different chromosomes that have been generated from genome sequencing data and also for characterization of gene spaces. Sequencing of mega-variety Varuna with long sequencing reads (60X data) is being carried out in collaboration of Arizona Genome Institute, USA.

Under the project functional validation of MAPK-3 gene and phosphoproteomic induction studies were carried out on defense against alternaria blight disease in Brassica expression. Gene constructs harbouring Arabidopsis MAPK2, MAPK3, MAP2K4, MAP2K9 and Brassica MAPK3 have been developed. Studies on plant defense signalling and molecular modelling had been elucidated.

Groundnut: In the project on integrated marker assisted selection to develop groundnut varieties for resistance to foliar fungal diseases -Rust and Late Leaf Spot, backcross lines of JL 24 and TMV 2 were multiplied and evaluated. In a multi-location trial consisting of 8 centers during the kharif 2016, disease resistant lines gave ~15% higher yield than the recurrent parent. Another 12 backcross lines were identified to be promising and the seed multiplication is on-going for these lines. Additionally, the QTL and markers linked to LLS and rust were confirmed through this marker-assisted backcross breeding

Soybean: The project aims at the elimination of off-flavor generating lipoxigenase-2 gene in kunitz

trypsin inhibitor (Kti) free soybean lines derived from JS97-52, NRC7, JS93-05, MACS450 and DS97-12 through marker assisted backcrossing. Sixteen SSR markers from different linkage groups were found to be polymorphic for all the 5 parental combinations. Twenty soybean homozygous lines (Ten lines each in CO 3 and JSS 35 background) with Phytophthora and powdery mildew resistance were developed through molecular markers.

Safflower: In the project on fortification with Omega 3 FA, metabolic engineering of oil biosynthetic pathway in safflower [*Carthamus tinctorius*] has been made for the production of alpha linolenic acid (C18:3) and stearidonic acid (C18:4) in safflower seeds. The genes of Delta-15 desaturase of Arabidopsis and Delta-6 desaturase of the borage plant were cloned and placed under the transcriptional control of the beta conglycinin promoter for seed-specific expression. Transgenic safflower plants were raised through Agrobacterium-mediated transformation. Seeds of Delta-15 desaturase safflower plants accumulated alpha linolenic acid. Plants co-transformed with Delta-15 and Delta-6 desaturase genes accumulated minute amounts of stearidonic acid. The work shows the potential to do metabolic engineering of safflower for the production of the omega-3 (alpha linolenic acid) and omega-6 (stearidonic acid) fatty acids in plant oils.

C. COMMERCIAL CROPS

Cotton: A study on genomics and improvement of fibre quality was carried out for development of saturated genetic linkage map for *Gossypium hirsutum* L. using SSR and SNP markers. SNP linkage map was constructed for allo tetraploids cotton *Gossypium hirsutum*. High density cotton SNP Chip with 51,347 probes representing 42,377 SNPs (distributed across all the 13 chromosomes) using Affymetrix's Axiom technology was developed. The SNP-chip was utilized in genotyping of 192 F8 Recombinant Inbred Lines (RILs) with high call rate (99.9%).

At CSIR-NBRI, 10 QTLs were identified for SL, tena and micr (staple length (SL), tenacity (Tena) and micronaire (Micr)) from data collected for fibre quality. For SL, two QTLs were identified on LG 18 and LG4. Similarly, six QTLs were identified for tena and two QTLs for micro.

Two new cotton leaf curl disease (CLCuD) resistant donors viz., *G. armourianum* and Synthetic amphiploid have been identified and they are highly tolerant to whitefly also. F_1 plants derived from synthetic amphiploid and American cotton crosses have been found to be resistant to CLCuD virus and back crosses with the recurrent American cotton parent are in progress.

Sugarcane: Genetic engineering of sugarcane for water deficit stress tolerance was undertaken by ICAR-SBI. More than 100 transgenic events (EaHSP70 – 35 events; EaDREB2 – 25 events; PDH45 – 24 events; EaDREB2 and PDH45 co-transformed – 44 events) with different abiotic stress tolerance genes were developed.

D. MILLETS

Pearl Millet: Work on QTL mapping for betacarotene [*Pennisetum glaucum* (L) R. Br.] in pearl millet was undertaken at TNAU. Water saturated n-butanol (WSB) spectrophotometric method was standardized for estimation of beta carotene for larger populations. Phenotyping of 250 RILs for beta carotene through WSB method was completed and two beta carotene rich lines (TNBG 0608053 & TNBG 0608207) (superior for high yield and beta carotene) were identified along with screening of 198 SSR. Genotyping with polymorphic markers in the 250 RILs is under progress.

A project on generation of mapping populations and identification of QTL(s) for Downy Mildew Resistance in Pearl Millet (*Pennisetum glaucum* (L.) Br.) was carried out. 13 genotypes have been screened (susceptible and resistant against all the three known pathotypes of

Sclerosporagraminicolaviz Delhi, Rajasthan, and Gujarat isolates, Sg561, Sg384, and Sg445, respectively). 65 out of 336 SSR markers and 51 AFLP markers were found to be polymorphic for Rajasthan isolate Sg 384. QTLs for Downey mildew resistance have been mapped using markers by Simple interval mapping and a total of seven QTLs have been mapped using SSR and AFLP marker.

Finger Millet: Isolation and validation of salt tolerant genes in Ragi (*Eleusine coracana* L.) was undertaken at TNAU, Coimbatore. The transcriptome map of finger millet was developed and the Salinity tolerant gene(s) were isolated and characterized.

Molecular characterization of calcium signalling and transport machinery of finger millet (*Eleusine coracana*) was undertaken for calcium biofortification. Finger millet germplasm with high calcium content (452.8mg/100gm) was registered (National identity, IC0614156; and registration number INGR16014) at NBPGR, New Delhi.

For enhancing the productivity studies on genomics for stresses related genes of finger millet was carried out. A set of 413 germplasm accessions with adequate diversity having medium duration of 110-115 days was formulated and evaluated under different field conditions. A reference set of 220 contrasting accessions for drought and 70 contrasting accessions for high temperature tolerance were formulated. Based on the drought susceptibility index (DSI) and thermo sensitivity index (TSI) for grain yield and biomass, the accessions GE- 1332 (tolerant) and GE-156 (susceptible) were selected for drought transcriptome analysis and; PES-110 (tolerant) and KJNS-46 (sensitive) for high temperature transcriptome analysis. Validation of expression pattern of a few genes identified. Expression analysis for few additional genes is underway. Cloning and characterization for a few additional genes is under process.

F. CEREALS

Rice: The genetic enhancement of rice pertinent to seed size/weight trait and yield was carried out through epigenomics, transcriptomics and molecular breeding studies. The whole genome, methylome and transcriptome sequence of diverse contrasting low and high seed weight rice accessions were decoded at a high-resolution scale. Maximum numbers of ~1500 genes in S3 development stage of high grain weight rice accession were preferentially expressed as compared to their low grain weight accessions. A genome-wide 84634 ISM (intron-spanning marker) and 16510 ILP (intron-length polymorphism) markers developed from the genes were made accessible through a user friendly web-resource, “*Oryza ISM-ILP marker*” database to expedite high-throughput genetic analysis in rice with optimal resource expenses. Diverse integrated genomic strategies were developed by using the high-throughput marker genotyping and yield trait-related field-phenotyping information generated from numerous natural germplasm accessions (association panel) and 12 different mapping populations of rice. This approach delineated functionally relevant molecular tags (12 genes, six QTLs/eQTLs) and 10 natural allelic variants/haplotypes regulating seed size/weight in rice. Two potential major QTLs/genes regulating seed weight and seed number were introgressed into promising Indian varieties through marker-assisted breeding for improving rice.

Through molecular mapping and introgression of stigma exertion trait in hybrid rice, parental lines important donor lines for breeding have been identified. Molecular resources have been developed (518 SSR/ 95 HvSSR/ 120 HRM markers/ 28 QTLs)) and validation is under process.

Characterization of *Xanthomonas oryzae* pv. *oryzae* strains for screening of Xop like effectors to investigate its role as virulence determinants to induce blight in rice, different Xoo races were mapped. Different races were characterized and

one race was found to be highly virulent. Role of Xop 3 effectors was identified and communicated.

Biotic stress resistant rice varieties have been developed through marker assisted breeding. Near Isogenic line (NIL), Pusa 1728-23-33-31-56 (IET24573) carrying bacterial blight resistance gene in the genetic background of Pusa Basmati 6 (PB6) has been released as “Pusa Basmati 1728” for commercial cultivation in various states.



Fig.1: Pusa Basmati 1728 developed through marker assisted transfer of two genes namely xa13 and Xa21 governing resistance to bacterial blight disease. The variety is released for commercial cultivation in Punjab, Haryana, Delhi, Uttarakhand and Uttar Pradesh in 2016

Marker aided incorporation of major genes conferring resistance to blast disease into genetic background of high altitude temperate rice was developed. Three pyramided lines carrying genes Pi54+Pi1+Pita in the genetic background of Mushk Budgi are advanced.

A project on rice improvement is being carried out for rice var HPR2143 focussing on blight and blast resistance. Co Dominant markers were identified linked to Pi9 and pyramid lines with four resistance genes namely Pi9, Pita, Xa21, Xa38) has been developed.

Improvement of Ahu rice cultivars with focus on drought tolerance suitable for upland ecosystem is being implemented using molecular breeding approach. Two promising lines namely CBMAS 14065 and CBMAS 14142 harbouring drought tolerant QTLs of Apo has been developed and are being evaluated under AICRIP (All India Co-ordinated Rice Improvement Program). Salinity tolerant

version of White Ponniis (IWP-saltol) developed and is under AICRIP evaluation.

At TNAU, Coimbatore pyramiding biotic and abiotic resistance was achieved through inter-mated F1 plants of improved *White Ponni*. In the study 10 different genes/QTLs controlling tolerance/resistance against drought, salinity, submergence, blast, BLB and gall midge have been pyramided.

Studies on marker assisted introgression of Pup1 into elite rice varieties for phosphorus uptake is continuing at Indian Institute of Rice Research (ICAR-IIRR), Hyderabad. Pre-breeding lines with Pup1 gene in genetic background of three elite rice varieties namely Improved Sambha Mansuri, MTU1010 and IR-64 have been developed. Two of the lines with Pup1 in genetic background in MTU1010 and IR-64 have been nominated for AICRIP trials during kharif 2016.

Wheat: As study on physical mapping sequencing of wheat chromosome 2A was carried out to generate a gold standard pseudo-molecule of wheat with minimum gaps. Approximately 4000 full length genes have been identified from the sequence assembly and more than 100 of these are mapped genetically onto the linkage map of chromosome 2A. More than 5000 SSR markers have been identified out of which more than 100 were mapped onto the linkage group for generating saturated linkage map. More than 3000 genes have been anchored to the chromosome 2A. NextGen shotgun sequencing resulted in assembly of only 65 per cent of the chromosome, thus necessitating the physical map based sequencing. So far, fingerprinting of more than 100 per cent BAC clones stands completed along with BAC-end sequencing of more than 1.3 lakh BACs of both the arms.

In a study on bio-fortification of wheat for micronutrients, efforts were made to develop high yielding wheat lines with higher grain micronutrient (zinc/iron) and development of marker. The study confirmed that Chromosomes

2A, 5A and 7A harbor QTLs for increased grain iron and zinc. Chromosomes from different *Aegilops* were transferred to the wheat stock PBW343 carrying genes for leaf and rust resistance and protein gene GpcB1. Introgressions from alien species bring a considerable linkage drag affecting phenology and yield.

Leaf rust, caused by *Puccinia tritica*, is amongst one of the devastating rust diseases of wheat. To address this, studies on leaf rust -*Puccinia tritica* genomics was carried out. Whole genome *de novo* sequencing of two fungal pathotypes/race namely *P. tritica* Race 77 and *P. tritica*, Race106 were carried out using genomic DNA from the urediniospores.

In a network programme mobilizing quality traits into high yielding varieties were developed in wheat varieties with high grain yield and improved grain quality for industrial end-products. Products such as bread, biscuit, cake, pasta, etc. were developed. Pyramided genes/QTL for high grain protein content (GPC), pre-harvest sprouting tolerance, grain weight, gluten strength, yellow pigment content, lipoxygenase, and leaf rust resistance were systematically and successfully transferred into 13 popular Indian wheat varieties (11 hexaploid wheat and 2 durum wheat varieties) using marker-assisted selection (MAS). Several of these MAS-derived lines are being evaluated in All India Wheat Improvement Project and 15 improved lines have already qualified the IPPSN 2015-16. One entry from PAU, Ludhiana was promoted to MABB trial. These improved lines have the potential for release as varieties for commercial cultivation as well as pre-bred material in future wheat breeding programme.

Advanced homozygous and significantly improved population had been developed using QTL/Genes for quality traits into high yielding wheat varieties through marker-assisted selection. Multi-location trial conducted in 2015-16, registered in NBPGR and recommended for varietal testing.

Maize: Among various micronutrients, deficiency caused by provitamin-A, Fe and Zn is wide-spread in the country. To address this, a study was undertaken on enrichment of micronutrient in maize. In the present project, Vivek QPM-9, a popular QPM maize hybrid was improved for provitamin-A (21.7 micro g/g of beta-carotene, compared to 2.6 micro g/g in original hybrid) by introgressing mutant allele of crtRB1 through MAS. The improved version of Vivek QPM-9 produced 5588 kg/ha and 5916 kg/ha of grain yield in NHZ and PZ, respectively under AICRP. The grain yield was at par with the original hybrid. It is country's first provitamin-A rich maize hybrid. Beta-carotene rich version of Vivek Hybrid-27 has were also evaluated under AICRP.

Sorghum: Marker-assisted gene pyramiding of brown midrib genes was undertaken for development of sorghum genotypes suitable for lignocellulosic biofuel production. A PCR-based marker (Sb-bmr12) was developed for the selection of brown midrib (bmr12) trait for use in marker-assisted gene pyramiding.

G. VEGETABLES

Chilli: In the project, DNA marker assisted mapping of anthracnose resistance in chilli (*Capsicum annum* L.), Polymorphic markers were identified. Single marker analysis was performed and a DNA marker putatively linked to anthracnose resistance in chilli was identified.

Tomato: NIPGR had developed RNAi lines of tomato and the molecular, biochemical and phenotypic characterizations of these tomato lines showed that fruits were with longer shelf life than control, and had no negative effect on vegetative growth, fruit development, days to maturity, seed production and yield.

ANIMAL BIOTECHNOLOGY

Livestock are vital to subsistence and economic development of our country. Continuous R&D support resulted in substantial increase in the

productivity of animals. However, the productivity of indigenous livestock is still very low in comparison to exotic breeds. The department continued R&D support both in basic and applied research of animal production. Some of the major achievements of the projects supported are as follows:

Reproduction: Availability of quality semen is a major constraint for successful implementation of artificial insemination programme in our country. To predict the fertility status of bull, transcriptomic profiling of bull spermatozoa was carried out at National Institute of Animal Nutrition and Physiology (NIANP), Bangalore. Initial results showed that the transcript profile of spermatozoa varied depending on fertility status of animal. This study will help in developing fertility diagnostic and identifying quality of semen of bulls selected for breeding purpose.

Autocrine / paracrine growth factors were found to be expressed in a regulated and stage specific manner in buffalo ovary in a study conducted in IVRI, Izatnagar. The results confirmed that the growth factors contribute to the extensive capillary proliferation associated with the increase in size, selection, and maturation of the pre-ovulatory follicle and formation and development of corpus luteum. This facilitates follicle maturation by enhancing the supply of nutrients, hormones, and other essential blood-borne signals to the follicle. The growth factors also play essential modulatory role in steroidogenesis and promote survivability of the follicular and luteal cells in buffalo. LH, IGF-1, and EGF treatment were found to have cytoprotective/anti-apoptotic effect and stimulate VEGF production in luteal cells and granulosa cells of bubaline pre-ovulatory follicles.

Analysis of neutrophil dynamics and changes in their gene expression profiling was carried out to identify possible markers specifically for early pregnancy detection or specific diseases in cattle at National Dairy Research Institute (NDRI), Karnal.

The neutrophils showed changes in their expression from day 12 to day 20 post insemination, and play an important role during peri-implantation period of embryo. The study also indicates down-streaming of adhesion molecules of neutrophils along with pro-inflammatory cytokines in pregnant cows. The preliminary results indicated that neutrophil activity and mRNA expression of genes isolated from neutrophils of cattle can be used as indicators to assess the health/physiological status of an animal.

At NIANP, Bangalore, gene expression profiling of various genes related to estradiol synthesis (CYP19A1), granulosa cell proliferation (CCND2) and Wnt signal components (WNT2, WNT4, FZD6, APC, AXIN2, DVL1, CTNNB1) in the ovarian granulosa cells of buffalo. The study confirmed that all three aspects viz. estradiol synthesis, granulosa cell proliferation and Wnt signal components play an important role in folliculogenesis and thus have a role in enhancing productivity. Gene expression studies confirmed a positive effect of Wnt canonical signaling pathway on estradiol synthesis both in medium sized and large sized ovarian follicles of buffalo. The Wnt signal confirmed its positive role in estradiol synthesis during early as well as in late folliculogenesis in buffalo / goat.

At Indian Institute of Science (IISc.), Bangalore, bovine and bubaline FSH were expressed in mammalian expression system, partially purified and found to be biologically active. Indigenous production of FSH and LH will help in reducing the cost of production of ET calves.

In another study at IISc, Bangalore, the microarray analysis of corpus luteum (CL) tissues collected from PGF_{2α} treated buffalo cow revealed differential expression of Cyp19A1 gene, responsible for estrogen (E₂) biosynthesis. The mining of differentially expressed genes for estrogen signaling and its target genes provided evidence that following rapid decrease of luteal E₂ concentration in response to PGF_{2α} treatment, a number of E₂ responsive genes were also

differentially regulated. Analysis of CL tissue suggest that expression of IGF1R and Akt survival pathway molecules are influenced by PGF_{2α} treatment, but their expressions were not restored following hCG and GH treatments.

The role of melatonin as a fertility marker as well as in fertility enhancement of Mithun was studied at National Research Centre on Mithun, Jharnapani, Nagaland. Melatonin implant at a dose of 3mM improved the biometry of scrotum, semen quality parameters, freezability and fertility of semen in different seasons. It also protects sperms from the adverse effects of free radicals due to heat stress during summer season as a potent powerful antioxidant.

Transgenic: A novel non-invasive technique for generation of transgenic rat model alpha thalassemia was developed at National Institute of Immunology, New Delhi by integrating transgene into the genome of the spermatogonial cells by testicular injection of DNA followed by electroporation. This efficient method will ease the generation of transgenic rats which is needed to create better disease models than mice, for certain human diseases.

At CCMB, Hyderabad, a transgenic mice model expressing Echidna anti-microbial protein (EchAMP) gene in its mammary gland was developed. Milk samples of transgenic mice confirmed expression of EchAMP protein. The whey protein of milk was isolated and confirmed for its anti-microbial activity. Exposure of mammary glands of EchAMP and wild type mice to LPS revealed a significantly lower inflammatory response. The expression of TLR4 gene, the receptor for LPS was also low in EchAMP transgenic mice indicating that EchAMP modulates the response of the animal LPS-induces inflammation. Immuno blot analysis revealed that the NF- κ B signaling pathway was not activated in EchAMP transgenic mice. The biophysical studies of recombinant protein (from *E.coli*) confirmed its folded nature and presence of an alpha helical

structure, a characteristic feature of antimicrobial protein.

Genomics: Genetic diversity study of selected cattle breeds viz. Sahiwal, Tharparkar, Gir and Vechur was carried out at National Bureau of Animal Genetic Resources, Karnal to identify selective sweep regions in their genome. A total 72 DNA samples (18 random samples/breed) were genotyped using 777K SNP chip and analyzed. Out of 7,77,962 SNPs genotyped, 4,79,277 SNPs were in Hardy Weinberg equilibrium, out of them 1000 markers were identified having potential to differentiate these cattle populations and also accounted for 39% of the genetic variation between the breeds. These breeds were classified into small and large sized breeds indicating shared ancestry of large sized milch breeds (Gir, Tharparkar and Sahiwal). Most of sampled animals (> 67%) from 4 populations were classified into their own group of animals called breed. The genomic regions containing highly differentiated SNPs with F_{ST} (> 0.25) were considered as selective sweeps. The selective sweep regions were annotated for the presence of genes and a total of 48, 30 and 60 genes were found under selective sweeps for Sahiwal-Tharparkar, Sahiwal-Gir and Tharparkar-Gir breed pairs, respectively.

High throughput exome sequence analysis of four buffalo breeds was carried out to detect single nucleotide polymorphisms (SNP) at AAU, Anand. A total of 9,23,964 high quality SNPs were identified in four buffalo breeds for milk production and fertility trait. Most of these identified SNPs of milk production were located in the genes which have been related to economically important traits in other mammalian species. Further gene ontology (GO) categories involved in various pathways and processes like lipid metabolism, carbohydrate metabolism processes etc. were found to be associated with milk globule formation, along with other milk component formation and their secretion.

Nutrition: The effect of dietary supplementation of omega 3 polyunsaturated fatty acid (PUFA) in

goats was studied at IVRI, Izatnagar. The findings confirmed role of omega 3 fatty acid in corpus luteum development, follicular growth, ovulation, higher plasma progesterone level on day 11 and 14 of the estrous cycle.

Various types of nano-formulations were developed and utilized as functional feed supplements on model animals (guinea pigs and wister rats) at IVRI, Izatnagar to confirm their effect on health and productivity. Zinc nanoparticles in the range of 20-50 nm particles were synthesized by chemical and green synthesis method and its availability was reported as 24-27% and 40-46% respectively. Selenium (Se) nanoparticles of 30-35 nm were also prepared by chemical method and their supplementation in guinea pigs and male Wistar rats feed at the level of 150 ppb improved their growth performance, digestibility humoral immune response etc. Supplementation of 20 ppm Zn nanoparticles had beneficial effects on growth performance, SOD activity, serum, liver and testes.

Biomining of selected white rot fungi (WRF) for the production of novel lignin peroxidase and manganese peroxidase for enhancing digestibility of crop residues was carried out at NIANP, Bangalore. Thirty eight strains of commercial isolates and thirty six wild isolates of fungi were screened qualitatively and quantitatively. The isolates with maximum activity were immobilized on different matrices for enhanced production. The purified enzyme was characterized and kinetics were worked out. Nine different straws were subjected to treatment with crude (t1) as well as purified (T2) lignin peroxidases produced by immobilized mycelia of wild white rot fungi, LPS1. The NDF, ADF and lignin of all the treated straws showed a decrease compared to the untreated control straws. IVDMD of all straws treated with both the crude as well as purified enzyme showed improvement though variations were recorded amongst the tested straws. High yields of LiP obtained through immobilization were effective in

enhancing the digestibility of various crop residues.

Various plant secondary metabolites viz. condensed tannin (CT), hydrolysable tannin (HT), saponins, combination of CT & HT, tannin (CT+HT) and saponin, essential oils were prepared and their effect to ameliorate methane emission was studied in livestock at NIANP, Bangalore. *In vitro* results indicated approximately 27% reduction in methane production with a combo preparation of CT & HT (1:1) of secondary metabolites supplemented at 30 mg/g level in basal diet. Saponin supplementation alone at minimum level (5 mg/g) also decreased ($p < 0.05$) methane production as compared to control one.

Animal Product: Animal cartilage of goat origin was successfully utilized as surgical implantation in Microtia and Rhinoplasty of human patient at S.G.Kar Medical College, Kolkata and West Bengal University of Animal and Fisheries Science, Kolkata. The acellular goat choncal cartilage was developed and tested for its *in vitro* immune-compatibility and cytotoxicity assay, qualitative and quantitative biocompatibility testing including studies on pro-inflammatory cytokines. The acellular cartilage was characterized and assessed for its suitability for xeno-transplantation in rabbit initially and also on human volunteers. Treated cartilage was implanted in 15 human patients (Rhinoplasty-9 and Microtia-6) with xenochoncal cartilage graft and 7 patients (Microtia: 3 & Rhinoplasty: 4) with autogenous cartilage graft with an average follow up period of 8 months. The rhinoplasty and microtia operation utilizing the treated acellular animal cartilage showed satisfactory recovery resulting improved facial look.

Poultry: Thermotolerance gene expression profile of *Salmonella typhimurium* and their thermal death time models applicable to poultry processing industry was studied at Central Avian Research Institute, Izatnagar. Growth profiling pattern of *S. typhimurium* was observed to be arrested at 50°C only. Gene expression analysis of heat stress

related genes in *Salmonella typhimurium* isolate revealed induction of *htrA*, *rpoE*, *rpoS*, *uspA* and *uspB* genes with heat stress at 42°C temperature as compared to control (30°C). Exposure of lethal heat stress at 50°C induced *htrA* and *rpoE* genes while expression of *rpoS* gene was lowered as compared to control (30°C) and *uspA* and *uspB* genes showed lowered expression relative to *rpoD* gene (reference gene). The results obtained were used for the thermal death time modeling of hardy *Salmonella typhimurium* on skin and dressed carcass treated with ASC or carvacrol and thermal treatment. The treatments found suitable were applied in actual processing conditions for ensuring microbial safety of carcasses without any affect on sensory attributes and organoleptic quality of meat.

Single nucleotide polymorphism detection in coding region of broiler genome and its association with feed conversion ratio has been taken up at Anand Agricultural University, Anand. So far, a total 192,119 high quality SNVs have been identified including 30,380 coding SNVs (cSNVs) in the experimental population. The missense SNVs in *PGM2*, *NOX4*, *TGFBR3* and *TMX4*, and synonymous SNVs in *TSNAX*, *ITA*, *HSP90B1* and *COL18A1* were found to be associated with FCR. Through SNV-trait association analysis, a total 896 SNVs were identified for FCR that will be of interest to achieve breeding goals for broilers. The study indicates that protein-altering mutations contribute little to the genetic component of broiler with Low FCR. A comprehensive replication study of coding and non-coding SNVs in an independent replication data sets was also carried out which suggests that *TMX4* variant may be associated with FCR in broilers. The SNVs along with the relatively high rate of non-coding variants should provide an excellent resource for future molecular breeding and genomic selection in poultry.

Animal Vaccines and Diagnostics:

Introduction: The mandate of Animal Health Division of DBT is to support the R & D programmes

for the development of point of care diagnostics and affordable new generation vaccines against animal diseases of economic and zoonotic importance. The emphasis is given to the collaborative translational research, consolidation of existing projects with potential leads and generation of network programmes around major animal diseases of national importance.

Major Initiatives: During the year, several new projects on studies of innate immune response during reproductive salmonellosis, diagnostic for bovine uterine neoplasia, Toll Like Receptor (TLR) agonist as adjuvants and prophylactic agents in chicken have been supported.

The Department organized a Brain Storming Workshop on “Transgenic Livestock: Technologies and Applications” to identify priority areas for initiating a network programme on transgenic livestock with special reference to agriculture and biomedical applications inviting several Indian and foreign experts.

Department of Biotechnology in collaboration with Indian Council for Agriculture Research has organized the International Conference on Brucellosis from 17th-19th Nov., 2016 at NASC, Complex, Delhi. The programme was inaugurated by Hon’ble Minister of State for Science & Technology and Earth Sciences, Shri Y.S. Chowdary, and presided over by Shri Sudarshan Bhagat, Hon’ble Minister of State, Agriculture and Farmers welfare. Three new diagnostic kits against brucellosis were launched along with announcement for launching of “Brucella Free Villages” for implementation on pilot scale in 50 villages covering 10 states. The International Brucellosis Conference 2016 has provided a technical platform for scientist and experts from all over the world. Scientists from 27 countries including India participated in the conference and in the three days deliberations addressed various issues on Brucellosis covering broad and interdisciplinary field of “One Health” concept

revolving around Brucella Pathogenesis & Host-pathogen interaction; Human Brucellosis; Epidemiology and Control; Brucella research in India; Canine and Wildlife Brucellosis; Diagnostic methods; and Vaccines & Immunology.



Participants from 27 countries in International Brucellosis Conference organized by DBT from 17-19th November, 2016 at New Delhi



Hon'ble Minister of State for Science & Technology and Earth Sciences, Shri Y.S. Chowdary, and Shri Sudarshan Bhagat, Hon'ble Minister of State, Agriculture and Farmers welfare launching new diagnostic kit against brucellosis along with announcement of “Brucella Free Villages”

Salient achievements

DBT Network Program on Brucellosis: The Network Program on Brucellosis has successfully completed the first phase. A repository was established for storing and cataloguing different Brucella species. A novel penside diagnostic, lateral flow assay kit, indirect ELISA kit against Brucella species and a hand held ELISA reader have been developed.

Translational Research Platform for Veterinary Biologicals (TRPVB): TRPVB is a unique novel partnership programme between Department of Biotechnology (DBT) and Tamilnadu Veterinary and

Animal Science University (TANUVAS) in the field of translational research for Veterinary Biologicals. The platform includes an integrated combination of academia / industry and regulatory experts to leverage and assist clients in various stages of product development. TRPVV is offering 13 biotechnology services, 6 cell line supply and testing services, 7 instrument usage services and 5 different diagnostic kits being directly sold to end users. During the year six proven business strategies were supported by case studies, the GMP compliant clean room facility at TRPVV was inaugurated and which is now fully operational. Three hands on workshop on Flow cytometry, Confocal Microscopy and in-vivo imaging were conducted during this reporting period.



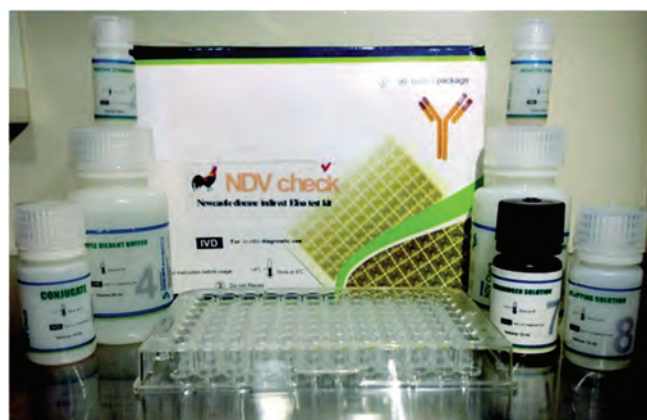
Bru Alert Kit for Brucellosis detection in livestock Surgical Scrub Kit



Progesterone impregnated nanofibers placed as a skin patch on bovine for oestrus synchronization

Vaccine and Diagnostics Research and Development: Recombinant vaccine against *Mycobacterium avium* for goats, vaccine for canine mammary tumor, Nano-Newcastle disease virus vaccine, recombinant antigen based diagnostics and chimeric plant virus-like particle based vaccine for infectious bursal disease virus (IBDV) were developed. Studies to develop dip-strips to detect acaricide resistant ticks, biosensors for detection of peste des petits ruminants (PPR), and economic diagnostics for surra have been done. Newcastle disease Virus Antibody Test Kit, NDV-Check was

also developed through the project supported by the department. A study was also carried out to assess the status of veterinary biologicals in India and as a result a book has been published on “Animal Biotechnology – Vaccines and Diagnostics- Markets and Investment Opportunities”. The book was released by Hon’ble Minister of State for Science and Technology, Shri. Y. S. Chowdary and Minister of State for Agriculture and Farmer’s Welfare, Shri. Sudarshan Bhagat on 17.11.2016 during the occasion of International Research Conference, Brucellosis 2016 at New Delhi.



NDV Check- Newcastle disease Virus Antibody Test Kit



Fig. Book released on “Animal Biotechnology – Vaccines and Diagnostics- Markets and Investment Opportunities

Under Animal Biotechnology Career Enhancement Programme (ABCEP) 10 students were successfully trained and Post Doc’s were involved in development of a kit to detect subclinical ketosis in bovine and a lateral flow assay for simultaneous detection of antibodies to canine parvo and rabies viruses.

Support was continued for studies on identification of disease related markers for the diagnosis of Subclinical Mastitis, development of recombinant

vaccine for control of salmonellosis in poultry, Animal Biotechnology Career Enhancement Programme (ABCEP)", development of recombinant antigen based diagnostics and chimeric plant virus-like particle based vaccine for infectious bursal disease virus and operation and maintenance of P3 facility (BSL-3) for studying dangerous pathogens with special reference to anthrax causing pathogen *Bacillus anthracis*.



Ketocheck Kit



Simultaneous CPV and rabies antibody detection using LFA

AQUACULTURE & MARINE BIOTECHNOLOGY

Aquaculture and Marine Biotechnology programme is being implemented to support projects for development of useful products and process from marine resources and also for enhancement of aquaculture production and productivity with the adoption of biotechnology tools and techniques. Some of the major achievements of the programme are highlighted as follows:

Fish Disease Management: A project was implemented at University of Delhi on understanding the mechanism of induced ulcerative disease syndrome (USD). The interplay of cytokines

and signaling molecules in fish resistant and susceptible to *A. hydrophila* was studied. The study reported that the cell death induced by the bacteria is apoptotic in nature and caspase-3 mediated. The role of TLR-4 as the transducer of Ca^{+2} signals consequent to *A. hydrophila* has been determined. The infection with live *A. hydrophila* did not induce any significant pro-inflammatory response however immunization with dead *A. hydrophila* followed by challenge with live *A. hydrophila* led to significantly upregulated pro-inflammatory cytokine production, reduced pathogenesis, efficient removal of bacteria and enhanced fish survival.

Studies on Comprehensive analysis on cyanobacterial Glutathione S-Transferases were carried out at Bharathidasan University, Tiruchirappalli. This was taken up considering the importance of Glutathione S-transferases (GSTs) as a second line of defense against various xenobiotic compounds from primordial photosynthetic prokaryotes. Twelve types of GSTs in cyanobacteria were identified through *in silico* approach. Evolutionary divergence of the GSTs among the cyanobacteria studied shown variations. *Oscillatoriales* and *Nostocales* have showed highly evolved forms. 10 isoforms chi type GST showed higher expression under pesticide stress namely acephate, carbendazim and glyphosate when compared to other types. Affinity of pesticides to chi was greater and this substantiated by *in vivo* studies.

Development of Diagnostics: Development of field level nanoparticles based immunodiagnostics for viral pathogens of shrimp and prawn was carried out at Agharkar Research Institute, Pune. White spot syndrome virus (WSSV) infection spreads rapidly leads to huge economic losses. A lateral flow immunoassay (LFIA) employing gold nanoparticles conjugated to polyclonal antibody against VP28 (envelope protein of WSSV) for detection of WSSV has been developed. The LFIA detected WSSV in ~20 min and showed no cross-reactivity with other

shrimp viruses. The limit of detection (LOD) of the LFIA was 103 WSSV particles. The LFIA could rapidly detect the virus in different tissues of *Litopenaeus vannamei* after 3 h, 6 h and 12 h of infection. Assay developed is rapid, field-usable and does not require skilled personnel. The antibody production against WSSV and immunodiagnostic test for detection of WSSV is completed.

Studies on genetics diversity of *C. botulinum* in seafoods and development of Lateral Flow Immuno Assay (LFIA) for toxinotyping were continued at CIFT Kochi. Prevalence of fish and fish products comprising of ready to eat, ready to cook, dried fish and fresh fish have been analyzed. Out of 250 presumptive *C. botulinum* cultures isolated eighteen positive samples, twenty three were found to be toxigenic in mouse bioassay. Work continued to study the genetic diversity of *C. botulinum* types isolated from diverse sources and to develop a Lateral flow immunoassay (LFIA) for *C. botulinum* toxinotyping.

Antimicrobial and Immunostimulants: A project on purification, characterization, functional analysis and structural elucidation of pattern recognition molecule - β -1, 3-glucan-binding protein and antimicrobial peptides from crustaceans was continued at Alagappa University, Tamilnadu. Isolation and purification of pattern recognition molecule α -GBP from the crustaceans and purified α -GBP have been characterized. Functional analysis demonstrated purified α -GBP involvement in the agglutination reaction acts as a first step in the activation of major humoral response like prophenoloxidase activity in dose dependant manner. Antimicrobial peptide crustin has been purified from the haemolymph of *E. tetragonum*. Antibacterial activity was explored through bacterial killing assay and antibiofilm activity against *Staphylococcus aureus* and *Enterococcus faecalis*. Immune molecule prophenoloxidase has been purified from green tiger shrimp *Penaeus semisulcatus* and functional activities of phenoloxidase (PO) were assessed by agglutination,

phagocytosis and encapsulation.

Studies on antimicrobial and immunostimulatory activities of actinomycetes in aquatic animal health management was continued at C.Abdul Hakeem College, Melvisharam. Actinomycetes isolated from different habitats screened for antiviral activity against WSSV. Two isolates have showed strong antiviral activity against WSSV (Fig.1). The pure active compound having antiviral activity has been tested *in vitro* using fish cell lines and *in vivo* using different life stages of shrimp. Attempts are being made to synthesize the compound chemically and to make use of this actinomycetes isolate as probiotics or co-inhabitant in culture system to control WSSV infection in shrimp.



Fig. 1 : Growth of Actinomycetes isolate (CAHSH2) having strong antiviral activity against WSSV on different culture media

Studies on immuno-prophylactic and therapeutic potentials of the hemi-parasitic *mistletoe* *Dendrophthoe falcata* in Asian seabass, *Lates calcarifer* was carried out at Vels University, Chennai. The polysaccharide fraction (PF) of *Dendrophthoe falcata* (DF) has shown excellent immunostimulatory properties. A significant enhancement of non-specific humoral immune has been observed on most of the post treatment days compared to the untreated control when administered intraperitoneally or as feed supplement. One week feeding of DFPF resulted in

Relative percent survival of 100 the maximum protection after a challenge with virulent *Aeromonas hydrophila*. Studies on the molecular interaction between aspartate semialdehyde dehydrogenase (ASADH) enzyme involved in the synthesis of essential amino acids of fish pathogen *Vibrio anguillarum* with natural product caulerpin found in marine macroalga. This has revealed that caulerpin inhibits ASADH and it can be used as a novel plant based antibiotic in aquaculture (Fig. 2,3). Further, marine fishes can directly feed on algae that produce caulerpin.

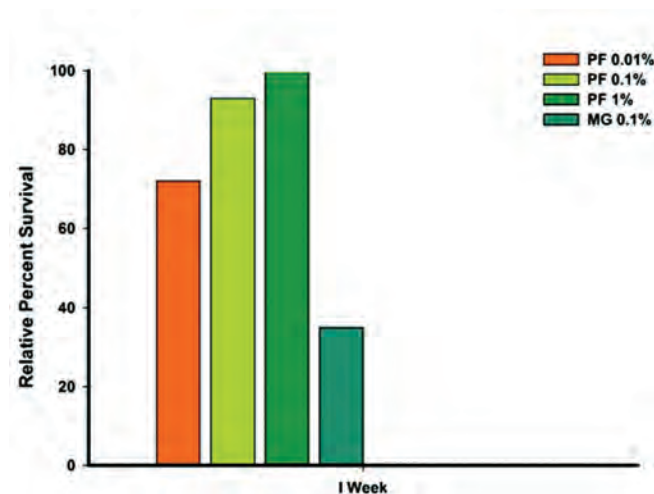


Fig 2. Relative Percent Survival (RPS) values of DFPF treated (as feed supplement) fish after the challenge with virulent *Aeromonas hydrophila*.

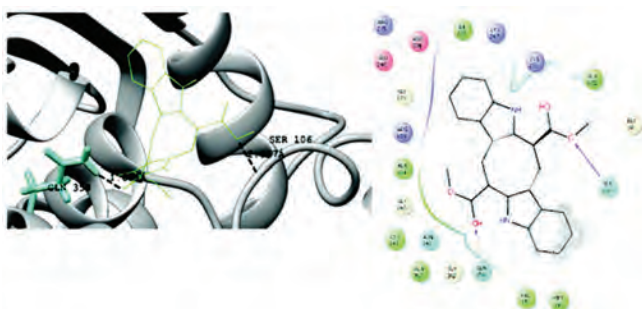


Fig. 3: Docking simulation of VA. a) Protein is shown as ribbon, Gln358 (blue) and caulerpin (green) as wires. Hydrogen bonds are shown as black dashed lines with distances. b) Same rendered by maestro. Structure of caulerpin is depicted as black lines surrounded by amino acids of the binding pocket. Arrows represent hydrogen bonds.

Fish Nutrition: A project on development of pelleted diet for *Catla catla* and *Clarias batrachus* using *Achyranthes aspera* were taken up at

University of Delhi. Evaluation of its immunostimulatory properties in pond culture system were carried out. Culture of fish, preparation of diets (diets for *rohu* and *magur*), feeding trails in laboratory and field conditions have been done. Fishes have accepted the prepared diets using *Achyranthes aspera*. Work on evaluation of immunostimulatory and disease resistance properties of plant ingredients in fishes are progressing well.

A project on periphyton enhancement for efficient nutrient utilization in seed rearing and grow-out carps culture was implemented at Central Institute of Freshwater Aquaculture, Research Station, Bangalore. The study on application of poultry manure reported was superior for periphytic growth on sugarcane bagasse substrate and *L. fimbriatus* young ones and adult can efficiently utilize periphyton as a food. Provision of substrate in addition to supplementary feed resulted in increased growth and substrate in tank bottom also shown increase in fish growth. *In vivo* digestibility study showed that periphyton is better digestible in *L. fimbriatus* compared to isonitrogenous pelleted feed. Periphyton grown on sugarcane bagasse has more planktonic genera compared to that in free plankton from the ambient water. Periphyton also shown contributing nutrients and digestive enzymes to grazing fish.

Spawning and Reproduction: A project on genetic and molecular endocrinological and its application no sex manipulation in common carp and its hybrid using Indian major carp, *rohu* was implemented at University of Hyderabad. Candidate sex-specific genes have been identified and analysed in normal *Cyprinus carpio*. Several essential genes related to gonadal development have been identified. Common carp breeding was standardized and Carp samples used to get different stage undifferentiated gonads. Growth rate, weight gain, histology and sex percentage were analysed between control and hormone treated samples. The

percentage of female population was significantly increased when compared to the control population. However, intersex population was also observed in different doses selected. Studies on development of genetic hybrids between common carp and Indian major carp *rohu* and impact of these genes in genetic hybrids are in progress.

At University of Madras, Guindy Campus studies were carried out to trigger ovarian maturation of *Penaeus monodon* in captivity. The follicular cells in crustacean have shown to secrete various hormones which are believed to play a central role in ovarian maturation. To understand the mechanism the studies were undertaken on serotonin or 5-HT detected in ovarian follicular cells of *P. monodon* was shown to stimulate ovarian maturation. It was informed that molecular signalling that is being regulated by serotonin and cocktail of inhibitors in attaining early oocytes maturation. Studies have also revealed higher expression of GnRH in serotonin treated animals in supraesophageal ganglion and thoracic ganglion. A significant increase in the expression of StAR in 5HT treated animals shown compared to untreated groups. This demonstrates the role of serotonin through GnRH in regulating oocyte maturation. The expression of Cyclin B1 and cdc2 were higher in serotonin plus cocktail of inhibitor treated animals compared to control animals, whereas the trend of expression of pcdc2 was vice-versa.

Fish Genomics and Transcriptomics: A network programme on whole genome sequencing and development of allied genomic resources in two commercially important fish - *Labeo rohita* and *Clarias batrachus* was continued at NBFGR Lucknow, CIFA Bhubaneswar, IASRI New Delhi and AAU Gujarat (Fig 4). Whole genome multi platform sequencing (Illumina, Roche 454 and Ion Torrent) have been completed for *L. rohita* and *C. batrachus*. SSR mining has been done from the assembled contigs in both the fish, followed by the development of webserver. Analysis of repeat

elements in *L. rohita* and *C. batrachus* indicated 41.62% genome of Rohu and 36.48% of genome of Magur, containing repeat sequences. Transcriptome sequencing has been done for *C. batrachus* (of both sex), tissues of brain and gonads, followed by transcript generation using Trinity. Mitochondrial DNA haplotypes were sequenced for generation of SNP markers for both the fishes. A total of ~55,000 BAC clones have been developed, with an average insert size of 115 Kb. This may serve as useful genomic resource for genome finishing, gene characterization and other genomic related studies in *C. batrachus*. 3686 BAC end sequences have been generated from the BAC clones.



Fig.4: Specimens of *L. rohita* (A) and *Clarias batrachus* (B) used for whole genome sequencing

Development of Cell lines: Studies on derivation and characterization of embryonic stem cell lines from the marine ornamental maroon clown fish *Premnas biaculeatus* was carried out at Central Marine Fisheries Research Institute, Kochi. Initiation of primary fibroblast cultures from various tissues of the humpback grouper *Cromileptes altivelis* for use in derivation of iPSCs have been done (Fig.5). Attempt has been made to culture blastomeres from various developmental stages of the embryo. It was found that the mid blastula stages containing 128 and 256 cells yielded better blastomere attachment and multiplication. Multiplication of blastomeres under *in vitro* conditions and formation of stem cell colonies were observed. ES cell cultures derived from mid blastula stage embryos exhibited morphology of typical ES cells with high nucleocytoplasmic ratio and prominent nucleoli. Culture conditions have been optimized with various growth factors and additives for successful passaging of the cultures without differentiation and the cells have been successfully cryostored and revived.

Protocol to re-programme the low passage fibroblast cultures derived from various tissues of *C. altivelis* using pluripotency transcription factors is being standardized (Fig 6). Work on Induced pluripotent stem cell lines (iPSCs) from the humpback grouper *Cromileptes altivelis* was also carried out.

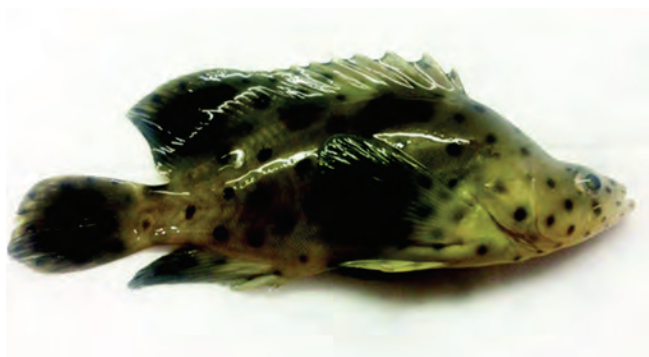


Fig. 5: *Cromileptes altivelis*



Fig. 6 : *Premnas biaculeatus* brood pair

At CUSAT work on cell culture studies in shrimp was carried out. Two shrimp specific vectors were constructed and transcriptional activities of these vectors have been confirmed in the primary lymphoid cell culture. Shrimp cell surface protein has been detected by monoclonal antibody of a shrimp antigen (proteins) on the surface of fusion cells. The hybrid cells were exposed to shrimp virus WSSV and cytopathic effect (CPE) was observed with nucleus enlargement and granular formation after 72 hours. RNA was isolated from the floating cells and VP28, DNA polymerase, WSSV Ie1, WSSV protein kinase-1 and WSSV endonuclease were amplified. The study reveals that hybrid cell line supported the growth of shrimp virus WSSV.

Bio-prospecting: In a network project studies on diversity (cultivable and culture independent), *ex-situ* conservation and bio-prospecting of marine actinobacteria for antibiotics, anti-tuberculosis, anti-HIV and immunomodulatory substances continued at Annamalai University, Periyar University and Sathyabama University, Tamilnadu. Out of 101 strains received from Annamalai University, 74 actinobacterial extracts have been prepared in Periyar University. Out of 74 actinobacterial extracts 16 showed antimicrobial activity have been selected as potential strains for further extraction of antimicrobial metabolites. The extracts of six actinobacterial cultures showed more than 75 % inhibition against clinical isolates of *M. tuberculosis*. These isolates were selected as potential strains for further extraction of anti TB metabolites. Standardization of methodology related to screening for anti HIV activities of these strains have been carried out.

A project on purification and characterization of bioactive compounds from a marine bacterium was implemented at Vignan University, Andhra Pradesh. The aim was to find out a bacterium that produces novel bioactive exopolymer (ECP). Screening procedure has been performed to detect ECP-producing bacteria. ECP producing strain was identified as *Acinetobacter* species by 16S rDNA analysis. The polymer produced by the isolate has been quantified purified and chemically analyzed. Various bioactivities of the purified ECP are being studied specifically for antioxidant properties.

DNA Barcoding and Molecular Taxonomy: A project on pattern recognition of Indian prawn with neural network was implemented at Sri Padmavati Mahila Visvavidyalayam, Tirupati. Automatic Recognition of Indian Prawn Species (ARIPS) software product developed. This helped in identification of Indian prawn species automatically using external morphological features like rostrum, carapace, abdomen and telson. Identification system for the Classification of DNA barcodes of prawn species using hybrid soft computing system

developed increases the accuracy by computer vision technology. The traditional method of the human subjective evaluation method is being replaced by an automated computer based systems.

A project on molecular taxonomy and phylogeny of cones (cone snails) and strombs (mollusca, gastropoda) of the Indian coast was implemented at Central Marine Fisheries Research Institute, Kochi. The work on inventorization and establishment of taxonomic status of cone snail and strombs (Mollusca) in Indian waters were carried out. 70 individuals from 20 species of the families Conidae and Strombidae were collected from 5 sites along the coast of India (**Fig.7**) Specimens were identified based on shell morphology; morphometric and meristic data were recorded. Tissue samples from the region of muscular foot or mantle were used for DNA isolation and fragments of the mitochondrial genes 12S rRNA, 16S rRNA, Cytochrome oxidase subunit I (COI) and nuclear H3 gene were amplified. Genes sequences were identified using BLAST search within nucleotide database to determine the highest homology. The presence of cryptic species in *Conus inscriptus* was observed from the collections made Vizhinjam and Tuticorin. Further confirmations are being made through molecular signatures.

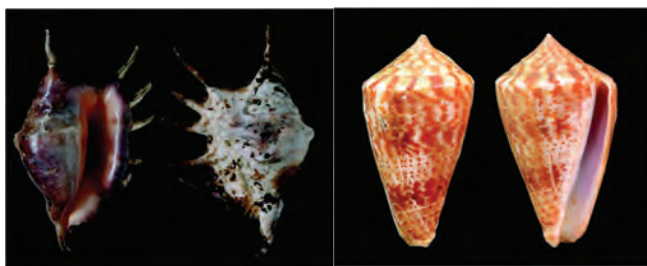


Fig. 7. Specimens Collected, a. *Lambis lambis*, b. *Conus inscriptus*

BASIC PLANT BIOLOGY, AGRICULTURE AND FRONTIER AREAS

Under basic plant biology, agriculture and frontier areas, the emphasis has been on gaining more understanding on biotic and abiotic stress

mechanisms and elucidating the signal transduction pathways during plant development. The focus has also been on identification of molecular markers governing disease resistance, male sterility in various crops to develop better plant varieties. In addition, thrust has been on biotechnological interventions in forestry, horticulture and plantation crops, germplasm characterization and improvement of crops using molecular biology tools.

Programs on Metabolomics, Saffron, Apple, and Solanaceae Phase II continued to receive support. Under the metabolomics programme, software modules have been developed for analysis of large data generated through metabolomics. Under apple network programme, apple germplasm has been characterized from apple growing states and germplasm repositories have been established. Seed-derived mother mapping population, as well as, clonal grafted population in apple orchard has been established at Zakura campus of Kashmir University. The program will be taken further to Phase II where in promising progenies identified will be used for cultivar improvement and dense linkage maps would be developed. Under saffron network program efforts are on to increase the aroma and quality of the saffron produced by understanding the regulation of biosynthesis and accumulation of apocarotenoids in saffron stigmas. Emphasis has also been on characterization of microflora of rhizosphere associated with saffron with a target to develop consortia of beneficial microbes. Various PGPRS associated with saffron were tested for antagonistic activity against bacterial and fungal pathogens. Projects on Solanaceae Phase II genome initiative are being supported with an aim to understand the basic development mechanisms, enhance nutrition, and engineer disease resistance in tomato plants. Research is being supported to isolate tomato mutants by TILLING with improved traits for nutrients and shelf life.

Basic Research: Various projects have been funded under basic research this year. At University of Delhi

South Campus (UDSC), New Delhi project was supported to generate marker free transgenic tomato plants with delayed fruit ripening. Transgenic tomato lines expressing mutant gene encoding ethylene receptor of Arabidopsis AtETR-1 under RIP1, a fruit-specific promoter have been generated. Ripening was delayed by about 2 weeks for both on vine and off vine tomato. Transgenic marker-free tomato plants showing delayed fruit ripening were also developed (Fig. 1).

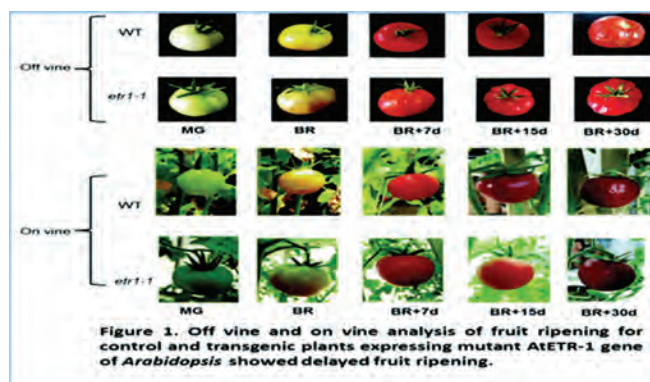


Figure 1. Off vine and on vine analysis of fruit ripening for control and transgenic plants expressing mutant AtETR-1 gene of Arabidopsis showed delayed fruit ripening.

Project was supported at Punjab Agricultural University (PAU), Ludhiana to understand the role of different cyclophilin genes in heat stress tolerance in wheat. 37 different genes have been analyzed so far at seedling stage. 16 genes showed expression at the seedling stage out of which eight different genes show regulation by heat stress. Further analysis revealed that different homologues of at least four different cyclophilin genes are regulated differentially by thermal stress. One of the cyclophilins, TaCypA-1, has been characterized in detail in *E. coli* and it has been demonstrated that this gene plays a key role in stress tolerance.

At university of Delhi South Campus (UDSC), Delhi studies have shown that arabidopsis CCX1 and CCX2 are highly upregulated by multiple abiotic stresses like salt, drought, osmotic stresses, ABA treatment and also under phosphate, nitrate and potassium deficiency. AtCCX1 provided tolerance to salt and heavy metals to mid1 mutant suggesting its possible role in stress tolerance pathway. It was also found that, AtCCX1 is a K⁺ independent Na⁺/

Ca²⁺ exchanger. Transgenic lines with T-DNA inserted mutant of AtCCX1 and 2 are being generated.

Projects have been funded for development of male sterile lines in various vegetable crops. At, (Punjab Agricultural University) PAU, Ludhiana the focus has been on development of male sterile and restorer lines using molecular markers in onion (*Allium cepa* L.). Sterile (S) and non-sterile (N) cytoplasmic plants have been identified in 25 onion populations. These plants were further amplified to genotype for fertility restoration (MsMs, Msms) and non-restoration (msms). Efforts are underway to develop putative male sterile, maintainer and restorer bulbs. In another study at PAU, Ludhiana, two markers linked to the nuclear sterility gene ms10 in chilli pepper (*Capsicum annuum* L.) have been identified and validated. Using these markers three new male sterile lines have been developed. These NMS lines can be used for hybrid development.

Host Pathogen Interaction: Study was supported at Sher-e-Kashmir University of Agricultural Sciences & Technology -Jammu to identify and characterize viruses of solanaceous crops in different agro-climatic zones of Jammu region. Diseased samples of tomato leaf curl virus plants were collected from different locations of low, mid and high altitude temperate zones of Jammu and Kashmir and also from cold arid region of Leh, Ladakh. The isolates collected from different locations showed very close (95.10 to 99.6 %) homology among themselves with respect to nucleotide sequence and revealed 99% homology with popular tomato leaf curl virus strains.

Study was supported at IARI, New Delhi to decipher the role of Xop-T3SS effectors of *Xanthomonas axonopodis* pv. *punicae* in the modulation of PAMP-triggered immune response in pomegranate. Full length sequence of Xop effectors (XopC2, XopE1, XopL and XopZ) have been generated based on sequences of Xop genes. Further, deletion mutants targeting effector genes, xopL, hrpG were also developed.

At Indian Institute of Horticultural Research (IIHR), Bangalore research was conducted for identification and breeding of Tospovirus resistance in chilli using molecular markers. Hundred and two chilli germplasm lines were screened and seven lines were found to be highly resistant, eight lines were resistant, seven lines were tolerant and remaining 80 were susceptible to Groundnut bud necrosis virus. Crossing was done with the identified resistant sources with elite susceptible line Arka Suphal to develop mapping population. In another project at IIHR, Bangalore robust genotypic markers for identification of *Phytophthora infestans* associated with late blight of tomato have been developed. Further, conventional and PCR time based assay has been developed for detection of tomato isolates.

At Institute of Life sciences (ILS), Bhubaneswar, study was supported to understand the interaction of TGA and WRKY transcription factors in regulating the activity of these promoters under stress. Under this project, 9 mutated CmYLCV (Cestrum Yellow Leaf Curling Virus) promoter constructs have been made. The transient activities of these promoters under SA stress in tobacco protoplasts indicated there are particular TGA and WKRY transcription factors present in CmYLCV promoter. Putative transgenic tobacco plants expressing the mutated constructs have been generated and further role of these transcription factors under stress will be evaluated.

Study is being supported at National Chemical Laboratory (NCL), Pune to characterize insect protease and protease-inhibitor complex to select potent inhibitors that could act as insecticide for crop protection.

Solanaceae Genome Initiative- Phase II: Support has been continued for various projects under SOL Phase 2 program in a network mode. At University of Delhi South Campus (UDSC), Delhi, transgenic tomato plants have been generated with overexpression of SIERF (Tomato Ethylene Response

Factor) constructs i.e; SIERF9, 11, 72 81 and 84 under fruit specific RIP Promoter. Constructs have also been developed for silencing by miRNA mediated approach. Further, transgenic plants will be raised. At National Botanical Research Institute (NBRC), Lucknow the focus has been on targeted manipulation of SIERF6 and SIERF8 in tomato and on understanding their role in regulating fruit ripening and productivity. It was found that transgenic SIERF6 over expressing lines show reduced ABA responses while antisense lines showed increased ABA response.

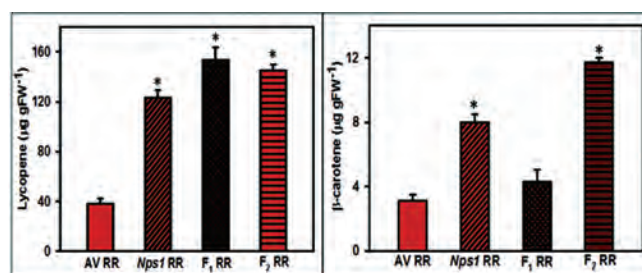


Figure 2: Enhanced accumulation of carotenoids in *Nps1*, *F₁* and *F₂* homozygous *Nps1*

Research is also being supported on introgression of begomovirus resistant genes in tomato (*Solanum lycopersicum* L.) using marker based and genomic approaches. At Indian Institute of Horticultural Research (IIHR), Bangalore, the focus has been on developing TOLCV resistant tomato cultivars by pyramiding of TOLCV resistance genes Ty2, Ty3, Ty5 and Ty6 using molecular markers. BC1 generation was developed to pyramid Ty-2 and Ty-3 in the background of tomato variety Kashi Vishesh and also to pyramid Ty-2, Ty-3 and ty-5/ty-6 in the background of Kashi Aman. Further, markers linked to putative resistance genes have been identified. Efforts will be made to introgress novel resistance genes and further to develop resistant tomato lines.

On genomic front at NIPGR, New Delhi the thrust has been to re-sequence parent varieties (TV55, LA1777, SB15 and H-88-78-1) for developing large-scale SNPs and construction of genetic linkage maps to identify the genetic determinants of ToLCNDV resistance. Genomes of four parental lines of two

TLCV (Tomato leaf curl virus)-resistance loci mapping populations have been re-sequenced at 40X-50X coverage. Mapping of sequence reads on the reference tomato assembly showed high SNP frequency for the wild resistant source *S. habrochaites* (LA1777).

At JNU, New Delhi tomato transformants have been generated with three *Rep* mutant constructs (D261A, D262A and K272A) of ToLCV. A total of 90 transformants have been hardened and some of them are being maintained in transgenic greenhouse.

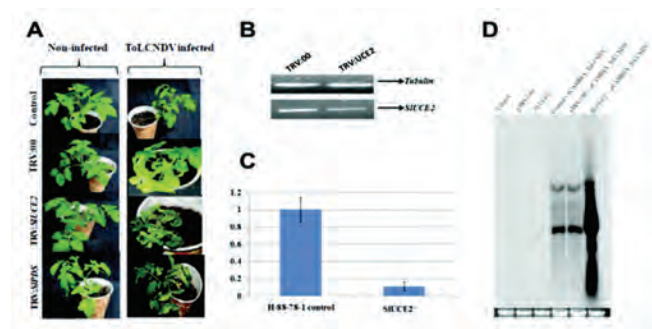


Figure 3. (A) Silencing of *SIUCE2* in tomato non-infected and ToLCNDV infected plants, (B) Semi-Quantitative PCR analysis, (C) Quantitative real time-PCR analysis to examine the level of *SIUCE2* at 21 day post infiltration of silencing construct, (D) Southern blot of tomato genomic DNA from HT and HT^{TRV-SIUCE2+T} hybridized with *Tomato leaf curl New Delhi virus* (ToLCNDV) specific coat protein (CP) gene as probe. Ethidium bromide stained DNA is shown for equivalent loading.

At NIPGR, Delhi study is on going to characterize ubiquitin/26S proteasome pathway related genes in tomato during ToLCNDV infection. *Solanum lycopersicum* 26S-proteasomal subunit RPT4 (SIRPT4), Armadillo-repeat protein gene (SIARM) Ubiquitin conjugating enzyme-2 (SIUCE2), have been functionally characterized by virus induced gene silencing (VIGS). The study suggested that silencing of SIUCE2 and SIARM leads susceptibility in tolerant cultivar. To identify the interacting partners of UPS component gene(s), SIUCE2 and SIARM were overexpressed in bacteria. Overexpression of SIRPT4 and SIUCE2 in susceptible cv. 'Pusa early dwarf' is in progress.

In phase-II of TILLING project, supported at

University of Hyderabad, Hyderabad large number of tomato mutants have been identified using Next Generation Sequencing (NGS) from an EMS-mutagenized tomato population of 768 individuals and the individual mutant lines are being characterized for correlation between genotype and the phenotype. The metabolic analysis of backcrossed population of delayed fruit deterioration cultivar into Arka Vikas revealed that longer shelf life of fruits is associated with lowering of fruit metabolism. In particular, the backcrossed fruits showed slower flux through the TCA cycle signifying slower rate of respiration.

Metabolomics: At University of Hyderabad, Hyderabad under tomato metabolome network program, folate and carotenoid enriched lines in tomato were identified. NBPGR72 was identified as beta-carotene rich line, SPA mutant as high lycopene line, PKM 1 as high folate cultivar and trifoliolate mutant as four-fold enriched with folate mutant in Arka Vikas background.

Programme Support on Genome Engineering of Tomato: Under a Programme Support on Genome Engineering of Tomato recently initiated jointly at University of Hyderabad, Hyderabad, Indian Institute of Horticultural Research, Bangalore, National Institute of Technology, Durgapur and University of Delhi South Campus, New Delhi, work has been undertaken on genome editing of tomato using CRISPR/CAS9 system. The ripening inhibitor (RIN) gene that is essential for tomato fruit ripening is being targeted for editing.

Apple Network Programme: In an ongoing network programme on apple, involving 5 institutions Kashmir University (KU) & Jammu University (JU) from J & K, Y. S Parmar University of Horticulture and Forestry (YSPUH & F) from HP, G.B. Pant Institute of Himalayan Environment & Development (GBPIHED) from Uttarakhand and Centre for Cellular and Molecular Biology (CSIR-CCMB), Hyderabad, a total of 529 apple genotypes (elite varieties/genotypes/plus trees) from the J&K, HP and Uttarakhand

through multiple surveys have been identified so far. DNA typing has been done using additional genotypes/SSR markers to complete the data for identified apple genotypes using >78 SSR markers. Mapping seedling nurseries have been established at Botanical department Kashmir University, Srinagar, and YSPUHF, Solan campus. Exchange of scion wood of identified apple genotypes has been initiated between partner institutes to establish in the germplasm repositories. To take the leads obtained under Phase I to a logical conclusion, Phase-II research project on apple genomics is being supported.

Saffron Network Programme: Support is being continued for an ongoing network programme on Saffron involving North Eastern Hill University, Shillong; University of Jammu, Jammu; Kashmir University, Srinagar; National institute of Plant Genome Research, New Delhi; School of Life Sciences, Jawaharlal Nehru University, New Delhi and IHBT, Palampur.

At IHBT, Palampur the focus of the research has been on increasing the size of cormlets through tissue culture. It was found that thinning increased the size of the cormlets effectively. Reduction in the number of shoots inoculated per flask containing MS medium supplemented with paclobutrazol resulted in significant increase in size and weight (4.0-4.5 g) of corms. In another study conducted at IHBT, Palampur evaluation of PGPR for growth promotion in saffron plants under controlled conditions revealed enhanced growth as compared to the control. *Bacillus siamensis* IHB B 18102, *Bacillus siamensis* IHB B 15650, *Bacillus aryabhattai* IHB B 18146 and *Pseudomonas azotoformans* IHB B 15160 showed significant increase in growth parameters as compared to control. Efforts are on to develop a cost-effective medium using different carbon sources including molasses.

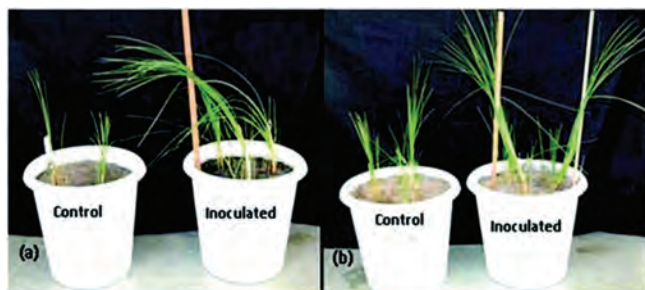


Figure 4: Growth promotion shown by efficient PGPR in comparison to control activated (a) Charcoal (b) Jaggery

At NEHU, early flowering was induced in saffron by GA3 application. Application of the hormone to apical buds during quiescent stage hastened floral anthesis by approximately two weeks and increased the number of flowers produced per corm. Apical bud and corm tissues from each harvest are in process for transcriptome profiling by NGS. In Planta protocol for transformation of saffron plant has been standardized.

At Jammu University, expression profiling of three additional genes of carotenoid biosynthetic pathway at different developmental stages has been completed. 5' UTR of two more genes have been cloned and their sequences characterized. Further, experiments for functional validation of promoters have been initiated.

At Jawaharlal Nehru University, New Delhi plants having flowers at different stages of stigma development have been harvested and are being processed for profiling for secondary metabolites (apocarotenoids/carotenoids) for analysis of changes in primary metabolites. Relative abundance of metabolites such as amino acids, fatty acids, organic acid and sugars in various floral tissues (stamens, tapels, stigmas) were quantified in the stigma of tissues. Comprehensive *de-novo* transcriptome assembly and characterization and genome wide discovery of microsatellites in saffron has been achieved. Further, RNA-seq of the stigma tissues at various developmental stages using Illumina platform is in progress.

BASIC RESEARCH IN MODERN BIOLOGY

The Department through Basic Research in Modern Biology funds research in a wide variety of biological science field with a goal of exploiting new knowledge to enhance-and where possible, transform-future capabilities. A number of research programs were supported during the period. Noteworthy achievements of some of the projects are presented below:

RAF kinases play a key role in cell division, proliferation and differentiation. Growth signal is mainly conveyed by CRAF: BRAF heterodimer and several regulators are reported to control the amplitude of the RAF mediated signaling. Scientists working on CRAF quality control and development of pathophysiological conditions at Bose Institute, Kolkata have for the first time established the role of Hsp90 and its co-chaperones in CRAF functioning. They have also revealed that Hsp90 acts as a recruiter of actin to CRAF kinase translocation across the cell. The insight gained from the research work has revealed a dual role of hsp90 that keeps a fine tuned growth signaling. The study might suffice to target Hsp90 and its co-chaperone modules as alternative means in RAF kinases based diseases including developmental disorders and cancers

Research work being carried out by scientists at Delhi University and IIT Delhi on development of potent small molecule inhibitors against dopamine beta-hydroxylase to combat cardiovascular diseases has led to the discovery of five small molecules as potent anti-hypertensives. These lead molecules were found to prevent elevated systolic blood pressure in L-NAME induced hypertensive rat model, with a promise for application as novel therapeutics against blood pressure/ hypertension. Figure 1(a) and (b)

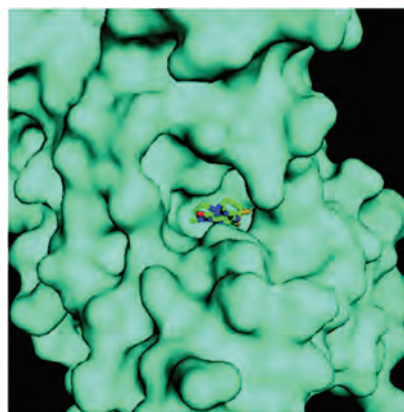


Fig. 1(a): Surface view of UDSC171 docked to dopamine beta hydroxylase. UDSC171 is a new molecule with potential to control peripheral blood pressure (hypertension).

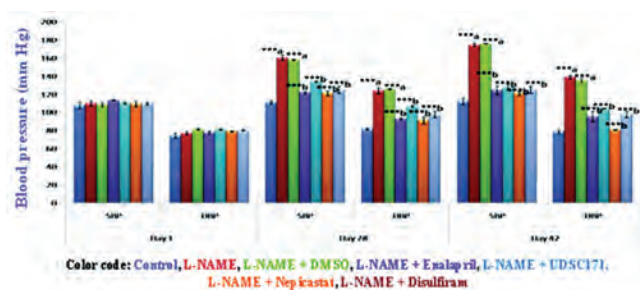


Fig. 1 (b): Preventive effect of UDSC171 on the blood pressure of L-NAME induced hypertensive rat model. 2mg/kg body weight of the inhibitor was administered intraperitoneally along with L-NAME from day 1 for 42 days. BP was measured on 1st, 28th and 42nd day. Enalapril was used as a positive control, since this drug is used to control hypertension. DMSO was the vehicle control and Nopicastat and Disulfiram are known inhibitors of DBH.

Researchers working to decipher protein interaction network of TAF4b (TBP Associated Factor 4b) involved in plant defense at NBRI lucknow have shown that TAF4b regulates immunity in plant. They have identified TAF4binteractome in *Arabidopsis thaliana*. Further, the group has also identify that Tip-1 regulate immunity against biotrophic and nactrotrophic pathogen. Research is ongoing to carried out to identify the molecular mechanism of Tip-1 mediated plant defense. Figure 2 (a), (b) and (c)

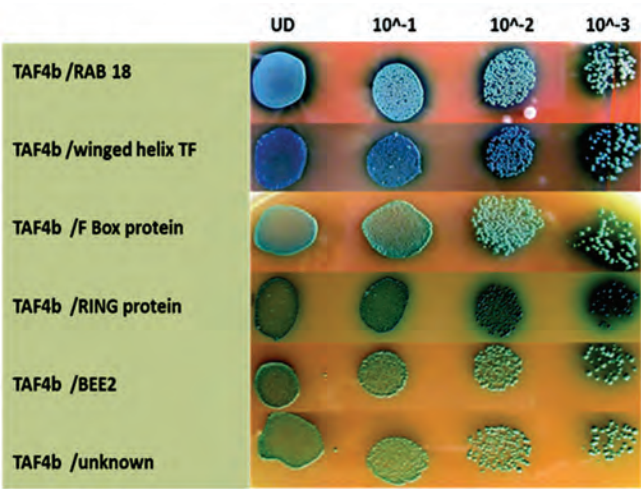
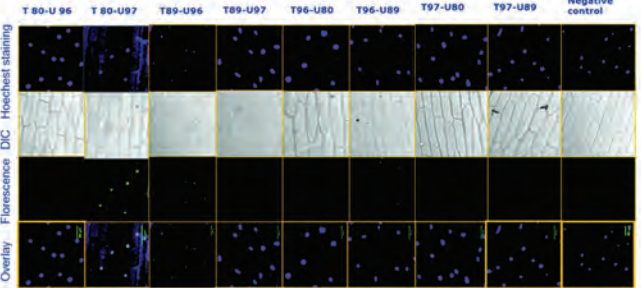


Fig. 2 (a): TAF4b interacting clones , dilutions were spotted on SD/- Trp/ - Leu/-His/-Ade/+ x- á gal/+ AbA.

S No	FDR corrected p-	
	value	Terms over represented in BINGO
1	1.70E-16	regulation of transcription
2	2.28E-15	macromolecule metabolic process
3	2.03E-13	response to hormone stimulus
4	2.03E-08	developmental process
5	9.54E-08	cytokinin mediated signaling pathway
6	1.05E-06	organ development

Fig 2(b): The overrepresented term in cytoscape network analysis.

Fig. 2 (c): Bimolecular florescence complementation assay; Taf4b and Tip-1 tagged with n'terminus and C' terminus eYfp and vector combinations were introduced in onion peel via particle bombardment. Samples were incubated for 48-72 hrs for fluorophore development and visualised under confocal microscope.



Research undertaken in IISc to understand whether FANCI helicase, whose mutation is known to cause Fanconi anemia regulate the fidelity of DSB repair in human cells has revealed that FANCI helicase is required for the error free repair of DSBs in human cells. Moreover, FANCI controls the extended copying during DSB repair indicating the likely role of FANCI in suppressing the gene amplification which is one of the hallmarks of cancer cells.

Study initiated at IISER, Pune aimed at resolving redundancy and sub functionalization, post gene duplication in animals using the Drosophila MADF-BESS genes as a model has led to the identification of a novel gene christened *brickwall*. This gene was found to be critical for determining stem cell development in the Drosophila female ovary. Further, Brickwall appears to have overlapping roles with the germ cell specification gene, stonewall. Figure 3

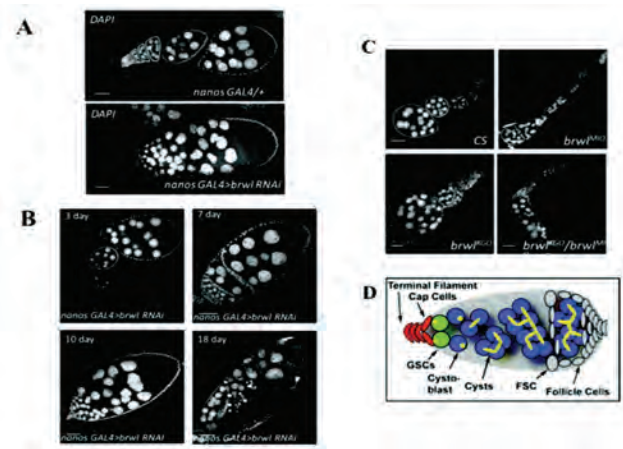


Fig.3: Brickwall/CG3838 has roles in Germline Cell Fate specification. (A)DAPI stained ovariolesusually show normal oocyte development from the anterior germarium? posterior egg cell (L?R). Reduction of brickwall(brwl) transcripts in the ovary of the adult fly using nanos-Gal4 leads to a repertoire of ovarian defects that include a fused ovariole and failure of oocyte specification. These defects depend on the age of the mother (B)The defects in brickwallmutanst are age dependent with initial manifestation in the adult female ovary 7 days after fly eclosionandenhancement with age. (C)Brickwall insertion mutants KGO and MIO mutants show defective ovarioles, when homozygous as does a KGO/MIO transheterozygote. (D) A schematic (adapted from Herzig et. al., 2014) of an oocyte germarium. Our data suggests defects in the development of the Germ Stem Cells (GSCs) in brickwall mutants.

Scientists working on elucidating molecular mechanisms in wound healing in the heart through regulation of the cardiac fibroblast AT1 receptor at SCTIMS, Thiruvananthapuram have shown that oxidative stress enhances AT1 receptor and collagen expression via local angiotensin II generation in cardiac fibroblasts by a complex mechanism involving the redox-sensitive transcription factors, NF- κ B and AP-1, which are activated by the co-ordinated action ERK1/2, p38MAPK and JNK. The study offers a novel perspective on the pathogenesis of cardiovascular disease known to be associated with oxidative stress.

Researchers at JNU, New Delhi and ICGEB, New Delhi working on genome –wide characterization of tRNA synthases and their paralogs from *leishmania* have provided genetic and chemical validation of several tRNA synthetases as drug targets and also identified several inhibitors that are *Leishmania* specific and inhibit both *L. donovani* tRNA synthetases and of *L. donovani* cell growth but do not affect host.

Studies conducted on design and development of novel phosphodiesterase 4(PDE4) inhibitors at Dr Reddy's Institute of Life Sciences, University of Hyderabad has led to the identification of a series of compounds as potent inhibitors showing selectivity ranging from 4-15 folds. The lead compounds developed reduced inflammation in adjuvant induced arthritis model of rats and disease severity in adult zebrafish EAE model. Further work is being conducted to characterize these compounds in different animal models.

Scientists working on determining the molecular basis for TIM-3-mediated immunoregulation of dendritic cells at IMTECH, Chandigarh have revealed the molecular mechanisms regulating TIM-3 expression in DCs and also identified c-Src as a target for improving the efficacy of nucleic acid-mediated anticancer therapy. Figure 4

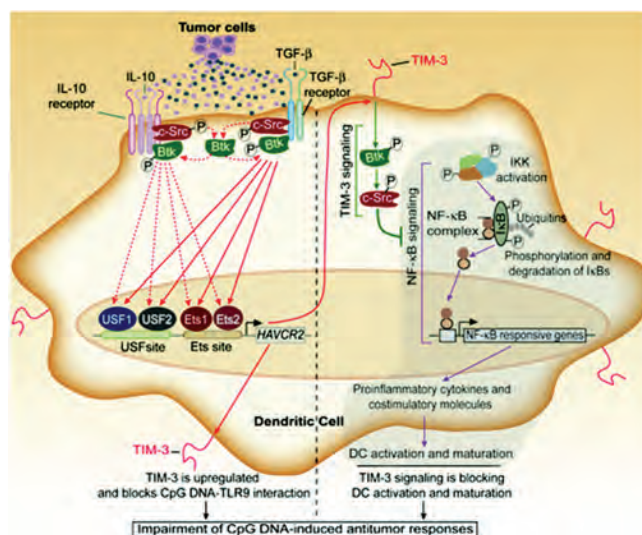


Fig. 4: Crosstalk between c-Src and TIM-3 in DCs suppresses the antitumor effects of CpG DNA. c-Src impedes CpG DNA-induced antitumor responses in two mutually nonexclusive ways (demarcated by dotted line). First (left side of the dotted line), in response to IL-10 and TGF- β secreted from tumor cells, c-Src activates the downstream signaling pathway (Btk!transcription factors Ets1/2, USF1/2) to upregulate TIM-3 expression on DCs. The upregulated TIM-3 then prevents the binding of CpG DNA to TLR9 and thereby attenuates the antitumor effects of CpG DNA. Second (right side of the dotted line), c-Src mediates the inhibitory effect of TIM-3 on DC activation and maturation by blocking the NF- κ B pathway thus suppressing antitumor immunity mediated by CpG DNA. The "grey" shaded area represents the events, which include NF- κ B-driven DC activation and maturation, blocked by TIM-3 signaling.

Ongoing research at CDFD, Hyderabad aimed at understanding the role(s) of a transcription termination factor Rho in different physiological processes have shown that mutations in Rho are synthetically lethal with deletions of different DNA repair genes such as *uvrA*, *uvrB*, *uvrC* *mfd* etc and mutations in Rho are sensitive to DNA damaging agents such as UV mitomycin etc. Further, the group has also shown that *in vitro* Rho is capable of releasing RNA from stalled elongation complexes at the damaged sites.

Scientists working on investigating the mechanisms of recruitment of DNA damage response factors to the sites of stalled replication at NII, New Delhi have discovered the factors which regulate the recruitment of BLM to the DSBs. The group has also shown that BLM is co-recruited to the DSBs with DNA repair proteins in a cell cycle phase specific manner.

Ongoing work aimed at studying the human pathogenic fungus, *Candida albicans* at JNU, New Delhi examined the relationship between invasive filamentous growth of the organism and its virulence factors that are present at the cell surface as GPI anchored proteins. The results obtained provided for the very first time a molecular level understanding of how the two processes mutually assist one another in order to promote infection by the organism.

Researchers working on structure and function of the ribonucleoprotein particles of *Entamoeba histolytica* retrotransposons at JNU have biochemically characterized the polypeptide encoded by ORF1 of EhLINE1(*E. histolytica* retrotransposons) and demonstrated RNA binding activity at N-terminal, protein-protein interaction domain at C-terminal, and nucleic acid chaperone activity. Although EhLINE1 belongs to the primitive R2 clade its ORF1p showed similarities with later evolving clades. The data showed functional conservation of EhLINE1 ORF1p on an evolutionary scale, although arrangement of functional domains is altered. Figure 5 and 6

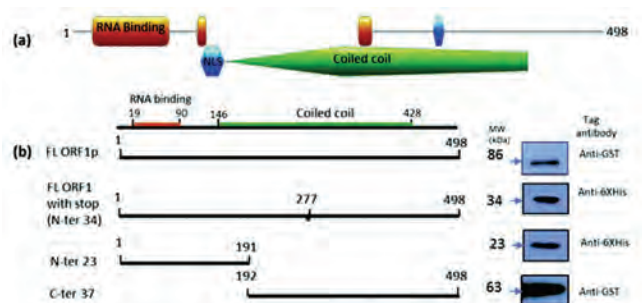


Fig. 5 : ORF1p and its sub fragments. a. Schematic representation of domain structure of ORF1p showing stretches of RNA binding (19-90,117-125 and 268-280aa) and a coiled coil domain (146aa to 428) as predicted by MARCOIL tool). Blue diamonds show predicted nuclear localisation signals. b. Full length ORF1p and sub-fragments were expressed and purified from different host vector systems. the purified polypeptides were detected by western analysis using tag-specific antibodies.

Fig. 6 (a) RNA binding ability of various ORF1p sub-fragments: Recombinant N-ter 23 (GST-tagged), N-ter 34 (His-tagged) and C-ter 37 (GST-tagged) sub-fragments were used to test the RNA

binding ability. In all EMSA experiments radiolabeled SINE1- RNA was used. C-ter 37 lacks RNA binding ability. Protein vs. RNA molar ratio ranged from 0 to 110.7 (N-ter 23), 0 to 123 (N-ter 34) and 0 to 64.6 (C-ter 37). (b) Protein-protein interaction domain lies at the C-terminus. Interaction of full length GST-tagged ORF1p with its sub fragments was studied by incubating it with 6X His tagged sub fragments (N-ter 23, N-ter 34 and C-ter 37). The sub fragments were incubated with glutathione sepharose bound ORF1p at 4% overnight with gentle rotation. Glutathione sepharose beads were subsequently washed, boiled with SDS loading buffer and electrophoresed. Western blotting was performed with anti- His antibody. Among the three sub-fragments, only two (N-ter 34 and C-ter 37) were able to interact with full length EhORF1p. GST protein alone was used as negative control (GST).

Ongoing research at NIT, Durgapur aimed at investigating the interconnecting roles of ZBF1/ MYC2 and HY5 in Arabidopsis seedling development and disease defence has shown a mechanistic view on coordinated regulation of MYC2 and HY5, two different classes of transcription factors, in the transcriptional activity of HY5 during blue light-mediated Arabidopsis seedling development.

Network Project: A multi-institutional project with the larger aim of resolving the mechanisms by which the pathogen, *Mycobacterium tuberculosis*, adapts within the host macrophage has collectively provided new insights into the mechanisms by which the pathogen, *Mycobacterium tuberculosis*, adapts within the host macrophage and regulates its function. Further, work is being carried out to integrate the resulting time series into computational/ mathematical models to obtain a view of molecular interplay between host cells and pathogen for efficient development of therapeutic strategies.

Centers of Excellence- Basic Research: Three new long term projects were sanctioned this year in the basic research area pertaining to studies on

epigenetics, proof reading and elucidation of structural aspects of HIV and TB pathogens. The salient achievements in few of the on-going projects are as below:

Combating MDR in pathogenic yeast *Candida albicans*: Drug-resistant pathogenic fungi use several families of membrane-embedded transporters to efflux incoming antifungal drugs from the cell. To identify the genes associated with the onset of MDR in an immune-compromised host, expression profile at transcriptome level was carried out in 6 hospital isolates (TW). Overall results demonstrated that genes involved in translation, metabolism, transport, respiration and MDR regulation were induced.

Molecular structure and intermolecular interactions by NMR spectroscopy: Molecular structure and inter-molecular interactions using cryogenically cooled NMR probe was exposed in biomolecules ranging from peptides to proteins and nucleic acids. Mimicry of α -strands, Telomere remodeling factors and ncRNA - protein interactions and Human Crystallin Protein are some of the molecules for which structure was determined.

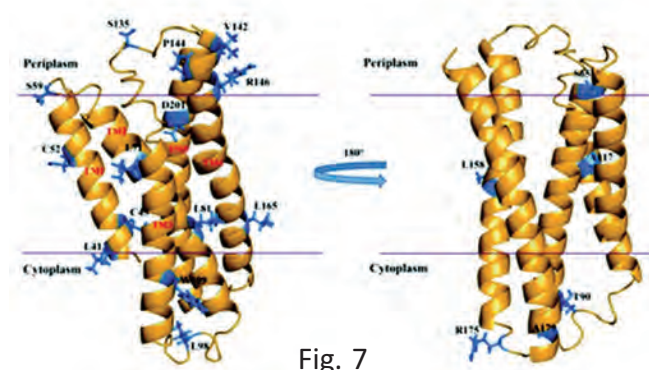


Fig. 7

Multiple long noncoding transcripts of *Drosophila*: Live imaging studies provided very significant insights about the biogenesis and life cycle of omega speckles in *Drosophila* cells under normal and stressed conditions. A very significant finding was that the omega speckles are assembled at the *hsrù* gene locus and that chromatin

remodellers like ISWI are essential for their biogenesis but not for movement of hnRNPs to the *hsrù* gene locus. Further a central collection of *Drosophila* stock repository with 1300 different mutant and transgenic lines are being maintained and provided to researchers across the country.

COE for microbial biology: Studies on physiology of the model bacterium *Escherichia coli*, showed that the action of the endoribonuclease RNase E on its various substrates (mRNA, RNA, and tRNA) jointly contribute to its essentiality for growth. Further potassium homeostasis is modulated by the product of an anonymous ORF *ycgO* (which functions as a putative cryptic potassium efflux system) and a phosphotransferase cascade Pts-PtsO-PtsN through an interesting cross-talk regulatory mechanism. The maintenance of ribose metabolism by the transketolase enzymes is required to sustain glycerol-3-phosphate pools for central carbon metabolite fluxes and that the Rho protein can terminate transcription redundantly, that is, either by itself when it binds to strong *rut* sites on RNA, or with the assistance of NusG in the absence of strong *rut* sites. All these studies would ultimately aid in design of new drugs for antibacterial resistance primarily antibiotics (Figure 8). -

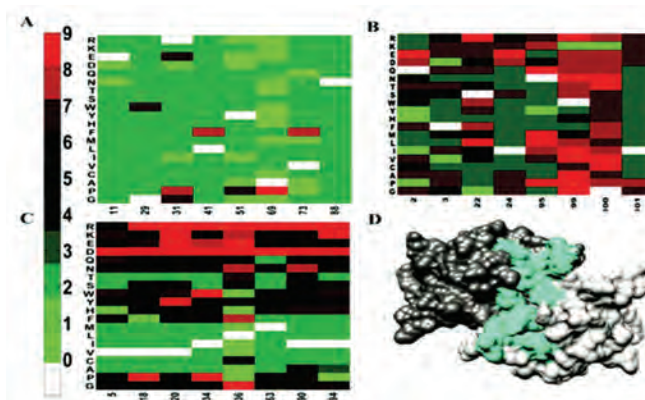


Figure 8: Mutational effects on CcdB protein activity inferred from phenotypic screening and deep sequencing (A), (B) and (C) show the mutational sensitivity (MS_{seq}) values for representative exposed-site (Accessibility >5%), all active-site residues and buried-site (Accessibility <5%), respectively. On the vertical axis, residues are grouped into (G, P), aliphatic (A–M), aromatic (F–W), polar (S–Q) and charged (D–R) amino acids. Residue numbers and substitutions are indicated on the horizontal and vertical axes, respectively. Each heatmap is colored

according to the MS_{seq} value of the mutant. Green to red color gradation represents increasing MS_{seq} values. Zero value (light green) indicates that the corresponding mutant was not observed in the library. WT residue at each position is indicated in white. Data for only representative residue positions are shown for clarity. (D) Active-site residues identified from the mutational phenotypes mapped onto the crystal structure of CcdB (PDB ID 3VUB).

Integrative approaches to understand of bacterial toxin-antitoxin systems: Comprehensive fold recognition and modeling of toxin-antitoxin (TA) complexes using bioinformatics and computational approaches are being extensively studied. A number of TA systems have been cloned and are being characterized. Preliminary results from single bacterial cell gene expression analysis using live cell microscopy and microfluidics, and quantitative proteomics to characterize endogenous TA complexes have been obtained.

BIODESIGN PROGRAMME

Biodesign program has been implemented as a flagship program of the Department for fostering and promoting development of indigenous affordable medical technologies and creating an ecosystem for med-tech innovations and entrepreneurship in the country. Under the umbrella, four centres/programs are implemented at School of International Biodesign centred at AIIMS and IIT Delhi; Centre for Biodesign and in-vitro Diagnostics at Translational Health Science & Technology (THSTI), Faridabad; Biodesign and Bioengineering Initiative program at IISc., Bengaluru; and Healthcare Technology Innovation Centre at IIT Madras, Chennai. Significant highlights are given below:

School of International Biodesign Program, Delhi:

School of International Biodesign (SIB) is a frugal medical device innovation program implemented by the Department jointly at All India Institute of Medical Sciences (AIIMS), Indian Institute of Technology (IIT), Delhi, in collaboration with Stanford University and other international partners. DBT has engaged Biotech Consortium India Limited (BCIL) for managing techno legal activities of this program. SIB focuses on training young innovators

in developing low-cost, high-impact medical devices for the common man. Innovators from India and from partner international universities are trained for 11 months at the school to identify unmet clinical needs with a special focus on public health. Eventually, using the Biodesign process the fellows develop technologies that aim to solve these problems. The process is facilitated through fellowships, conducting workshops in partner universities and organizing an annual MedTech summit.

During this year, 8 Fellows have been trained under this program wherein 4 Indian Fellows, 3 Fellows from Queensland University of Technology and 1 from Tottori University were enrolled. Two medical technology innovation workshops conducted at Tottori University and at Queensland University of Technology. During this year, three inventions were conceptualized and filed as provisional patents with the Indian patent office:- a) Multipurpose Endoscope System; b) Aspiration Monitoring Device c) Ocular Screening. Two Industrial design applications were filed for FlexioH; Three complete non-provisional patent applications and PCT applications were filed for Apparatus for Manual Ventilation, Hemorrhoid treatment device, Endonasal Air Purification device. National Phase proceedings were filed in different jurisdictions for:- a) A non-reusable Intra-Osseous Access Device and method thereof; b) A breathable and customized cast for immobilization of fractured limb. During 2016-2017 two technologies were licensed: a) 'Ostomy Management Device' was licensed to M/s. Crimson Healthcare Pvt. Ltd., a Start-up Company; and b) 'Patient Transfer Device' was licensed to M/s. Vista Furnishing Pvt. Ltd., Ghaziabad. The 10th edition of MedTech summit was organised in this year wherein over 200 delegates attended the summit from universities and medical device industry in India, Japan, America, Singapore, Australia, Europe and Africa. At the summit, the world's first foot operated newborn resuscitation system 'NeoBreathe'

developed by Windmill Health Private Limited, an alumni company of School of International Biodesign was launched by Chief Executive Officer, NitiAyog, Mr. Amitabh Kant in presence of the SIB team. In addition, collaboration agreements were formally executed by Dr. Mitsuo Ochi, President, Hiroshima University, Japan and representatives of Biodesign partnering Institutes from AIIMS, IIT Delhi and BCIL. Under this agreement, the Hiroshima University will send a Japanese Fellow to SIB for the iFellowship program.

Centre for Biodesign and In-vitro Diagnostics,

THSTI: The Center for Biodesign was established as a niche center of THSTI with the mission to undertake innovation in medical technologies for affordable health care in India utilizing the bio-design concept and support services that extend from strategic bench work to commercialization. During the year 2016, Centre has developed diagnostic tests for TB meningitis and also developed *in vitro* proof of concept for phenotypic rapid antimicrobial susceptibility testing. Three patents have been filed on: a) monoclonal antibodies specific to *Salmonella typhi* flagellin for diagnostic use; b) production of recombinant Cytolethal Distending Toxin B protein and its uses as diagnostic tool thereof; c) Aptamer based system and method for the diagnosis of Tuberculous Meningitis (TBM). Two entrepreneurial ventures are undertaken- a) Tritex Innovation Pvt. Ltd. (Faculty founded start-up); b) AptaBharat Innovation Pvt. Ltd. (Innovation awardee founded start-up). Another major initiative being undertaken is alliance against Anti-microbial Resistance – a multi-disciplinary alliance in collaboration with engineering and medical schools to fight against the diagnostic challenge of antimicrobial resistance.

Biodesign& Bioengineering Initiative Program,

IISc: The Biodesign-Bioengineering programme at IISc Bangalore was implemented in collaboration with St. John's Medical College and Narayana Hridalyala Bangalore, with an aim to facilitate

collaboration amongst the faculty in the Indian Institute of Science and clinicians in Bengaluru hospitals. During the reporting year, the team has standardized a new method to characterize hemoglobin variants from hemolysate as well as hemoglobin isolated from dried blood spots on blotting paper. A customized database of hemoglobin variants has been developed with mass spectra analysis including mutants relevant to India. The main goal towards hemoglobin variant characterization is to use it as a standard diagnostic procedure in Indian hospitals and clinics. An Advanced Intensive Care Unit (ICU) simulator, developed in collaboration with IISc and St. John's National Academy of Health Sciences, underwent clinical trials in 2016 following its launch in 21st Annual Conference of the Indian Society of Critical Care Medicine in 2015. The simulators are tested on mechanical ventilation, ultrasound/ECHO, and hemodynamics. The process of commercialization of the simulator is under process. In another initiative, a perfusion culture system was developed with multiple standard wells integrated miniature peristaltic pumps, electronics, and media reservoir. This device enables high throughput culture of cells under conditions closer to human physiology than the usual Petri dish culture, in biological research studies. This device is now being commercialized with further development by a start-up company from IISc, namely BendFlex as Perfusion Enabled Cell Chamber. This device can be used in standard CO₂ incubators and is amenable for live cell imaging at high magnification. Other interesting studies are being conducted on understanding the mechanobiology of breast-cancer cells and studies on cellular traction force-microscopy technique.

Healthcare Technology Innovation Centre (HTIC),

IITM: Healthcare Technology Innovation Centre (HTIC) of IIT Madras is an R&D centre established by DBT. HTIC has evolved into a unique and leading med-tech innovation ecosystem in the country bringing together more than 20 medical institutions,

industry and government agencies. HTIC, collaborating with these institutions, is developing affordable healthcare technologies for unmet healthcare and clinical needs. HTIC has developed the first indigenous point-of-care instrument for quantitative immunodiagnosics in collaboration with the company, J Mitra & Co Pvt. Ltd. The developed instrument, named iQuantAnalyser, is designed to read multiple test kits directly from the test kit without the need for a separate calibration chip. The product is meant for small to medium labs to meet market needs and requirement in the community for affordable test kits for non-communicable diseases such as HbA1C (diabetes), Vitamin D, etc. The product has completed first batch of production and is scaling up production. Expanding on this technology, a comprehensive platform for automated, high throughput, rapid quantitative diagnostic products, is under development. HTIC, Forus and Narayana Nethralaya are collaborating to create India's first infant eye screening device for tackling Retinopathy of Prematurity (ROP), a leading cause of blindness in premature born infants. To achieve this goal, HTIC is developing the image analytics for the "Shishunetra" device, including algorithms for real time video enhancement to aid in image acquisition, image mosaicking to create a wide field of view and data driven analytics for identification of disease signs and staging the disease, using deep learning techniques. VITALSENS technology platform is another initiative of HTIC for reliable and automated activity tracking along with ECG which eliminates need for manual activity logging otherwise required for typical Holter monitors. Currently, the setup has completed pre-clinical trials in a controlled setting on 20 volunteers. Clinical validation with identified clinical collaborators has been initiated. The VITALSENS platform has also been used to develop a range of wearable devices. The expertise

developed in the hardware and algorithm domain has paved the way to start collaborations with various industries.

School of International Biodesign (SIB)



Launch of ' Neonatal Resuscitation Device - NeoBreathe' developed under DBT supported School of International Biodesign (SIB)



Formal Signing Ceremony of SIB-Hiroshima University, Japan for Collaboration under DBT supported School of International Biodesign (SIB)

HTIC-IIT Madras



iQuant project pathway and status



VITALSENS technology summary

Biodesign and Bioengineering Initiative-IISC, Bangalore



An ICU simulator undergoing clinical testing at St. John's hospital, Bengaluru



Perfusion-enabled Cell-chamber (PECC), developed by BendFlex, a spin-off from the DBT-funded project in IISc

BIOENGINEERING

Bioengineering is an interdisciplinary area of research involving knowledge and expertise from cross disciplinary fields like physics, chemistry, mathematics and engineering sciences to render solutions to important biological and medical problems. During the year, Department has supported various projects in the identified areas of Bioengineering. In addition, special emphasis was given to generate research initiatives on the theme titled "Total/partial organ development and assisted technologies using bioengineering methodologies". More than hundred concept papers were received, screened and only few ideas were finally shortlisted for financial support. Some of the

significant achievements during the year include:

Novel Computational Methods for Optical

Molecular Tomographic Imaging: Scientists at IISc, Bangalore are developing technologies to extract quantitatively accurate information from molecular imaging modalities as well as make images available in real time to clinicians for better prognosis/diagnosis. Under this project, the near infrared light is delivered through optical fibers to the tissue under investigation and diffused light is collected on the boundary using the same fibers. These boundary measurements are used in a model-based iterative technique to compute the optical images, which have the capability to reveal the patho-physiological changes in the tissue. An analytical algorithm has been developed for light propagation in thick tissue. Investigators have also implemented direct sensitivity based data-optimization approach to curtail the algorithmic complexity and implicitly reconstruct optical absorption image based on direct sensitivity approach. The performance of the proposed method was validated using numerical and gelatin phantom data indicating that this perturbation-like approach can quantify embedded regions with good accuracy and is free of bias errors associated with regularization approaches. The algorithm was tested on human data for fast pulsatile diffuse optical imaging and found to provide the required high level of optimization.

Photoacoustic Imaging technique for Non-Invasive deep tissue imaging:

Scientists at IIT, Indore are focusing on photoacoustic imaging technique as disease diagnostics. Non-invasive characterization of tissues with abnormalities is an important problem with respect to disease diagnostics and therapy. Under this project, photoacoustic imaging as a diagnosis technique. Photoacoustic imaging has been applied to quantitatively differentiate blood clots from blood which can be further utilized as a diagnostic technique for thrombosis related applications. Empirical wavelet transform based photoacoustic

spectral response technique has been applied onto human breast masses to quantitatively differentiate human breast masses (normal, benign and malignant) based on tissue mechano-biological properties.

Microfluidic device for Cell sorting: A microfluidic device has been developed by scientists of IIT Madras with focusing and spacing control for resistance-based sorting of droplets and cells which could be potentially used for sorting of normal and diseased cells. The device has two modules: focusing and spacing control module and sorting module. Investigator has developed novel hydrodynamic technique for sorting of deformable objects based on size. The variation of hydrodynamic resistance of biological cells was studied with the cell size (different size of HeLa cells) and stiffness (different cells of same size). Young's modulus of different types of cells was compared and the deformability index of these cells was studied using microfluidics. MDMB 231 and HeLa cells of same size (25 μm) were sorted based on the difference in their stiffness or deformability in a microfluidic channel.

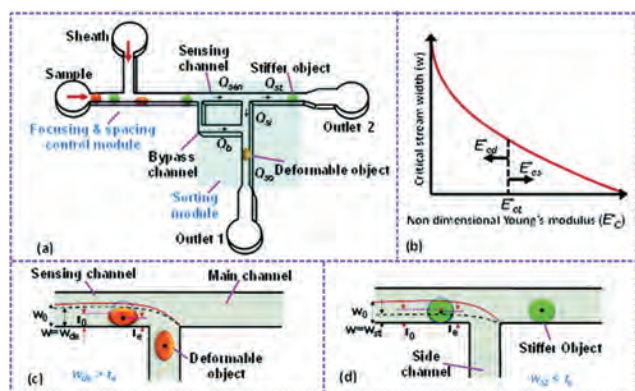


Figure 1: Schematic of the (a) stiffness-based sorting device (b) variation of instantaneous critical stream width with Young's modulus (c) deformable objects of effective radius $<$ critical stream width are sorted to the side branch (d) stiffer object of effective radius $>$ the critical stream width continue to flow along the main channel

Fluorescent Probes for Biosensing Applications: Researchers at NIIST, Thiruvananthapuram designed and synthesized a novel series of 1, 2-dihydropyridine (DHP) based fluorophores for

detection of phosphatases and have synthesized for sensing intracellular pH. A pH dependent reversible interaction between bovine serum albumin and squaric acid nanoparticles was exploited for the design of an array of sensors for the monitoring of small variations in pH. The ratio between the protein and the dye nanoparticles is extremely crucial in tuning the pH sensitivity and these ratios were fine tuned to design sensors for detecting pH fluctuations in live cells. Dihydropyridine based fluorophores were synthesized through multicomponent protocol and 1,2-DHP showed remarkable photophysical properties with high and long-lived fluorescence in the series. It exhibited greater than 90% cell viability in HeLa (cervical) cell lines and was found to localize in the cytosolic region of the HeLa cells. Further it was also demonstrated that a non-phosphorylated tyrosine appended to the optimized fluorophore with a suitable linker exhibited 60% more fluorescence than its phosphorylated congener. These results indicated that the fluorophore could be used as a chemosensor in tyrosine phosphatase activity.

New Generation Caspase Sensor FRET Probe Expressing Stable Cancer Cells for Anticancer Drug Screening: Scientists at RGCB, Thiruvananthapuram developed robust model of live cell real-time detection of caspase activation and G1-S phase cell cycle phase. Several cancer cells stably expressing FRET probes were developed for caspase activation with nuclear localization signal for effective segmentation and automated quantification and validated for caspase activation. The cells were utilized for real time caspase activation profiling in time lapse with limited photobleaching. The same cells when stably expressed with cdtKuzabira orange, allowed real time visualization of cell cycle and cell death. Further stable cancer cells were developed for sensing all phases of cell cycle and cell death by expressing the caspase FRET probe with nuclear exclusion signal and G1 and G2 marker at the nucleus. The nuclear targeted FRET probe emerged

as the best quantitative live cell based caspase sensor tool in 3D culture models and also performed well in HTS ratio imaging.

Novel Photo Changeable Fluorescent Proteins:

Scientists at ACTREC, Mumbai are aiming to create novel photo switchable fluorescent molecules by directed chemical evolution method. They are in process of generating novel photo-convertible fluorescent proteins with high after conversion quantum yield or with novel pairing of emissions. Under this project, they generated mutant library of 1200 mutants, out of which 6 improved mutants were screened and finally got one improved mutant, mEos3.2. The improvement in brightness of mutant protein was verified. The optimum fluorescence of mutant protein increased almost double as that of optimum fluorescence of wild type. Other fluorescent properties of mutant protein remain similar as that of wild type mEos3.2. The process is underway to create different fusion proteins with improved variant and express them in mammalian cells and subsequently test the efficacy of improved mutant in super resolution microscopy.

Modification of Orthopedic Implant to Improve Osteogenesis and Osseo-Integration:

Scientists at IIT Kharagpur are exploiting drug loaded *A. mylitta* fibroin protein on titanium surface as an influential method to achieve altered surface topology in nanoscale, controlled drug release and enhanced osseo-induction and osteogenesis. Antibiotic loaded fibroin nanoparticle depositions efficiently influence microbial adhesion and proliferation. Altered nano-topography enhanced initial attachment of osteoblast cells followed by increased cell proliferation and differentiation. The improvement of osteogenesis and inhibition of bacterial growth using the modified drug loaded silk nanoparticle titanium surface showed great potential. The titanium surface modification with fibroin nanoparticles found to be promising for bone tissue engineering.

Micro-Diffractive Interference Contrast Cell Imaging:

A group of scientists at IISc, Bangalore are working on quantitative phase imaging of cells and sensing of mechanical properties of a cell using a diffractive technique. A rigorous model for imaging has been developed using micro-diffractive interference contrast. With the model they investigated the 4 main aspects: a) effect of cell proliferation, b) effect of cell migration, c) effect of cell shape changes and d) effect of sub-cellular structures. The optical setup for imaging and demonstration of the imaging technique has been completed. The experimental investigation was carried out with this set-up to distinguish 0.5 micron polystyrene (PS) beads from 3 micron PS beads. The yeast cells were also used in order to demonstrate that the system is capable of detecting cell proliferation.

Multi-layer Customized Skin Graft for Full Thickness Wound:

A highly porous, fluffy 3D nano-patterned, self-assembled, microfibrillar PCL/chitosan fibers with core-shell architecture has been developed by scientists at IIT Kharagpur. The architecture and composition of the scaffold promoted efficient cell attachment, migration and proliferation *in vitro*. Further, scaffold provided platform for surplus synthesis of ECM proteins and development of stratified epithelial layer. Presence of nano/microfibers with high interconnected porosity promoted efficient cellular attachment, infiltration and proliferation. The scaffold supported extracellular matrix protein expression and stratified epithelialization *in vitro*. Effective integration and attachment of scaffold with full thickness excision wound created in a rat model leading to accelerated healing within three weeks endorsed the scaffold as a promising material for skin tissue regeneration.

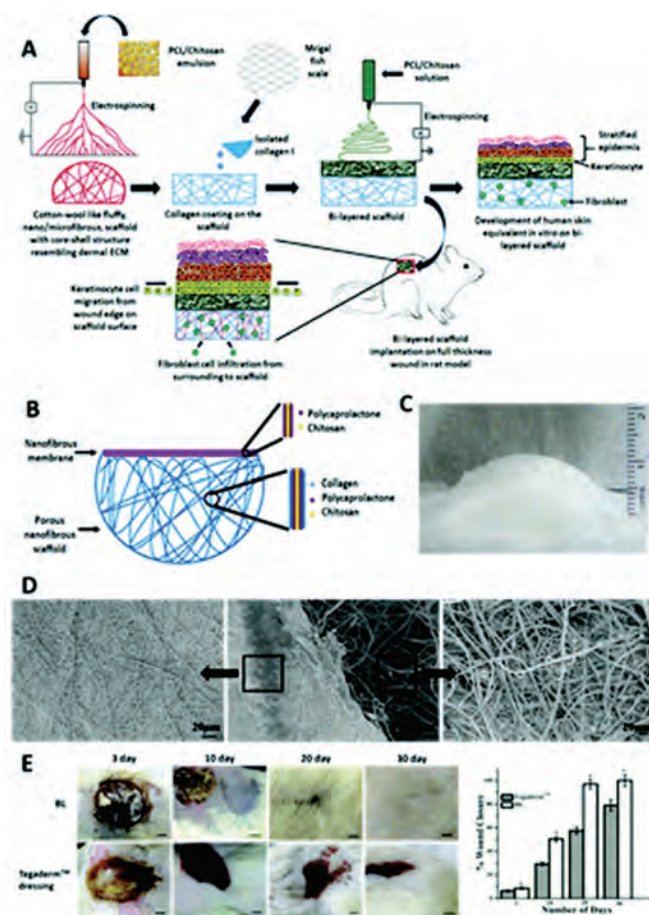


Figure: 2 (A) Schematic representation of bilayer scaffold development and its application in vivo for wound healing and in vitro for development of human skin equivalent. (B) Schematic diagram of the developed bilayer scaffold. (C) Optical image of fabricated bilayer scaffold with cotton-wool-like fluffy structure and nanofibrous membrane. (D) Morphological appearance of bilayer scaffold through SEM showing distinct variation in pore size and fiber diameter. (E) Wound healing effect of bilayer scaffold compared to Tegaderm™ standard dressing as control in rat burn model. Scale bar 0.5 cm. BL- bilayer scaffold

ENVIRONMENTAL BIOTECHNOLOGY

The Environmental Biotechnology programme of the DBT supports research and development programme in the areas relevant to development of microbial technologies for waste management & environmental improvement, environment friendly treatment processes for industrial effluent, bioremediation/ biodegradation of xenobiotic pollutants, environmental genomics and metagenomics research for waste management & pollutant mitigation, conservation of viable habitat and restoration of degraded habitats using the bio-

restoration technologies, and research towards development of mitigation technologies for climate change like carbon sequestration etc. Some of the salient achievements of the projects are highlighted as follows:

Bioremediation/ Biodegradation: A project on genomic and biochemical characterization of bacterial isolates degrading atrazine and its application in herbicide bioremediation is being attempted at NEERI, Nagpur and IITB, Mumbai. Many isolates were screened from NEERI culture bank for atrazine biodegradation and ten best were identified and selected. The atrazine degradation pathway has ten genes and the presence of these genes in the ten bacteria was screened by PCR. *atzA*, *atzB*, *atzC*, *atzD*, *atzE* and *atzF* were present in most of the isolates. *Pseudomonas* sp. AAN5 was successfully grown with atrazine as Nitrogen source. *atzA* and *atzB* were monitored in the presence of atrazine and it was demonstrated that the two enzymes are inducible. Analysis of the metabolic products indicated that the bacterial isolate was mineralizing atrazine.

Study on improving biomethanation and bioremediation efficiency of *Cassava sago* effluent by nitrogen amendments and *Spirulina* cultivation under HRAP system for safe recycling being carried out at TNAU, Coimbatore. The detailed studies have been carried out in lab scale to show the enhancement of biogas production with nitrogen amendment. The results shows cyanide removal during biomethanation in lab scale. Its transformation is being studied to understand the toxicological potential of the treated effluent.

Project on development of a process for enzyme assisted bioremediation of lipid (FOG: Fats, oil and Grease) based waste is being carried out at TERI, New Delhi. Results shows that identified bacterial strain *Bacillus* spp. (TERI Fb) has the significant potential for lipase production from low cost agro industrial waste. The partially purified lipase was monitored for its biodegradation potential of Fat,

Oil, Grease (FOG) contaminated waste water collected from local restaurant. It has demonstrated significant potential for biodegradation of FOG contaminated wastewater and the process may be up-scaled for demonstration of domestic water.

In the project on development and optimization of technology for bioremediation of chlorpyrifos (CP) in constructed wetlands at KIIT, Bhubneshwar, biostimulation and bioaugmentation studies in constructed wetlands using *Ochrobacterium* CPD-03 on the CP degradation at different conditions i.e. stimulated (addition of N, P, and K in a ratio of 80:40:40) and non-stimulated (no additional nutrients) were performed. Nearly 88% CP degradation was observed in stimulated condition as compared to the 66% degradation in nonstimulated conditions. This suggests that CP degradation is stimulated by addition of nutrients which had also provided a suitable environment for degrading CP. Overall, three CP degrading strains: *Ochrobactrum* CPD-03, *Microbactrum* CPD-20 and *Bacillus* CPD-33 were identified. This information can be used for designing potential consortia for biostimulation experiments.

Phytoremediation/ Bio restoration: Phytostabilization of mine tailings in the Sukinda chromite mining area is being jointly carried out by Chilka Development Authority, Bhubaneswar and KIIT, Bhubaneswar with an overall aim to develop and optimize a PGPR (plant growth-promoting rhizobacteria) based technology. Potential PGPR strains are being used in further experiments. Native plants such as *Saccharum spontaneum*, *Tephrosia purpurea*, *Eragrostis ciliaris*, *Alternanthera sessilis*, *Eragrostis ciliaris* and *Desmodium triflorum* have been identified from the overburden sites and these plant species are being assessed with PGPR inoculants for phyto-stabilization attributes.

Project on bio restoration of degraded mangrove forest along the embankment of the river Ramganga and related molecular study for the loss of mangrove ecosystem homeostasis is being done at WBSU,

Kolkata. Planting of *Myriostachya withiana* with its sub-surface rhizome network has successfully prevented the mudflat from erosion, and subsequent establishment of *Porteresia coarctata* on such mudflats have provided the successful lead for stabilizing the mudflat from tidal erosion. Some species perpetuating in high saline natural mangrove areas have been proved to be high accumulator of osmolytes. The species distribution across the natural mangrove forests along a salinity gradient may further help in deciding species composition of the sites for restoration effort.

At Shivaji University, Kolhapur, phytoremediation treatment process has been developed for the degradation of dyes from textile industrial effluent. The study showed that Macrophytes – *Ipomea aquatic*, *Alternanthera philoxeroides* (a massively rooted macrophyte) and *Salvinia molesta* had a potential for textile dyes and effluent treatment. *A. philoxeroides*, *S. molesta* and *I. hederifolia* can efficiently be used for the treatment of textile industry effluent at large scale (constructed wetland system) through rhizofiltration approach. Further, field application of *I. aquatica*, *S. molesta* and *A. philoxeroides* in wastewater lagoon systems has been successfully carried out. Studies to explore these plants in a constructed wetland system for textile effluent treatment at an industrial scale are underway.

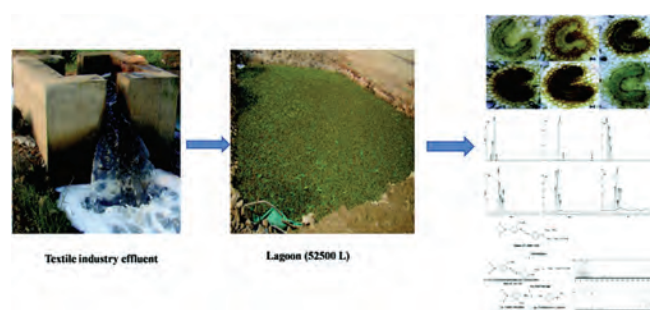


Figure: *Salvinia molesta* in constructed lagoon treated 52,500 L of textile effluent

Environmental Metagenomics: In the network project on understanding genome organization and

gene expression in response to different Hexachlorocyclohexane (HCH) isomers in HCH degrading bacteria and the HCH dumpsite carried out at University of Delhi, IITB, Mumbai and University of Hyderabad. *Sphingobium indicum* B90A was sequenced (using 454 GS FLX and Illumina) and further sequencing gaps were filled by using SMRT technology. This led to designation of the assembled sequence data into respective replicons i.e. chromosome and plasmids. Further, the genomes of the HCH degraders were sequenced and annotated to reveal their genomic ability to survive in high HCH concentrations (450mg/g) and to metabolize different HCH isomers. The information so obtained was utilized to perform comparative genomics of *Sphingobium* spp. which revealed the ongoing evolution of *lin* pathway (HCH degradation pathway) among HCH degraders. Investigators have used multiple strategy to study HCH degradation and precisely concluded that use of in-situ consortium will be best option for bioremediation of HCH degradation and biostimulation would be a better approach.

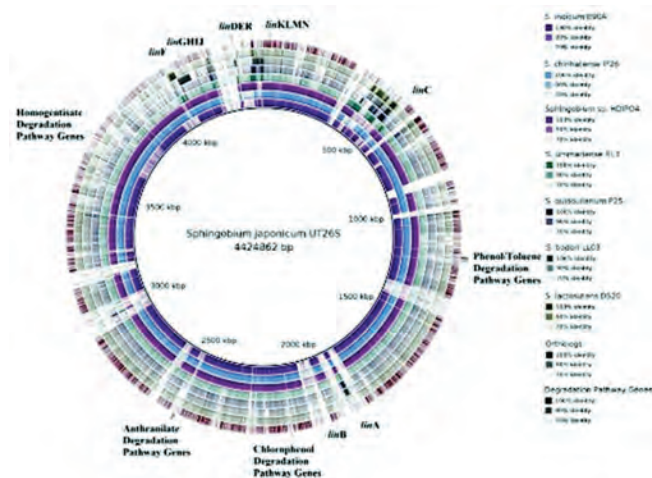


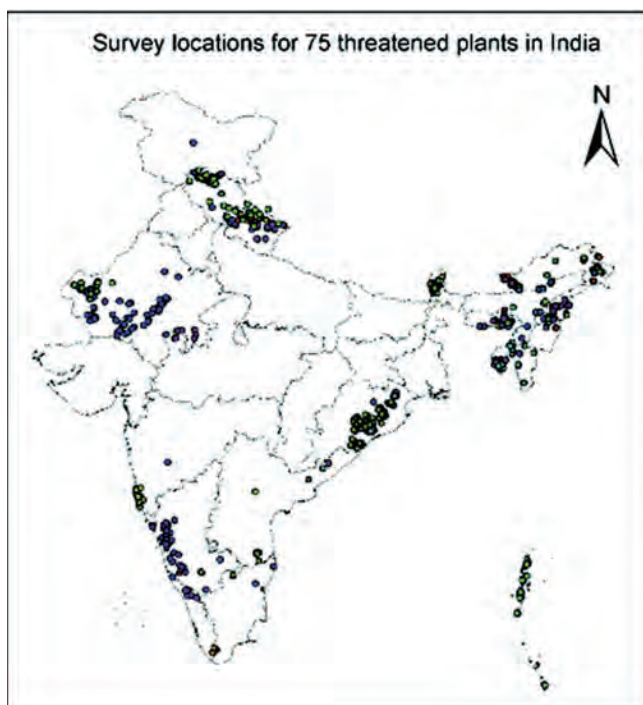
Figure: Comparative genome map of *Sphingobium* spp. *S. japonicum* UT265 used as a reference genome over which other strains were mapped. Genes for HCH, Phenol/Toluene, Chlorophenol, Anthranilate and Homogentisate degradation pathways were identified in the outermost region of the figure. Outermost circle: Orthologous genes, circle 2: *S. lactosutens* DS20, circle 3: *S. baderi* LL03, circle 4: *S. quisquilarium* P25, circle 5: *S. ummariense* RL3, circle 6: *Sphingobium* sp. HDIPO4, circle 7: *S. chinhatense* IP26, circle 8 (innermost circle): *S. indicum* B90A. (Darker color intensity represents higher percentage identity).

Biodiversity Conservation and Characterization: Meta-Population dynamics studies of tigers in the Malenad-Mysore landscape of Karnataka is being jointly carried out at CWS, Bangalore and NCBS, Bangalore. Investigators have generated genomic data (using tissue/blood samples) and identified over 10,000 SNP markers. These SNP data were used to elucidate relationships between Southern Indian tigers and other tiger populations of India. Results showed that contrary to previous microsatellite-based results, Southern India forms a separate genetic cluster and it is genetically closest to Central India, from which it may have recently separated. It has also been concluded that genetic diversity is high in South India. Combination of genetics and demographic studies are important and knowledge generated in the project may be useful in the wildlife conservation programmes.

A study has been jointly carried out at ATREE, Bangalore and UAS, Bangalore on conservation of critically endangered and economically important species – *Myristica malabarica* in the Central Western Ghats: using ecological niche models as a tool to identify areas for conservation. Species distribution maps of *Myristica malabarica* have been developed using GIS tools. The niche models indicate the ecological niche of the species and provide a range of habitat from highly suitable to unsuitable. It provides an explicit test of the ENM with respect to the plant functional traits, regeneration ability and genetic diversity of populations along a habitat suitability gradient. Based on these results viable species conservation and restoration programmes have been carried out in identified habitats.

In the Pan – India network project on preventing extinction and improving conservation status of the threatened plant species the reasons for regeneration failure of 18 threatened species have been ascertained, and large-scale multiplication protocols for 55 species have been standardized. At least 40 species have been successfully

introduced to the natural habitats for augmenting their natural populations. A total of 65,282 individuals of 75 threatened plant species were discovered from their natural habitats using Ecological Niche Model-based field survey. This has improved the conservation classification of several threatened species. Based on the population data, at least 30 threatened plant species have now been reclassified. Several new species/rediscovery of species/geographic extension of species have been reported. Taxonomic identity of several species has been established using molecular profiling. It has been established that one of Indian ginseng species has high ginsenoside (Rb1) content as compared to American and Japanese ginseng. This provides the scope for value addition of a high value resource.



Climate Change/ Carbon Sequestration: In the project on carbon sequestration and seed oil biosynthesis in *Pongamia pinnata* at University of Hyderabad, 15 elite *Pongamia pinnata* accessions with consistent high yielding potential have been identified. The transcriptome of *P. pinnata* seed along with leaf, pod and flower tissues was

sequenced and assembled. Transcripts and transcription factors involved in various physiological processes and metabolic pathway were identified. The expression patterns of lipid biosynthetic genes at different developmental stages revealed ACCase, SAD and FAD8 as candidate genes during seed maturity. This may be helpful in the functional and comparative genomic studies to improve oil and seed yield related traits.

GENOME ENGINEERING TECHNOLOGIES AND THEIR APPLICATIONS

A Task Force on genome engineering technologies and their applications has formed very recently to promote research in the emerging areas of genome analysis and engineering technologies and to foster innovations to make such technologies affordable and available for basic and applied research in life sciences. The current priority areas are development of new methods, tools, processes and platforms for genome-wide studies and novel applications and improvements of genome wide technologies platform as well as genome-editing methods. A range of activities were initiated for overall growth and promotion of the program. The highlights of the activities undertaken during the year are mentioned below:

Advancing Research and Fostering Innovation: Programs are being implemented in the priority areas of research and innovations which are at the initial stage of implementation across the institutions. Some of the recently implemented programmes are highlighted below:

Studies were initiated at L V Prasad Eye Institute, Hyderabad to create zebra fish models of retinal dystrophy using genome editing methods. The study aims to employ CRISPRs as the genome editing tool to generate near-identical zebra fish models of human genetic mutations implicated in the disease

and also to understand the effect of mutations in retinal development and function. The team has been working towards design, construction and preparation of guide RNAs for genome editing in zebra fish.

Studies were undertaken at National Agri-Food Biotechnology Institute (NABI), Mohali Punjab to improve the nutritional qualities of wheat using genome editing tools. CRISPR-Cas system is being used for modifications of certain genes those are involved in metabolic pathway and could be manipulated for trait development. The studies include development of an efficient monocot specific CRISPR-Cas system and stable integration of the developed vector system in wheat.

The long-term goal of this project is to develop an efficient method for stable genome editing tools in cereal crop like wheat. At IISER, Pune, studies were initiated to investigate spatio-temporal organization of oncogenes, tumor suppressor and cancer associated genes by live-imaging using CRISPR-Cas technology in models of cancer initiation and progression. Studies involve the serial introduction of genes to transform human mammary epithelial cells. CRISPRi system is being used as a toolbox to investigate novel regulatory mechanisms of synapse formation by long non-coding RNAs" at National Brain Research Center, Manesar, Haryana. This study will illustrate novel RNA based mechanism of synapse formation and will also demonstrate application of new tools to explore RNA based mechanism involved in cognitive functions and will provide clues to develop possible therapeutic intervention tools towards the amelioration of neurodevelopmental disorders. At CCMB Hyderabad, CRISPR-on-in System is being used for simultaneous differential repression and induction of target genes in vertebrate model organisms" Centre for Cellular and Molecular Biology, Habsiguda, Hyderabad. The studies include generation and validation of CRISPR-on-in-Hipp11 ES cell line/mouse line and in Zebrafish line.

Human Resource Development: *Overseas fellowships:* Activities were initiated through IUSSTF program for overseas fellowships with the following two modules: (a) *Genome Engineering/Editing Technologies Initiative (GETin) - Overseas Fellowship* for Indian citizens (i) Student Internship and (ii) Fellowships and, (b) *Genome Engineering/Editing Technologies Initiative (GETin)-Visiting Fellowship* to attract highly skilled researchers working overseas in the cutting-edge area of Genome Engineering/Editing Technologies to pursue their R&D interests in Indian institutions or to mentor Indian scientists in their projects.

Advance Training: Activities were also initiated on Genome Engineering/Editing Technologies Initiative (GETin)- Training with CCMB to provide advance training to students and young faculties in the areas of genome editing and engineering technologies. Detailed modalities are being worked out with CCMB for implementation of this program such as eligibility criteria, duration, training schedule, intake/year, logistics and financial implications.

Workshop & Symposia: One day technical workshop on "Practical Considerations of Applications of Genome Editing" was organised at Hyderabad on September 23, 2016 in association with Biotech Consortium India Limited (BCIL) to deliberate on advances in genome editing on prioritization of areas of research and explore potential collaborations. The symposium was attended by eminent scientist and industry representatives working in the areas of genome engineering and gene editing technologies. Deliberations were focussed around Evolution of modern genome engineering technologies and their applications in Plant Science/Agriculture, health/animal sciences and, understanding Global Policies on Gene Editing.

A plenary session was also organized in 104th Indian Science Congress, 2017 with eminent speakers and panellists deliberated on Gene Editing Applications

in Medicine, Animal and Agriculture Sciences - Regulation and Ethics” in the session.

GLUE GRANT SCHEME

Glue Grant Scheme was initiated aiming to link Basic, Clinical and Public Health Research Departments in an inter-institutional linkage(s) leading to long-term partnership programs to bridge the gap between laboratory/field research and its application to clinical and policy outcomes with a potential for translational research and technological innovation and capacity building efforts.

The on-going programs under Glue Grant scheme have received support for implementation of a collaborative program between Translational Health Science and Technology Institute (THSTI), National Brain Research Center (NBRC), Regional Centre for Biotechnology (RCB) and the Civil Hospital, Gurgaon for creation of “bench to bedside” or the “bedside to bench and back to the bedside” model for clinical and translational research. This program has strengthened clinical care in the district hospital, provided basic training in clinical and research protocols to establish a core group of research clinicians and resulted in collaborative research studies which have major public health significance.

A collaborative research program between clinicians from AIIMS and basic scientists from THSTI/NII has focused on improving understanding of the biological basis of kidney disease, asthma and blood cancer in children. Completely functioning platforms in microscopy, flow cytometry, tissue culture/molecular biology labs have been established in St. John’s Medical College under this scheme. The genomics platforms using the NCBS campus have generated substantial progress in HLA multiplexing and pathogen discovery. Also, fully functioning “crisper” platforms around the MIR-182-CML Notch project have been established.

HUMAN DEVELOPMENTAL AND DISEASE BIOLOGY

Maternal and Child Health Programme: A Task Force on Human Developmental and Disease Biology (HDDDB) has been giving emphasis on research activities related to pregnancy complication, factors of adverse pregnancy outcome, antenatal development, congenital anomalies and problems and diseases of early childhood. The projects supported so far focus on preeclampsia, IUGR, recurrent miscarriages, effect of maternal nutritional status on pregnancy outcome, development of neonatal immune system, neonatal sepsis and aspects of congenital anomalies. The overall goal is to support both basic research and application centric discovery under the programme. Major new initiatives taken under the programme are as follows:

Human Placental Research: Fetal growth and development is regulated in a very complex manner and critically hinges on the growth and development of placenta. This unique organ of fetal origin has been indicated to predict not only the outcome of a pregnancy, but also the long term health of the baby. Difficulties in real time assessment in pregnancy due to largely inaccessible position of the placenta have hampered studies and it is thus called the ‘least understood’ human organ. Since placentas are being collected in the deliveries happening in the Preterm Birth programme where the plan is to enroll about 8000 pregnant women, it was an important resource to be utilized appropriately. A call for LoIs was published inviting Letters of Intent from investigators/basic and clinical researchers who desire to develop and hone their skills in Placental Research. The goal of this advertisement was to support studies on this least understood human organ and also to mobilize more basic scientists to take up this challenging area as there is a clear dearth of scientists working in the

placental biology. In response to the same, the Department had received about 120 Lols out of which 25 have been recommended for development of full proposals.

DBT-ICMR Joint Working Group: A call for proposal under Maternal & Child health programme was made under the Joint working Group with ICMR which endeavours to identify invention and early-stage development of new medical technologies, early translation, development of innovative tools & technologies in the identified areas. This year a call for LOIs was made focussing on Preeclampsia, Neonatal Sepsis & Birth Asphyxia, against which 187 Lols were received and out of which 41 have been shortlisted for development of full proposals.

DBT-CIHR programme: International research collaborations are proven and effective way of answering both national and global priority health problems/challenges. The rapidly rising prevalence of obesity and risk of non-communicable diseases in India warrants the best minds and efforts to find solutions and mitigate the challenges in India. Collaboration with the world's leading scientists would therefore add value to whatever is developed as an original idea by the Indian researchers and vis-à-vis the Indian scientists interactions would add value to the ideas generated by the researchers in other countries. Considering this, DBT has partnered with Canadian Institute of Health Research (CIHR), Canada for a Healthy Life Trajectories initiative (HeLTi) which is a multi-country effort where interventional cohorts will be established in India, China & South Africa. Considering the importance given to evidence based recommendations in India, this programme is important as the outcome would be relevant for development of future Government policies in this direction.

The Department has signed a Program of Cooperation (PoC) with CIHR, Canada after many rounds of detailed discussions. A Call for RFAs was made in September-October following which a team

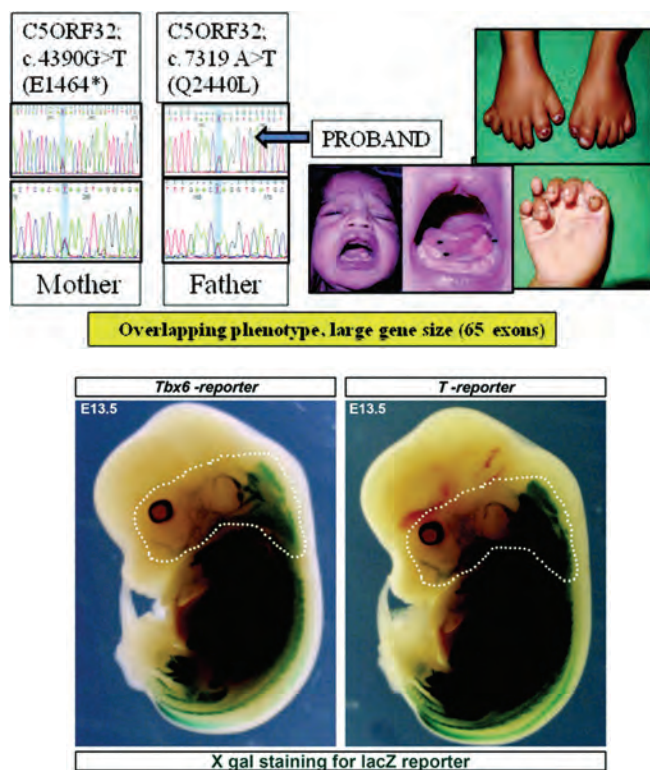
was selected which attended the strengthening workshop in Geneva for development of a proposal for linked international cohorts sharing the SOPs/ protocols with other countries.

Salient achievements in ongoing programme are as follows: Congenital anomalies: Intellectual disability is believed to affect about 1% of the population, and a complex genetic interaction among gene variants is thought to underlie some such forms. One of the major genes implicated in childhood Intellectual disability is FMRP, the protein product of which regulates the signal-dependent synaptic functions in neurons. It has been found that the Lafora disease protein malin – an ubiquitin ligase - regulates the cellular levels of FMRP. Thus, loss of malin leads to an abnormal increase in FMRP levels, and the concomitant decrease in the level of FMRP targets. A hitherto unknown regulator of FMRP has been uncovered for the role for FRMP in Lafora disease. In another study on the genome wide analysis of sub-microscopic genetic aberrations in children with idiopathic intellectual disability/ multiple congenital anomalies, the analysis has revealed that among the 63 patient samples analysed, 31 were detected to have pathogenic molecular variants, previously described in OMIM, amounting to a yield of 49%. In this context, it is important to mention that the international literature has reported an yield of 20-25%. In the current study, the yield is significantly higher, may be due to high prevalence of consanguinity in this part of the country.

In a study, with regard to limb malformations and related syndromes, till date 60 patients with malformations of limbs have been evaluated and samples of the probands and family members are stored for DNA analysis. Detailed pedigrees and photographic documentation have been collected. Sanger sequencing of candidate genes for cases with monogenic phenotypes identified pathogenic mutations in 8 of the 17 cases. Chromosomal microarray identified copy number variations in two

cases out of 10 cases. By homozygosity mapping, two candidate genes were identified in a patient which was further subjected to exome sequencing due to its large genes. Consanguinity is common in India and is of great help in identifying mutations by exome sequencing as was seen in 2 cases of Arthrogryposis renal cholestasis which is rare and serious lethal disorder and confirmation of diagnosis by mutation detection is of great help in providing genetic counseling and preventing recurrences by prenatal diagnosis. Many such results are novel, interesting and useful for the patient and families.

Oro-facio-digital syndrome CRF0532 gene mutation identified by exome sequencing



Arthrogryposis, renal dysfunction, cholestasis syndrome: Two infants from different consanguineous families: Homozygous mutations in VPS33B gene (Exome sequencing was done on stored sample after the death of the children)

The heart as well as the muscles in the head are derived from the embryonic cell population known as head mesoderm. The chambered heart and the

head musculature of vertebrates are highly complex and elaborate compared to the closest invertebrate relatives. Current idea in the field is that the expansion of the head mesoderm cell population is crucial for the evolution of vertebrates. In one study, the aim is to understand the developmental program controlling head mesoderm. Work accomplished in the past year, using mouse genetics approaches including analyses of mouse mutants, has uncovered a surprising role for Tbx6, an important mesoderm transcription factor, in head mesoderm. Prior to this study, Tbx6, which is a key factor in establishing mesoderm identity, was considered to be required uniquely for the mesoderm cell population below neck. This finding suggests that the differences between the developmental programs of head mesoderm and the mesoderm below neck arise downstream of Tbx6 function. Presently, the investigators are studying the mechanisms by which unique identity is conferred to head mesoderm.

The figure shows embryos from novel transgenic reporter mouse lines generated for the study. It provides evidence for the hitherto unknown expression of Tbx6 in head mesoderm. The expression in head mesoderm derivatives in Tbx6-reporter, highlighted by dotted line, compares with that of T, a gene with previously reported expression in head mesoderm. E13.5 – embryonic day 13.5.

The detailed biology of conception, gestation and pregnancy complications is another important aspect taken up under this programme. Several projects have been supported on aspects of pregnancy complications. Among them is a major Inter-institutional Grand Challenge program on Pre-term Birth (PTB) coordinated by pediatric biology centre at THSTI, Faridabad. Annually, 3.6 million preterm births occur in India, and over 300,000 of them die each year, contributing to 25% of the overall global preterm related deaths. Despite

considerable introduction of several therapies for prevention, the problem persists and contributes notably not only to neonatal and infant deaths but also to significant acute and long-term morbidity. This multi institutional programme envisions to address the multiple strategic priorities in preterm discovery.

A hospital-based cohort of pregnant women at the Gurgaon Civil Hospital (GCH), Haryana, has been established as part of this effort, till now 2663 women were found to have pregnancy with period of gestation (POG) < 20 weeks on clinical assessment and by the last menstrual period (LMP) after screening 8281 women attending the antenatal clinic at GCH. Out of these 1801 were confirmed to have a uterine pregnancy < 20 weeks POG on ultrasound (USG) evaluation and were enrolled. The group's attempt is to enroll women as early in pregnancy as possible. More than a third of women were enrolled in < 11 weeks (35.09%) and more than a half (58.97%) were enrolled before 14 weeks. Initial results shows that out of 953 determined outcome; 902 deliveries had happened out of which 144 (16%) were Preterm, remaining 51 were abortion (26), MTP(5) & IUDs (20).

HUMAN GENETICS AND GENOME ANALYSIS

Under the aegis of Human Genetics and Genome Analysis program, during this period, a base paper on Unique Methods and Management of Inherited Disorders (UMMID) was prepared and the modalities on different components was worked out to evolve different programs for common genetic disorders prevalent in India. Brainstorming meetings on Lupus and Hemophilia were organized to develop a consortium mode projects involving various stakeholders. A network project for diagnosis and management of celiac disease has being initiated during this period. As an ongoing activity, various R&D projects were implemented

for population based study, molecular study and pharmaco-genomics. At the Centre of excellence under this program, study on genome sciences and predictive medicine, human mycotic keratitis were carried out including development of drug delivery systems for treating inflammation, allergy, cancer etc. via self-drug-delivery technique.

Advancement in human genetics and genomic sciences and the corresponding explosion of biomedical technologies have deepened current understanding of human health and revolutionized the biomecal research. Under the human genetics and genome analysis program, DBT has prioritized certain thematic areas such as 1.) Genomics to Biology, Genomics to Health and Genomics to Society with major emphasis on monogenic disorders for initial five years. 2.) A base paper on UMMID (Unique Methods and Management of Inherited Disorders) has been prepared that gave an outline of a proposed approach to the diagnosis and management of genetic disorders at a national scale once it would be piloted. The plan was discussed by the Task Force on different components under UMMID and worked out to evolve a program in the coming years. At the initial phase, the focus can be given on the common genetic disorders, viz.

New born screening for treatable diseases

Down syndrome Screening

Thalasemia

Sickle Cell anemia

Neural tube defect screening

Hemoglobinopathies

More emphasis will be given on inter-ministerial participation and utilization of existing machinery of National Health Mission. A comprehensive training program will be designed for skill development at different levels.

A brainstorming meeting on Hemophilia was organized to discuss on patho-physiology of this

disorder, understanding the mechanism of disease, proper documentation of prevalence in the country, means to control the disease and screening & diagnostic techniques.

A brainstorming meeting on Lupus was organized to develop a consortium mode project involving all stakeholders such as basic researchers, clinicians, clinical immunologists and experts of genome measurement and analysis.

Keeping in view the unmet need in the diagnosis and management of celiac disease, a multi-institutional network project on Celiac disease is being initiated at AIIMS, New Delhi, IGIB, New Delhi, SRM Institute of Medical Sciences, Chennai, Postgraduate Institute of Medical Sciences, Chandigarh, Sardar Patel Medical College and Hospital, Bikaner, Rajasthan, and Gauhati Medical College, Gauhati with an objective to develop a national biorepository, identification and validation of a non-invasive biomarker for enteropathy present in celiac disease and to understand genotypic and phenotypic correlation in celiac disease.

In addition, conscious efforts are being undertaken for promoting the scientific advancements in its various identified areas and other emerging areas. Some of the significant achievements made during this period are:

Population study:

Epidemiology and biology of thalassemia in Tribals of Maharashtra

The scientists from Moving Academy of Medicine and Biomedicine, Pune are aiming to investigate (a) existence of other forms of hemo-globinopathies and their characterization at the molecular level, (b) study their health implications in general and (c) effect they exert when two or more hemo-globinopathies co-exist in the same person (Comorbidities). The project was conducted in 313 class XI and X school children belonging to Katkari

(35), Bhil (62), Kokana (65) and Thakar (151) communities.

In the present study the gene deletion $-a^{3.7}$ was observed as the dominant lesion. Further molecular study shows that the deletions belong to the subset $-a^{3.7}$. More than 80% of the population in each tribe carried the deleted gene. This is perhaps the highest prevalence of the deleted alpha Hb gene in the world. Interestingly, some of the sample does showed concomitant presence of mutations characteristics of Hb E, which is highly prevalent in tribes in the North-East. Analysis of the cases of α thalassemia showed that in addition to commonly prevalent mutations seen in Indian population, a few show mutations similar to those reported in Chinese and Iranian tribes, an observation that may provide clues to migration of these tribes.

Polymorphisms in the physiological anti-hypertensive peptide catestatin in an Indian population

The scientists at IIT, Madras are aiming to study polymorphisms in the physiological anti-hypertensive peptide catestatin in an Indian population and discovered a naturally-occurring, common genetic variation, Gly364Ser, within the anti-hypertensive peptide catestatin (CST), a proteolytic fragment of the prohormone chromogranin A (CHGA) that is expressed in secretory vesicles of endocrine, neuroendocrine and neuronal cell types. The 364Ser allele was associated with profound elevated blood pressure (up to ~ 8 mmHg systolic and ~ 6 mmHg diastolic) and enhanced risk (by $\sim 48\%$) for hypertension in its carriers in two geographically/ethnically-distinct Indian populations ($n=4000$). Functional characterization of the Gly364Ser variant using cellular/molecular biological experiments (viz. peptide-receptor binding assays, nitric oxide [NO], phospho extracellular regulated kinase [ERK] and phospho endothelial nitric oxide synthase [eNOS] estimations) and computational approaches (molecular dynamics simulations for structural

analysis of wild-type [CST-WT] and variant [CST-364Ser] peptides, and docking of peptide/ligand with beta-adrenergic receptors [ADRB1/2]) suggested that the CST-364Ser allele enhanced the risk for hypertension via diminished endothelial NO production due to altered interactions of CST-364Ser peptide with ADRB2 as compared to CST-WT.

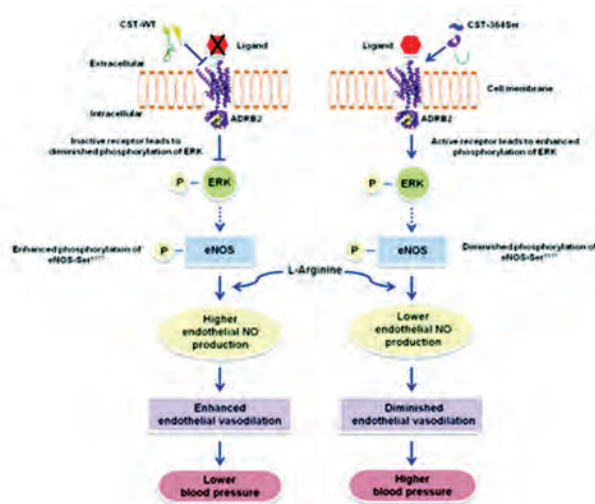


Fig.: Plausible mechanistic basis for the effects of catestatin peptides on blood pressure via modulation of nitric oxide pathway

The CST-364Ser peptide does not interact at the ligand binding site of ADRB2 unlike CST-WT owing to differences in their secondary structures. Their differential interactions with ADRB2 result in diminished antagonization of ADRB2 and enhanced activation/ phosphorylation of ERK by CST-364Ser. The altered ERK activation between the CST peptides may result in diminished phosphorylation of eNOS-Ser¹¹⁷⁷ and consequently lower eNOS activity in the case of CST-364Ser. These cellular/ molecular processes lower the NO levels in vascular endothelial cells in the carriers of CST 364Ser allele leading to endothelial dysfunction and thereby increasing their risk for hypertension.

Genetic Screening of Microdeletion of Y-Chromosome in Infertile Patients from Population of Eastern India

The scientists at AIIMS, New Delhi performed genetic analysis in clinically diagnosed cases of azoospermia & oligozoospermia with respective controls (n=380) to determine the cause of infertility in men. Chromosomal analysis showed significant structural and numerical variation with respect to the controls. Karyotypes (ISCN2013) demonstrated interstitial deletion (-12p11.3) and translocation between D/G group chromosome including structural variation of X-chromosome (Xq22.1-24), appearance of ring chromosomes and XY/XXY (mosaic).

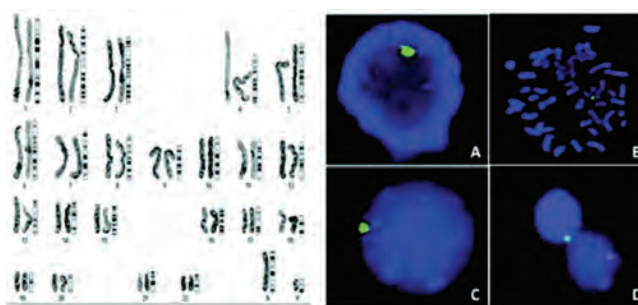


Fig. 1 Karyotype infertile case showing XY chromosome. FISH showing the Sry (+) ve (fig.A-B), & sry (-)ve (fig. C-D) in interphase and metaphase stage.

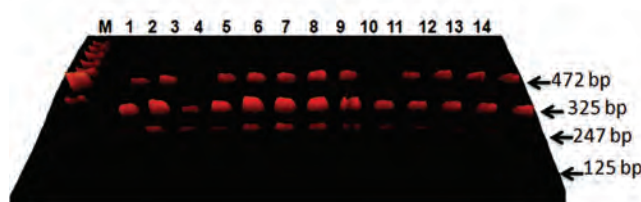


Fig.2. 3-D image analysis of multiplex PCR product of infertile cases (1-14) showing mutation in Lane 1 of AZFc 472bp, 325bp, 247 bp & 125bp of AZFb, and in lane-10 (472 bp of AZFc).

Genetic Association study of Polymorphisms related to Chronic Obstructive Pulmonary Disease and its Measures, in North Indian Population: COPD Genetics Consortium

The scientists from Public Health Foundation of India, New Delhi in collaboration with scientists from University of Delhi; All India Institute of Medical Sciences, New Delhi; VP Chest Institute, University of Delhi; Post Graduate Institute of Medical Sciences, Rohtak; Post Graduate Institute of

Medical Sciences and Research, Chandigarh; PS Medical College, Gujarat are aiming to constitute a consortium of clinicians, epidemiologists, statisticians and geneticists to determine the genetic factors related to chronic obstructive pulmonary disease (COPD) in North Indian population with a primary objective to create a bio-bank of 3000 COPD cases and controls to be able to validate GWAS loci related COPD and lung function in North Indian population. Under this collaborative project, the COPD genetics consortium has been successfully developed in India that has helped in the recruitment of 3483 participants from Delhi, Punjab, Haryana and Gujarat and bio-bank of 3483 serum developed and plasma and DNA samples related to COPD stored in required temperature in laboratory of PHFI, Gurgaon.

Pharmacogenomics:

Developing Pharmacogenetic Algorithm to Individualize Dosing of Tacrolimus + Mycophenolate Sodium in Patients with Kidney Transplantation

The most important immunosuppressive drugs given during kidney transplantation are tacrolimus and mycophenolic acid. These drugs possess narrow therapeutic index and wide inter-individual variability that may cause severe adverse events. A study undertaken at Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad aims at genotyping of CYP3A5 and ABCB1 for precise prediction of dose of Tacrolimus by developing appropriate algorithm in order to prevent adverse events associated with either low or high dose of Tacrolimus.

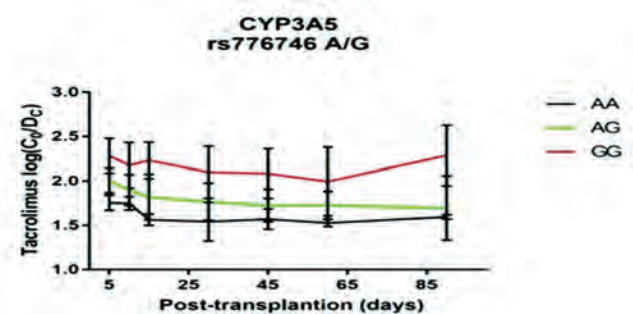


Fig. 1. Tacrolimus blood concentration in relation to CYP3A5 variant

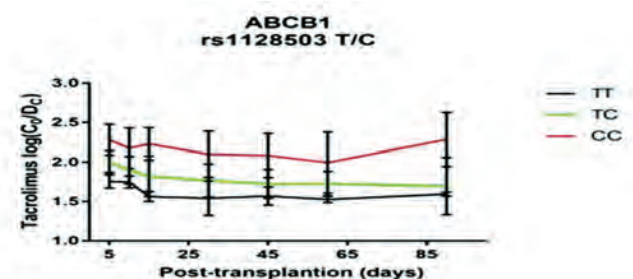


Fig. 2. Tacrolimus blood concentration in relation to ABCB1 variant

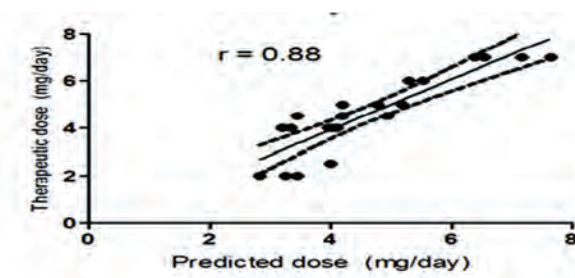


Fig.3: Correlation between therapeutic dose and predicted dose of tacrolimus (Predicted dose was calculated from multiple linear regression model)

Molecular Study:

Contribution of genetic heterogeneity of major histocompatibility complex (MHC) in the phenotypic presentation of systemic lupus erythematosus (SLE)

Genome wide association studies carried out at Nizam’s Institute of Medical Sciences, Punjagutta, Hyderabad have identified several novel susceptibility genes involved in immune-regulatory pathways in SLE patients including T cell B cell activation and signaling, phagocytosis, interferon regulation and production and antigen presentation. Among all the identified genes, HLA genes are extensively studied as strong candidate genes in different ethnic groups. It was observed that HLA-DRB1*07 allele is significantly associated with increased risk of Indian SLE. Statistical analysis revealed glycine at 11, thyracine at 13, Aspartic acid at 70 and glutamine at 74 of DRB1*07 protein showed significant association with SLE group, indicating these amino acids might have involved in defective presentation of self antigens leading to autoimmune SLE disease.

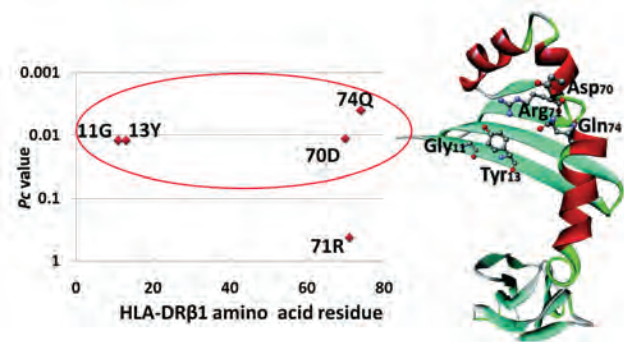


Fig.: Key amino acid residues in DRB1*07 protein α chain associated with increased SLE risk in Indian patients

Structure Function relationship of defective beta myosin heavy chain (MYH7) in Hypertrophic Cardiomyopathy

The scientists at PGIMER, Chandigarh are aiming to study the structure-function relationship of four novel defective beta myosin heavy chain (MYH7) in Hypertrophic Cardiomyopathy (HCM) patients employing three different approaches i.e. confocal microscopy, electron microscopy and functional genomics. The comprehensive study revealed the molecular basis of these MYH7 gene mutations in the pathogenesis of HCM/DCM via formation of

defective MYH7 protein. The significant findings of this study suggests that these mutations result in defective MYH7 proteins which may form protein aggregates and inhibit the incorporation of defective protein into thick filaments. Mutated protein aggregates may also impair the sarcomeric contractility and increase cellular stress, which finally leads to cellular hypertrophy.

Quantitative Proteomic Analysis of Human Follicular Fluid in Polycystic Ovary Syndrome

The scientists at NIRRH, Mumbai are aiming to carry out the quantitative proteomic analysis of Human Follicular Fluid in Polycystic Ovary Syndrome. A multipronged approach of protein-peptide separation coupled to LC-MS/MS was utilized to catalog normal follicular fluid proteome, which lead to the identification of 480 proteins in follicular fluid, of these 320 proteins were detected in follicular fluid earlier. The presence of lectin-induced complement pathway was detected in follicular fluid. Further, follicular fluid proteome collected during IVF from women with PCOS and normo-ovulatory women was compared using iTRAQ-LC-MS/MS. Total 770 proteins were identified, of which 186 were found to be differentially expressed (87 up regulated and 99 down regulated) in PCOS. Combining the proteins identified from follicular fluid cataloging and iTRAQ experiment, overall 978 proteins have been identified in follicular fluid.

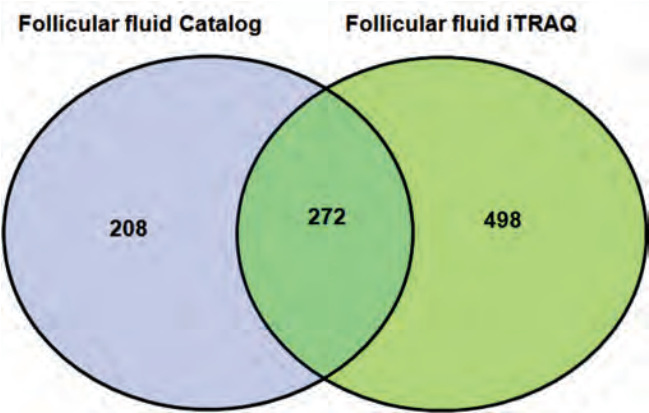


Fig.: Overlap of proteins identified in follicular fluid by cataloging and iTRAQ method.

The organization and expansion of COC matrix is known to affect oocyte maturation. Alteration of several proteins of COC matrix indicated reduced COC function in these women. Oocyte quality has been reported to be compromised in PCOS and dysregulated COC matrix functioning may contribute to it. Establishment of follicle vasculature, which is essential for its maturation, occurs at the preantral stage and this stage coincides with follicular growth arrest in PCOS. Angiogenesis is also required for maintenance of corpus luteum, while dysfunctioning of corpus luteum is reported in PCOS. These observations suggest that dysregulation of follicular angiogenesis may contribute to PCOS pathophysiology.

Identification of Rare Variants and Copy Number Variations in Schizophrenia

The scientists from University of Delhi South Campus and Dr. Ram Manohar Lohia Hospital, New Delhi have focussed on identification of rare protein disturbing variants using whole exome sequencing (WES) of ~25 multiplex Schizophrenia families. Using the hypothesis free WES approach, they identified a rare heterozygous variant (c.545G>T; p.Cys182Phe) in Trace amine associated receptor 1 gene (*TAAR1*) in one family. *TAAR1*, a GPCR, is a modulator of monoaminergic pathways and interacts with AKT signalling pathways. Interestingly, six additional variants have been identified in this intronless gene on screening two independent cohorts of north Indian (n=475) and African-American/Caucasian ancestry (n=310) but not in controls (n=410). The rare variant burden analysis performed on this variant data set from *TAAR1* screening showed a significant enrichment (p=0.036) in case group. Novel genetic evidence for the role of *TAAR1* in Schizophrenia etiology provided by this study is well supported by a large body of animal model based pharmacological and functional data.

Novel Causative Gene(s) For Parkinson's Disease

The scientist from University of Delhi South Campus, All India Institute of Medical Sciences, New Delhi and Parkinson's and Aging Research Foundation, Bangalore in collaboration are aiming to focus on identification of novel genetic determinants for parkinson's, if any, using NGS tools and the valuable familial PD resource available in our population.

In a family with autosomal recessive juvenile Parkinsonism (ARJP), a novel homozygous frameshift insertion c.85_90 CGTCGCCGTCGCCGTCGCCGTCGCCGTCGCC, in exon 1 of *PODXL* was identified. Besides, three additional mutations in sporadic cases were also obtained. With this strong genetic evidence for a novel PD causal gene, functional characterisation of the mutations was undertaken. The neurite branching pattern of PC12 cells transfected with WT and three other mutant constructs and differentiated to neurons were investigated. On immunostaining to ascertain the neurite branching profile, all three mutants showed higher number of branches per cell (Mann-Whitney p<0.0001) and R294Q showed a significant increase in neurite length per cell (Mann-Whitney p<0.0001) as compared to the wildtype, confirming the pathogenic nature of these novel mutations.

In another family with ADPD, a novel heterozygous non synonymous variant c.169C>A, p.P57T in exon 2 of *RIC3* was prioritised as the most probable disease causing variant. Functional characterization of these mutations in *RIC3*, a known chaperone of nicotinic acetylcholine receptors (nAChRs) in PC12 cells showed a significant (Mann Whitney p<0.0001) difference in and lower colocalisation between *RIC3* (wildtype vs both mutants) and *CHRNA7* as well as in quantitation of the number of endogenously expressed *CHRNA7* transported to the plasma membrane of PC12 cells which was also confirmed by western blots, thus suggesting

the possible pathogenic status of these mutations. In another ARJP family with consanguinity from eastern India, a novel homozygous mutation (c.1376C>G, p.Arg459Pro) in *SYNJ1* was identified by WES. These novel findings provide the first genetic evidence for the involvement of the neuro-developmental and/or inflammatory pathway via *PODXL*, and cholinergic pathway via *RIC3* to PD.

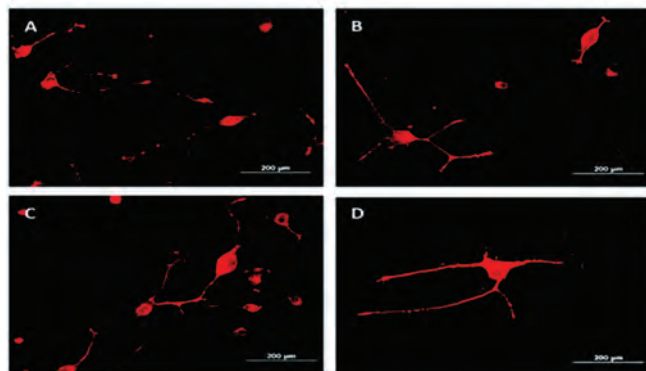


Fig.: Neurite branching profile in wild-type (WT) and mutant stable PC12 cells differentiated into neurons. (A–D) Representative images captured under 20× objective, on Olympus BX51 fluorescence microscope. Stable PC12 lines expressing podocalyxin-like (PODXL)-myc-DDK: (A) WT. (B–D) Mutants P429T, S373N and R294Q, respectively. Significant difference ($P < 0.0001$) was observed in neurite branching between WT and the three mutants; and in neurite length per cell between WT and R294Q.

Unraveling Monogenic Causes of Mental Retardation Using Contemporary Tools

Intellectual Disability (ID) and the conventional linkage, contemporary whole exome sequencing and copy number variation estimation approaches. Genetic determinants in four families with ID have been successfully determined in this study. Salient findings include: (i) Identification of a duplication of ~0.5Mb genomic region at Xp11.4 encompassing *BCOR*, a known ID gene in all the three affected sibs in family #1. (ii) Discovery of a novel gene *MID2* with a missense mutation (NM012216.3 c.1040G>A; Q9UJV3 p.Arg347Gln), hitherto unreported for ID, which encodes ubiquitin ligase E3 as the likely cause of ID in a large family with X-linked ID. This was achieved by custom target re-sequencing of the linked region (Xq21-Xq24) and prioritization of the novel variants by *in silico* softwares. (iii) In a third

Indian family, no causal variant on WES data analysis but a putative causal *de novo* deletion at 13q14.2-q21.1 shared among two siblings with mild ID, congenital cataract and other phenotypes was detected by array CGH analysis. (iv) An unusual finding with two different phenotypes namely Seckel syndrome in three male siblings and mild ID in the fourth male sibling, in a family of north Indian origin and identification of two distinct sets of X-linked rare variants segregating with the two phenotypes was made by WES.

Centre of excellence

Centre of excellence on Genome Sciences and Predictive Medicine (Phase-II)

The major focus in Phase-I of the COE on Genome Sciences and Predictive Medicine, by the scientists at University of Delhi South Campus, All India Institute of Medical Sciences and University of Delhi, Delhi was on discovery genomics and big data generation. The studies demonstrated that for common complex traits there is very limited replication of genetic findings from Caucasian populations. Therefore, in efforts were made to identify the genetic factors conferring susceptibility to two common but complex traits in humans namely Rheumatoid arthritis (RA) and Ulcerative colitis (UC) by employing an interdisciplinary approach of Genome Wide Association Studies (GWAS) and machine learning methods. In the first ever GWAS in the genetically distinct NI population, using a two stage study design a significant association of a novel gene *ARL15* ($P_{\text{combined}} = 2.26 \times 10^{-6}$; OR=1.46) in the combined analysis besides reaffirming a few previously reported GWAS findings was observed in RA.

Similarly in UC, seven novel genes namely *MICB*, *BAT2*, *MSH5*, *HSPA1L*, *SLC44A4*, *CFB*, *RDBP* and *NOTCH4* from three novel MHC independent UC loci were observed. In addition, notable strides in structural, biochemical and functional characterization of the SNPs, helpful for rational

drug design in pharmacological relevant candidate genes such as Dopamine receptor D4 (DRD4) and Dopamine α -hydroxylase (DBH) were made and a few lead molecules for DBH have been developed successfully.

Based on the successful interdisciplinary research collaboration to address the global challenge of complex disease trait genetics, biology and other promising findings, some with near future translational potential in the area of diagnostics/lead molecules, Phase-II of COE aimed at translational medicine was initiated. This Phase was however, restricted to RA with the specific objectives of **i)** Functional analysis of the susceptibility genes in RA obtained from multiple approaches from Phase I of the COE; **ii)** Construction of cell type specific networks, pathways to understand disease biology and identification of potential lead molecules; and **iii)** Provide proof of principle for lead molecule development for targets identified in Phase I and in (i) and (ii) above, with a one-time industry participation.

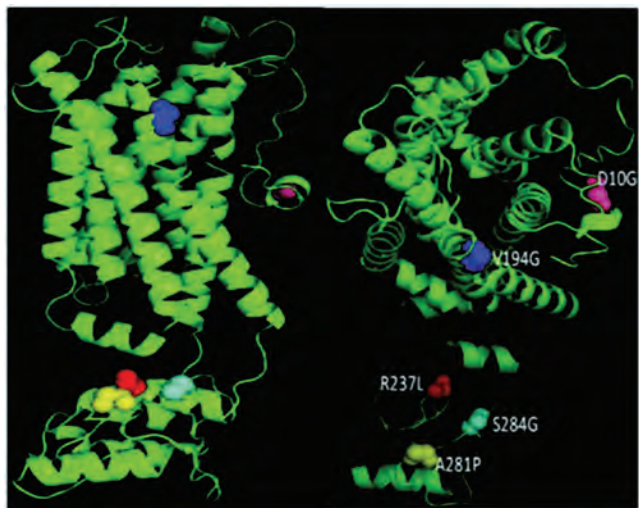


Fig.1. First three dimensional structure prediction of Dopamine receptor D4 showing location of a few variants

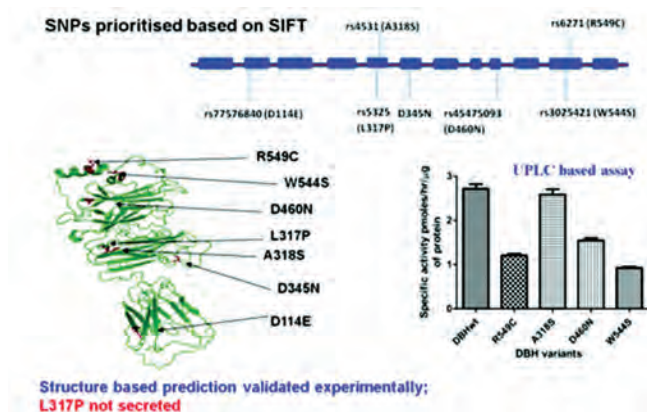


Fig. 2: *In silico* and functional characterization of variants in dopamine α -hydroxylase gene

2. Programme support on an interdisciplinary approach towards developing drug delivery systems:

An interdisciplinary approach towards developing drug delivery systems has been exploited by the scientists at Indian Association for the Cultivation of Science, Kolkata for treating inflammation, allergy, cancer etc. via self-drug-delivery technique. Supramolecular gels (hydrogels and methyl salicylate gels), amphiphilic co-polymer and metal complexes were used as a tool to deliver drugs at the target sites. The cytotoxicity and anti-inflammatory or anti-cancer activities of the modified drug delivery systems were also studied in details indicating its suitability as drug delivery vehicles.

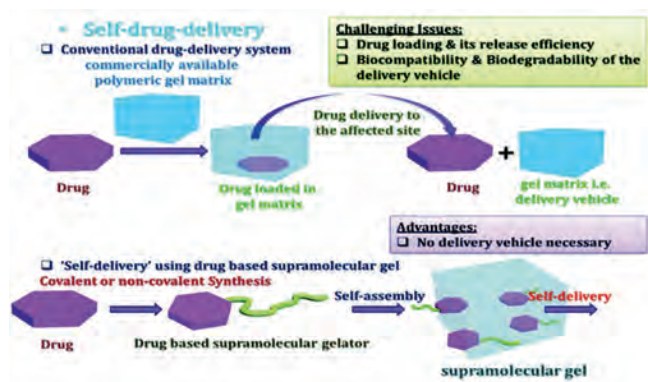


Fig.: Schematic representation of the self-drug-delivery system

3. Programme support for research on human mycotic keratitis

To understand the mechanisms that result in inflammatory response in human mycotic keratitis the scientists at Aravind Medical Research Foundation, Madurai carried out in-depth profiling of the proteome of tear from *A. flavuskeratitis* patients. This combined with detailed pathway analysis of the proteins identified in tear from keratitis patients in comparison with that of the healthy controls enabled them to identify the key events that are activated in the host in response to *A. flavus* infection.

INFECTIOUS DISEASE BIOLOGY

In India, the range and burden of infectious diseases are enormous. Tuberculosis, Malaria, Filariasis, Visceral Leishmaniasis, Leprosy, HIV infection, Japanese Encephalitis have caused serious epidemics in recent years. Bacterial resistance is a growing threat because of the widespread misuse of broad-spectrum antibiotics. Visceral Leishmaniasis prevalence has also increased. Inadequate containment of the vector has resulted in recurrent outbreaks of Dengue fever and re-emergence of Chikungunya virus disease. Other infectious diseases caused by faecally transmitted pathogens (enteric fevers, cholera, hepatitis A and E viruses) and zoonoses (rabies, leptospirosis, anthrax) are not in the process of being systematically controlled.

In order to address various issues and concerns related to infectious diseases, DBT has constituted a Task Force (TF) on Infectious Disease Biology to focus on Research and Development and Capacity Building with the aim to develop policy, planning and strategic thinking for infectious disease biology research and translational medicine on short-term, medium-term and long-term basis, guidance on setting-up 'Theme based Research Units',

suggesting novel and topical areas for R&D and developing partnerships and collaborative programs. Some of the salient achievements of the programme area are highlighted as follows:

In a study on effect of DENV Non-Structural 1 (NS1) protein and 3D cultures, the NS1 protein of all four serotypes of dengue viruses inhibited the cell growth of SK Hep1 cells in the 3D cultures. DENV 2 NS1 showed maximum inhibition. Interestingly, the 48 hr post exposure data point showed significant inhibition of the small and large colonies.

For the first time the human hepatic endothelial cell SK Hep1 was adapted to growth under 3D under hydrogel conditions and maximum growth inhibitory effect of DV2 & 3 NS1 was seen by direct exogenous exposure. Moreover, the nature of proliferation of the SK Hep1 cells in differential colony growths in 3D cultures also indicated a physiological uniqueness of this cell line not reported till date.

A study on the influence of single versus multiple Dengue serotype concurrent infections on clinical manifestations and the B cell response showed that Dengue infection leads to massive expansion of antibody secreting B cells (ASC or plasmablasts), the expansion of which varies dramatically between individuals, raising the question as to whether these cells or the subsequent humoral response might have a role in dengue immunopathology during an ongoing infection. The study recruited 817 children suspected with dengue like symptoms. Clinical analysis of differences in disease outcome between patients infected with different serotypes and patients infected with one or multiple serotypes is currently being performed. Humoral antibody analysis by dengue-specific IgM and IgG ELISA's revealed that 60% of children recruited have IgM greater than IgG that are considered as primary dengue and the rest 40% have IgG greater than IgM that are typically considered as secondary cases.

In a study on platelet associated molecular targets for inflammation, vascular integrity,

thrombocytopenia and disease severity in dengue infection, flow cytometric analysis revealed an increased expression of CD molecules (such as CD62P, CD31, CD29) that were associated with platelet activation in dengue cases compared to healthy control platelets. Within dengue cases, platelet glycoproteins were up regulated in the samples collected within 24 hrs of admission compared to samples collected at day 3. Further, a significant reduction was observed in the convalescence/day 7 samples compared to its respective baseline samples indicating the reduction in disease infectivity and improvement in recovery from illness.

A study on generation of culture-differentiated innate memory Cluster of Differentiation (CD8) cells with toll-like receptor expression and responsiveness to pathogen/danger-associated molecules resulted in the development of a novel method to generate CD44⁺, CD122⁺ and Eomes⁺ innate memory-like CD8⁺ T cells in culture from CD4⁺CD8⁺ double positive (DP) thymocytes of normal C57BL/6 mice. The *in vitro* expansion of CD8⁺ T cell subset could be utilized in clinical settings. Nonconventional CD8⁺ T cells generated in culture have discriminating power to sort pathogen-associated molecular pattern (PAMP) from danger associated molecular pattern (DAMP). This culture system is important for expansion of PD1⁺CD8⁺ T cells or PD1⁺CD8⁺ T cells *in vitro* for conducting immune therapy.

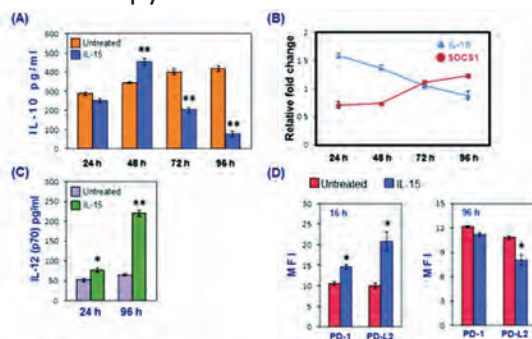


Fig. 1: Analysis of cytokine expression and regulatory molecule induction of viable B-1a cells by IL-15. (A) The release of IL-10 in untreated and IL-15-treated culture supernatants was quantified by ELISA at the indicated time points. The bar diagrams represent the mean \pm s.e.m. of three separate experiments, each performed in triplicate. ** $P < 0.005$. The data given are representative of three independent experiments. (B) The ratio of IL-10 and SOCS1 expression in an effect of IL-15-treatment are shown. The mean \pm s.e.m. for each time point from three separate experiments are indicated. (C) The release of IL-12 (pg/ml) in untreated and IL-15-treated culture supernatants was quantified by ELISA. The bar diagrams represent the mean \pm s.e.m. of three separate experiments, each performed in triplicate. * $P < 0.05$, ** $P < 0.005$. (D) The expression of PD-1 and its ligand PD-L2 on IL-15-treated and untreated cells at 16 h followed by their absorption at 96 h. The data given are representative of three independent experiments. The bar diagrams show the mean \pm s.e.m. of three separate experiments. * $P < 0.05$.

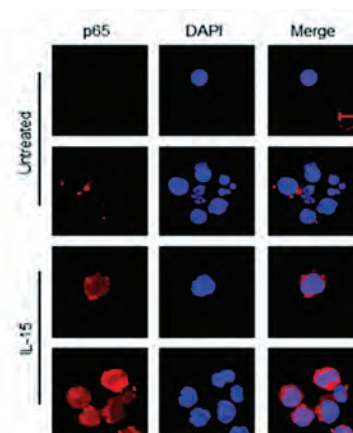


Fig. 2: IL-15 induced activation of NF- κ B in B-1a cells. Immunofluorescence showed IL-15 mediated nuclear translocation of p65 subunit of NF- κ B onto the nuclei of B-1a cells.

A study on investigating the effects of HIV-1 proteins in retinal blood brain barrier degeneration investigated changes in tight junction components in Muller glial cells exposed to the HIV1 coat protein Tat. The ability to attract monocytes on exposure to clade B and clade C HIV-1 Tat in Müller glia cell line MIOM1 was investigated. The ability to attach Peripheral Blood Mononuclear Cell (PBMC) is a defining step in AIDS progression. Activated Muller glia showed greater attachment of PBMC suggesting Muller glia transfected with Tat, can attach larger number of monocytes thus aiding in diapedesis. Transfection with Tat plasmid of both clade B and clade C variants show significant difference in their ability to attach.

A study on characterization of hepatitis E virus RNA-dependant RNA polymerase and its associated proteins in the replicase complex showed the capability to characterize HEV RdRp by optimizing methods for its purification and analyzing RNA synthesis *in vitro* by developing a non-radioactive assay. This is for the first time a non-radioactive assay for HEV RdRp has been established.

National Bio-Bank Facility at Institute of Liver & Biliary Sciences: A National Bio-bank facility for R&D activities in Hepatitis C Virus infection at ILBS, New Delhi with the involvement of laboratory and clinical researchers has been funded. This facility

would serve entire country as a bio-bank for future research & understanding of the patho-biology of HCV liver diseases and function as a nodal agency for collection & supply of HCV related tissue samples throughout the country.

A study on assured-chip, an accurate, affordable and rapid microfluidics-based diagnosis of Hepatitis-C virus was demonstrated as fully integrated isothermal PCR assay onto a POC (point-of-care) device for rapid and on-site molecular diagnosis of Hepatitis-C virus. A soft lithography-based protocol is developed to produce microchannels of 100 μm in heights by replica molding in an economic way out of the clean-room. For visual detection, a LED-based device that can be integrated to the PCR device has been fabricated. A prototype design has been developed as shown below in Figure.

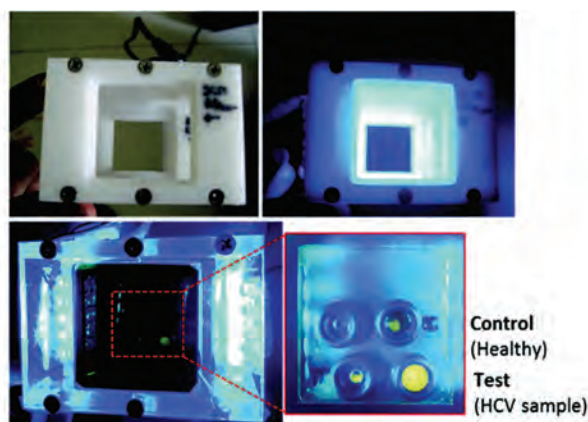
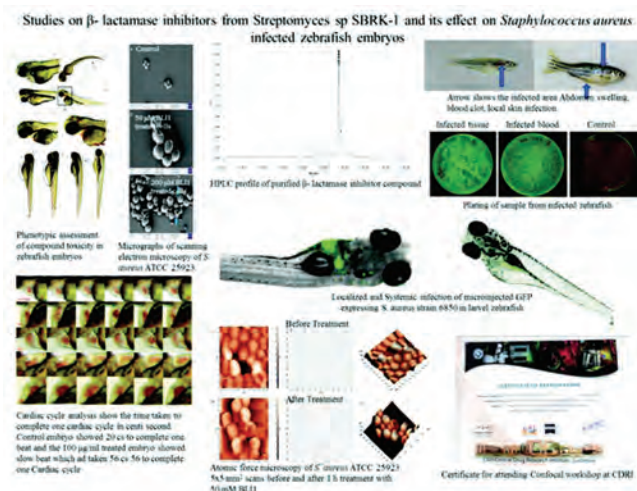


Figure. Photographs of two-channels ASSURED chip and lab-made portable LED device for on-site molecular diagnosis of Hepatitis C-virus. Isothermal amplification was performed with (Test channel) and without (Control channel) sample and detected visually (instrument-free).

Studies on beta-lactamase inhibitor(s) from *Streptomyces* sp SBRK-1 and its effect on *Staphylococcus aureus* infected zebrafish embryos established the zebrafish model of infection. A rapid systemic infection in zebrafish larvae was established by microinjecting GFP- expressing *Staphylococcus aureus* strain 6850 containing the plasmid pALC1743 directly into the blood circulation via caudal vein. The pathological examination showed significant variation on phenotype, surface

colonization, blood analysis and histopathology. The infected zebrafish showed blood coagulation, swelling in abdomen and thoracic cavity was observed. The details are shown in Figure below.



For the first time in India, the expression of RND pumps and outer membrane proteins were studied that are implicated in the antibiotic resistance of *A. baumannii*. No significant difference was noticed in the expression of efflux pumps among CRAB (carbapenem resistant *A. baumannii*) and CSAB (carbapenem susceptible *A. baumannii*) isolates. Other than efflux pumps and outer membrane proteins; class-D beta-lactamases ($\text{bla}_{\text{OXA-23}}$, $\text{bla}_{\text{OXA-24}}$, $\text{bla}_{\text{OXA-51}}$ & $\text{bla}_{\text{OXA-58}}$), class-B beta-lactamases (IMP-1, VIM-2, SIM-1 and NDM) and ampC beta-lactamases were also studied. Multi Locus Sequence Type (MLST) of *A. baumannii* isolates was performed and looked for the clonal spread of *A. baumannii* in various ICUs and wards of Nehru Hospital. A total of 47 Sequence Types (STs) were identified. Out of 47 STs, 28 were assigned as novel STs represented by 41 isolates and rest 19 STs already existed found in 56 isolates. ST-451 was found out to be most common ST, represented by a total of 13 isolates. ST-451 is the 'Founder ST' for 41 isolates in this study.

Center of Excellence in Infectious Disease Biology: Molecular Machinery of *Plasmodium*: Signaling, Autophagy and UPS: This Center of Excellence is directed at understanding mechanisms that drive

critical processes like signaling, trafficking, protein degradation and autophagy in malaria parasite.

Program Support on Molecular Parasitology: One of the major objectives of this program support is training, outreach and distribution of parasites. As part of these programs, debate competition, conferences and workshops on different parasites (at least one every year) have been organized and an internship program for training masters' students in Parasitology has been conducted. Parasite cultures/DNA/RNA were also distributed to individual researchers along with custom training on parasite cultivation.

Molecular Dissection of and Inhibitor Discovery against Motors Associated with Protein Translation in Malaria Parasites: The OSRP grant awarded to understand the roles of critical protein translational machinery proteins in parasitic diseases like malaria. Efforts have been directed towards structure-function studies that can probe these motors as new drug targets. Towards this, the three dimensional structures of N terminal GST-like domain of multi-synthase complex (MSC) component protein p43 from *Plasmodium falciparum* and *Plasmodium vivax* have been determined. Crystal structure analysis and biochemical characterizations have been carried out for *Plasmodium falciparum* and *Toxoplasma gondii* in organic pyrophosphatase (PPase).

Malarial Parasite Biology: An Avenue to Discover New Drug Targets: Studies in Phase I of the project established that curcumin- arteether combination therapy is very effective in the treatment of parasite (*P. berghei*) recrudescence and cerebral malaria in mice. The studies have been extended to nanocurcumin (PLGA-curcumin) to examine whether it is superior to native curcumin in view of the poor bioavailability of native curcumin.

Hepatitis C Virus – Phase II: Studies with pure natural compounds (Corilagin) extracted from *Phyllanthus amarus* has revealed that in addition

to preventing HCV entry and replication, Corilagin can also prevent the host from HCV induced ROS production and subsequent liver damage. This is mediated by inhibition of the TGF- α mediated upregulation of the NOX4 pathway. The results have also demonstrated Corilagin successfully inhibits HCV induced EMT progression in the infected cells. A unique neutralizing epitope encompassing C terminal 45 aminoacids of the HCV envelope (E2) protein was identified. Further, the monoclonal antibodies (A8A11 and C10E8) generated using the 45mer synthetic peptide (E2C45) successfully neutralized HCV infection (upto 80%) in infectious cell culture system. The combination of mAbs were effective against both gt2a and gt3 virus which drastically reduced the number of infectious foci in infectious cell culture system. Using HCV-like particles (HCV-LPs) corresponding to genotype 3a three mAbs (E3D8 and A10F2) have been obtained specific for the E2 protein that significantly inhibited virus binding to hepatocellular carcinoma cells. Screening of herbal extracts using the HCV-LP liver cell interaction assay showed identification of a flavonoid, termed rutin isolated from *Prunus domestica* (Plum fruit) as a new entry inhibitor against HCV. Rutin significantly inhibited HCV-LP binding to hepatoma cells, and inhibited cell-culture derived HCV (HCVcc) entry into hepatoma cells. The present investigation has also demonstrated preferential delivery of phyllanthin and corilagin to liver cells using functionalized amine terminated mesoporous silica nanocapsules to inhibit HCV in the infectious cell culture system.

Salient achievements of the achievements from the projects funded are as follows: Immunodiagnostic kits for detection of specific IgG and IgE antibodies to *Aspergillus fumigatus* in sera of patients of bronchial asthma and Pulmonary tuberculosis was Indigenously developed and clinically validated. The AfuPEP kit is becoming available as a "capture reagent to detect IgG and IgE in serum of suspected Afu infected cases" to Indian as well as foreign companies having interest

in development and manufacturing of *Aspergillus* screening and/or diagnostic assays. This is a ready to use, validated, low cost, assay technology having better diagnostic efficiency as an indigenous alternative to ImmunoCAP for Indian, Regional and Global diagnostic industry.

Data on differential diagnosis of patients with *A. fumigatus* infection having similar clinical picture to that of Pulmonary tuberculosis would be made possible for further clinical exploitation in national TB program in order to support these patients with antifungal therapy for a promising prognosis. In another study on rapid diagnosis of *Aspergillus*, a Dot Blot format has been developed. In comparison to the commercial kit, the monoclonal antibodies rapidly detected the presence of the galactomannan antigen, indicative of *Aspergillus* infection.

Sepsis, including neonatal sepsis, is an important and a major cause of death and suffering. Many of the patients of sepsis are admitted to the Intensive Care Units and do not survive. Today, there is not a single drug molecule that is specific for sepsis, pointing to lack of precise understanding of the biological phenomena underlying this condition. A program in sepsis was supported with the objective of identifying modifiable factors that impact the outcome of sepsis. In this study, blood samples are collected from human subjects with sepsis at various time points. By diligent analysis of circulating cellular gene transcripts, a robust set of genes associated with the advanced stage of sepsis have been identified. This novel finding provides a possible explanation for some of the complications seen in survivors of sepsis.

Tuberculosis:

Tuberculosis (TB) is an airborne infectious disease caused by organisms of the *Mycobacterium tuberculosis* complex. Although primarily a pulmonary pathogen, *M. tuberculosis* can cause disease in almost any part of the body. In many

low-income and middle-income countries, TB continues to be a major cause of morbidity and mortality.

DBT has been supporting research on Tuberculosis for the past two decades with major focus on disease biology, drug discovery and vaccine research. DBT has implemented various projects and also supported Centres of Excellence (CoE) that involves various institutes for research activities that ranges from basic sciences to translational research. In the CoE team supported at University of Delhi South Campus and International Centre for Genetic Engineering and Biotechnology, a new improved method was developed to evaluate the inhibitory potential of a candidate compound against *Mycobacteria* residing in phagosomes. In another project involving All India Institute of Medical Sciences, New Delhi and Indian institute of Science, Bangalore CoE team has developed a Vitamin 'C' model as a valuable system to probe host interactions with dormant MTB that will provide an understanding of cellular events in host-directed therapeutics. Under the network programme implemented at National Institute of Biomedical Genomics, West Bengal, International Centre for Genetic Engineering and Biotechnology, New Delhi and Jawaharlal Nehru University, New Delhi the team has been working on pathways regulating host cellular homeostasis that are more relevant than pro-inflammatory cytokines for governing *Mycobacterial* growth at early stage of infection.

Taking into account the fast spread of multidrug resistant and extensively drug resistant Tuberculosis in the country focused efforts to generate proposals was anchored.

Further, DBT and ICMR has signed a MoU on Biomedical & Health Research wherein Tuberculosis was marked as critical area of partnership with prime focus on TB diagnostics. The purpose was to strengthen the locally developed technologies. A project on validation of indigenously developed

technologies for diagnosis of pulmonary tuberculosis and multi-drug resistant tuberculosis, four major institutions and two Indian companies are involved in a tightly governed exercise. The TrueNat RIF kit is found to be comparable to the GeneXpert in-terms of sensitivity and specificity. An operational feasibility studies are now planned to be conducted to find its implementations at District Medical centers under Revised National Tuberculosis Control programme.

Furthermore, DBT is supporting a drug trial Open-Label, Non-Randomized, Two –stage, Dose Finding study of Verapamil(IR) Tablet formulation in Adult tuberculosis Patients in Continuation Phase of Anti-Tuberculosis treatment carried out by National Institute of Tuberculosis for Research , Chennai. The study is the final phase of stage I. The study aims to find the correct dose of Verapamil to be administered along with Anti-Tubercular drugs in order to reduce the duration of the Chemotherapy.

NANO-BIOTECHNOLOGY

Nano-biotechnology Task Force has been engaged in advancing research and fostering innovations in cutting edge area of Nano-biotechnology to address various issues in health, agriculture and environment. Research outcomes arising out of the projects are evaluated for translational potential and support is extended for development of an application of the knowledge with translational values. Some of the highlights of the research work accomplished during the year are presented below:

Preclinical research was carried out to evaluate gold nanoparticles coated PLGA/PNVCL based therapeutics for treatment of cancer in a collaborative effort by IIT Bombay and ACTREC, Kharghar. As an outcome, Toco-Photoxil® was developed which is core-shell type nanostructure, where core consist of TPGS (d-alpha Tocopherol Polyethylene Glycol Succinate) emulsified PLGA, and the shell is made up of biocompatible inorganic Material-Gold.

Novel polymer nanoparticle based drug releasing systems were developed at RGCM Trivandrum to improve the efficacy of drug administration in cancer therapy. It was demonstrated that Poly (lactide-co-glycolide-polyethylene glycol [PLGA-PEG] folate based nanoparticles-encapsulation improved the solubility of curcumin in aqueous medium and gel form, which further enhanced its efficacy to induce apoptosis in cancer cells. Tumour reduction study conducted using HeLa xenograft models in female NOD-SCID mice demonstrated that folic acid conjugation of PLGA Nano-curcumin improves the chemosensitizing efficacy of curcumin. In similar studies, methacrylic based copolymer was developed by micro emulsion polymerisation technique and studied for in vitro drug 5-Fluorouracil (5-FU) release. Biological evaluation of the nanogel confirmed that the gel can be successfully used as an efficient vector for pH sensitive and controlled delivery of drugs specifically to colon.

Studies were carried out at NCCS, Pune to develop peptide nanoparticle mediated drug/siRNA delivery system to suppress progression of tumor vasculature and angiogenesis in breast and prostate cancers. The invention led to improved solubility, bioavailability and specificity of anti-cancer therapeutic agents by ligand-receptor mediated targeting of tumor using cyclic-peptide (arginine, glycine and aspartic acid, serine) conjugated chitosan nanoparticles (cGRGDS-CHNP). cGRGDS-CHNPs were synthesized with high drug loading and well-defined physicochemical properties and loaded with various anticancer drugs such as raloxifene, andrographolide and curcumin alone or in combination. Enhanced uptake of cGRDS-CHNPs was demonstrated using FITC (Florescence Isothyocyanate) in $\alpha 5 \beta 3$ integrin over-expressing cells. cGRDS-CHNPs also enhanced the inhibitory effect of drug loaded CHNPs on cell viability, cell motility and *in vitro* angiogenesis in breast cancer cells. Tumor imaging Cy5.5 conjugated cGRDS-CHNPs showed substantial accumulation with high contrast in breast tumor grown in NOD-SCID mice

and significantly inhibited the breast tumor growth which suggest that cGRDS-CHNPs could be an effective strategy for targeted therapeutic delivery in breast cancer.

Translational research studies were continued at IISC Bangalore to develop plant virus-like particles (VLPs) as Nano carriers for therapeutic purposes. *Sesbania mosaic virus* coat protein (CP) was genetically engineered with the B domain of *Staphylococcus aureus* protein A (SpA) at the α H- α L loop, to generate SeMV loop B (SLB), which self-assembled to virus like particles (VLPs) with 43 times higher affinity towards antibodies than protein A. Chimeric SLB VLPs were shown to enter mammalian cells and deliver the antibodies pre-bound to them and were shown to be functional in neutralizing the effect of the target protein more effectively than the corresponding antibodies which usually cannot enter the cells. Another interesting lead obtained that DNA intercalating drugs/dyes such as Doxorubicin/DAPI can be easily infused into the native virus that remains bound to the genomic RNA and can be delivered to cancer cells. The structure of the chimeric VLPs expressing the B domain of SLB has demonstrated the plasticity in the CP and could be engineered into various other peptides of therapeutic interest. Thus, the study has shown that chimeric VLPs are potentially capable of delivering therapeutic antibodies and drugs. It has also shown that the delivered antibodies/drugs work at much

lower concentrations. This important finding if proved *in vivo* can reduce the cost of treatment and minimize side effects. Preclinical studies are in progress.

An intrinsically fluorescent self-assembled organic nanoparticles was developed at CSIR-IICT, Hyderabad to deliver active molecule such as Si RNA in tissue specific environment. The developed Nano system is intrinsically fluorescent and are surface functionalized with material that is non-toxic. It was shown that the Si RNA encapsulated in the Nano system protects Si RNA from endonucleases and are permeable to cells with good clearance and non-toxic to cells. In a similar effort, pH sensitive dual carrier biocompatible liposomal nanoparticle delivery system was also developed for the delivery of more than one therapeutic molecules. This pH-sensitive liposomal Nano carrier effectively delivers chemotherapeutic drug and siRNA, and significantly inhibits cell proliferation and reduces tumor growth. This present invention also provides the effective tumor targeting with chemotherapeutics through pH dependent manner.

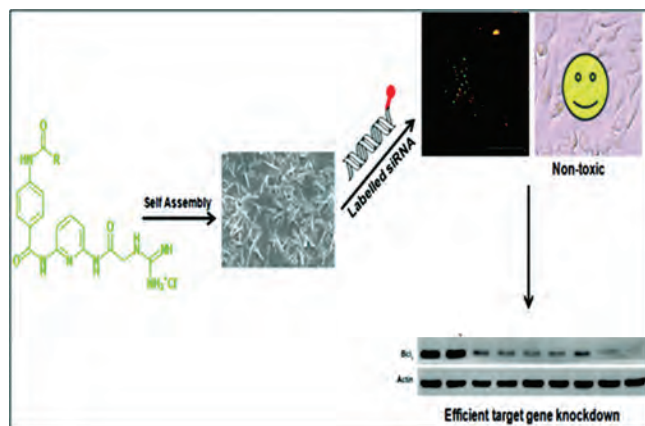
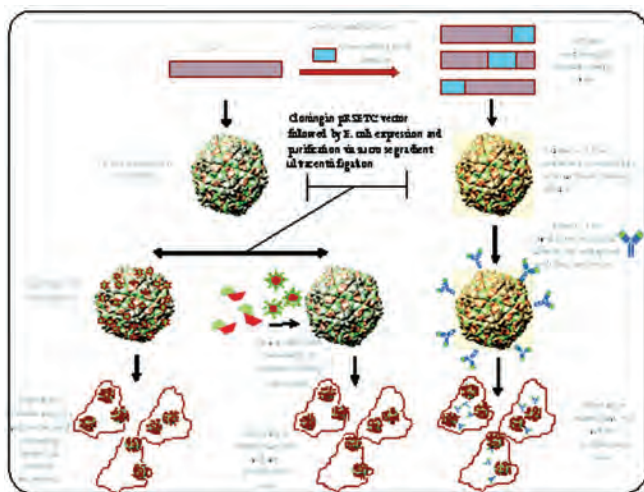
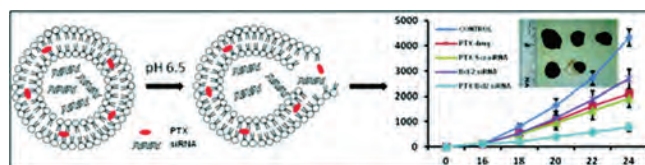


Fig Si RNA delivery nanosystem



At Anna University, Chennai, a bio-integrating surface with rapid bone remodeling and resistant towards corrosion and wear was developed using simple sol-gel technology. Heat treatment of the single layer made up of mixed metal oxide like ($\text{TiO}_2 - \text{ZrO}_2$, $\text{TiO}_2 - \text{SiO}_2$, $\text{TiO}_2 - \text{Nb}_2\text{O}_5$ and $\text{TiO}_2 - \text{Ta}_2\text{O}_5$) and the second layer constituted of strontium incorporated hydroxyapatite (Sr-HAP) gave the coating stable adherence and resistance to dissolve in the electrolyte rapidly. The fabricated Sr-HAP provided a good platform for the integration of the bone with the implant surface. The dissolution of Sr ions in the initial stages help in the rapid recruitment of the osteoblast cells which aids in rapid bone remodeling. Also the surface modified Ti provide a niche for cells to adhere, proliferate and differentiate. Further studies are in progress to develop an application of the system in orthopedic implants.

Studies were carried out at NCL, Pune to develop inorganic metal nanoclusters based fluorescence probes for bacterial quorum sensing detection. Development of fluorescent Au and Au-Ag bimetallic nanoclusters were functionalized with different bacterial signal molecules of the family homolactone serines. The structure of the composite was designed such that the bioactivity of the signal molecule, vis-à-vis their binding sites to the receptor proteins, is intact after interacting with the fluorescent nanoclusters. This material is hence capable of selectively identifying the bacteria based on the type of signal molecules used. This probe also targets the binding sites for QS molecules within bacterial cells and not the concentration of signal molecules produced which is the current practice. This property makes these systems independent of cell density and can be used before the bacteria attain a virulent quorate state.

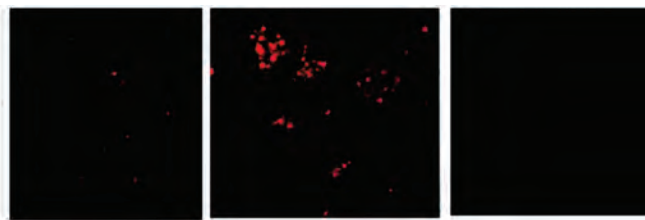
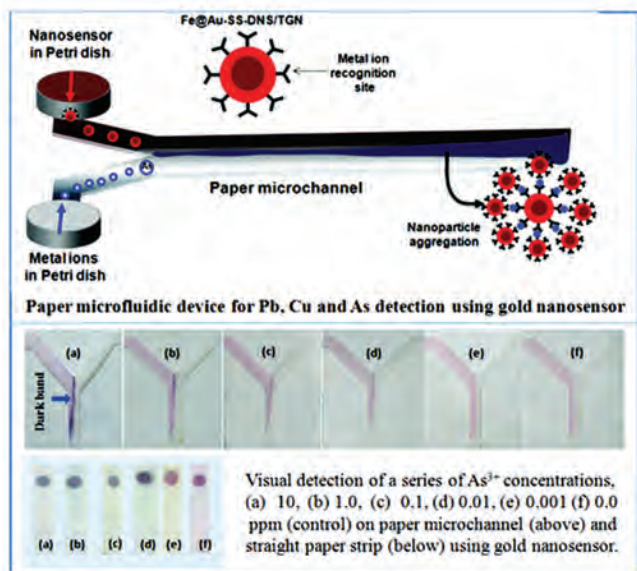


Figure 1. Confocal fluorescence images of bacteria incubated with different probes functionalized with different signal molecules: (left) E coli with C6 signal molecule (middle) C sakazaki with C12 signal molecule and (right) C sakazaki with C6 signal molecule. This indicates that we can identify the bacterial strain by varying the signal molecule functionalisation.

Disposal of the fleshing waste is a major challenge faced by the tanners worldwide due to the strict environmental regulations. Hence, studies were undertaken by CSIR-CLRI, Chennai for utilizing the fleshing waste to generate a value added material. Fleshing was converted into nano-fibers through electrospinning as a sound absorbing material for acoustics application. In similar line of studies, a novel silk fibroin based nanofibrous scaffold with antioxidant properties was also prepared by electrospinning method. These scaffolds contain fenugreek, a natural antioxidant and they accelerate the wound healing process by reducing adverse effects of reactive oxygen species generated at the wound site. In addition, these scaffolds showed superior thermal, mechanical properties and biocompatibility than the pure silk fibroin nanofibrous scaffolds.

At CSIR-CMERI, Durgapur studies were carried out to develop Gold-Iron Oxide Based Smart Magnetic Nanosensor for Detection and Separation of Heavy Metal Ions. A set of new fluorescent probes, DNS-SS, AMC-SS and TGN-SS was synthesized and immobilized on the surface of gold nanoparticle (AuNPs) to develop the initial gold nanosensors, i.e. Au-SS-DNS, Au-SS-AMC and Au-SS-TGN. While DNS-SS and TGN-SS could rapidly detect very low concentrations of Pb^{2+} , Cu^{2+} and As^{3+} respectively,

on the other hand. AMC-SS remains non-responsive to any of the ions. The nanosensors develop visible bluish-black color in solution and microdevice, because of the formation of nanoparticle aggregates upon binding with metal ions. (Figure below)



A novel electrospun polycaprolactone (PCL) based composite scaffold having potential application for bone tissue engineering was developed at SreeChitraTirunal Institute for Medical Sciences & Technology, Trivandrum. The study aids in providing solution for improving the surface wettability and tuning the biodegradation behavior of PCL. Incorporation of nHAP and blending with the synthesized copolymer polycaprolactone-polyethylene glycol-polycaprolactone (CEC) improved the overall biodegradation, hydrophilicity, mechanical properties and biocompatibility of PCL scaffolds. The study provides appropriate composition of PCL/CEC blend ratio and the electro spinning process parameters suitable for fabricating scaffolds with superior properties. The fabricated PCL/CEC/nHAP composite scaffold has the potential to be used as bony constructs for tissue engineering applications.

A gold nanoparticle based dipstick format for detection of mushroom toxin was developed at

Department of Agricultural Biotechnology, AAU, Jorhat. Antibodies were generated against the Phallacidin (PCN) toxin present in poisonous mushrooms which is a bicyclic heptapeptide belonging to the phallotoxin family is highly hepatotoxic. The antibodies showed high sensitivity and selectivity towards the cyclopeptides group of toxins such as Amatoxins and Phallotoxins. The immunoassay format developed can detect a limit of Phallacidin of 13.01 ng/ml whereas for α -Amanitin, it was 7.64 ng/ml. Dipstick based detection was developed and can detect toxins with high sensitivity. The developed immunoassay can be used as a potential and convenient quantitative tool for screening of toxin in wild mushrooms.

NATIONAL BIORESOURCE DEVELOPMENT PROGRAMME

The National Bioresource Development Board (NBDB) was set up in 1999 with a mission to evolve a broad policy framework for R&D for sustainable utilization of bioresources and an effective plan of action for economic prosperity of the nation through accelerated R&D using modern tools of biosciences. NBDB focuses on the application of biotechnological and related scientific approaches for R&D and development of new products and processes sustainably utilizing the rich biodiversity of our country.

During the 12th Plan period, the thrust under National Bioresource Development Board on value added products from Biomass and Bioresource. With the rich Biomass and Bioresource reserve, the main emphasis is to move towards a Biobased economy. To achieve the goal projects are being supported for both basic and translational research. The three major categories of the programme are:

Energy Biosciences Programme (Biofuel)

Bioresource Development and Utilization

Plant Tissue Culture (National Certification System for Tissue Culture Raised Plants (NCS-TCP)

Some of the salient achievements of the programmes are highlighted as follows:

A. Energy Bioscience Programme (Biofuel)

Recognizing the need for alternate energy for transportation, Department of Biotechnology has been promoting R&D for biofuel technology development. Many leads have been achieved from the research since last 5 years with potential translational value in field. Mission Innovation which is one of the major initiatives being coordinated by Department on behalf of Government of India, was launched in November 2015 in Paris with a common aim of 23 participating countries to reinvigorate clean energy innovation with a shared commitment to double the investment in R&D and Demonstration to make Clean Energy accessible and affordable. India has committed for doubling of investment in Clean Energy R&D by 2019 as announced by Minister S&T during Mission Innovation Ministerial held in June 2016 in San Francisco. This has been launched through collaborative efforts have of the Department in consultation with other concerned Ministries / Departments like DST, MNRE and Ministry of Power. DBT is also participating in the Swachh Bharat Mission through a range of initiatives and one of them is generation of energy from wastes. Proposals have been invited and selected to develop and demonstrate technologies for sustainable utilization municipal solid waste for cleaner and pollution free environment as well as generation of the energy.

Technology Transfer of 2G cellulosic ethanol technology developed by DBT-ICT Center to Oil Marketing Companies (HPCL and BPCL) for commercial plant. While progress is made for commercialization of 2G ethanol technology, the efforts are continued towards development of next generation biofuels like algal oil, bio butanol and bio hydrogen. Capacity building in Bioenergy was strengthened by launching Bioenergy Awards in

Cutting Edge Research (B-ACER) and continued support to Energy Bioscience Overseas Fellows and Chair to pursue research in Indian institutes.

Under Partnership for Advance Clean Energy Research (PACE-R) between India and US, the Joint Clean Energy Research and Development Center (JCERDC) has been designed to promote clean energy innovation by teams of scientists and engineers from India and the United States. This bilateral activity is also coordinated by DBT. Public private consortia are jointly funded in three priority areas; Solar Energy, Energy Efficiency of Buildings and Second Generation Biofuels. During last year this research cooperation extended further by launching a new research track in Smart Grids and Energy Storage in collaboration with DoE US and DST India. While ongoing projects on Sustainable biofuel development is progressing well by Consortium led by IICT Hyderabad, opportunity has been given to two more consortia lead by IIP Dehradun and JNU New Delhi to address the existing challenges in biofuel development.

In 2016 more than 100 research papers published and about 10 patents filed by Investigators from 04 Bio-energy Centers and R&D projects supported by DBT at various other institutes.

Under the bio-energy scheme promoted by DBT Center of Excellence, R&D projects, International cooperation and Capacity building through fellowships and awards were sanctioned. The Road Map for the Bioenergy sector outlines the long term goals to achieve cost effective clean energy development.

Bio-energy Centers: Following four DBT-Bioenergy Centers exist with specific goals and targets set by Department aligned to the National Biofuel Policy.

DBT-ICT Centre for Energy Biosciences, Matunga, Mumbai

DBT-IOC Centre for Advanced Bioenergy, Faridabad

DBT-ICGEB Centre for Advanced Bioenergy, New Delhi

DBT-Pan-IIT Center for Bioenergy (participating 5 IITs)

DBT-ICT Centre for Energy Biosciences, Institute of Chemical Technology, Mumbai

This is the first Bioenergy Center of Department and currently support extended for Phase II to take forward the leads from Phase I activities. Following are the highlights of achievements:

The Lignocellulosic Ethanol Phase II Demonstration Plant based on the DBT-ICT 2G-Ethanol Technology was erected by India Glycols Limited at their site at Kashipur, Uttarakhand. The demonstration plant was inaugurated on 22 April 2016 by Hon. Dr. Harsh Vardhan, Minister of Science and Technology and Earth Sciences. This technology is ready for commercialization. BPCL and HPCL would set up a 400 tonnes plant to produce 100L tonnes of ethanol per day (3 crore liters/year) by 2018.



The Centre has designed and implemented novel continuous, faster, and smarter enzymatic saccharification process for cellulose with the lowest enzyme dosage. This technology with much wider application to a number of biochemicals and chemicals is currently operational at the India Glycols Ltd. 10 ton/day lignocellulosic ethanol demonstration plant at Kashipur.

A complete robotic platform for enzyme screening and engineering has been designed and erected in collaboration with Perkin Elmer, Germany/India. This unit with a colony picker, a liquid handling device and other molecular biology tools has provided a great impetus to the synthetic biology and meta-genomic screening efforts at the Centre.

The Centre has developed a novel technology for algae based sewage treatment technology that is both efficient and rapid and results in near drinking quality water.

A total of five (5) patents have been granted in the year 2016 for various technologies developed at the Centre. One Australian and one Philippines patent has been granted for '*Methods for production of Fermentable Sugars from Biomass*'. One Canadian and one Japanese patent have been granted for "*Fractionation of Biomass*". A patent for "*Enzymatic process for fat and oil hydrolysis*" has been granted in Singapore. Eight (8) new provisional patent applications have been filed during the year 2016.

DBT-IOC, Centre for Advanced Bioenergy Research, Faridabad

DBT IOC Centre has completed four years and the major thrust of the centre has been to develop viable 2nd generation biofuel technologies in new areas of second and third generation biofuels, such as ligno-cellulosic ethanol and algal fuels. The Centre got equipped with state of art facilities in Enzymes scaleup & Fermentation such as for SSF Bioreactor from Infors (first in India), Industrial scale filter press for enzyme scaleup, Membrane filtration system for enzyme concentration, Refinery Gas Analyzer etc. Major achievements of this Centre in last year are as below:

Bench scale process optimization done for high titre enzyme production in mutant strains (8-10 FPU & productivity of 80-100 FPU/litre/hr) at 5 litre scale. Enzyme production scaled up in 150 litre Fermenter

facility. This enzyme is benchmarked against world's best enzyme & its successive trials shall lead to large scale enzyme production at toll manufacturer site and supply to 2nd Generation Lignocellulosic ethanol plants. This is first such attempt in India.

Novel step pretreatment process developed at 250 kg/day pilot scale for rice straw & bagasse at lower cost and low acid concentration to produce high sugars at minimum inhibitors.

The centre has optimized Simultaneous Saccharification & Co-fermentation process (SSCF) using available ethanologenic GMO for fermentation efficiency of Xylose / glucose in terms of yield, productivity, inhibitor tolerance.

BERC is in the process of integration of whole process from Biomass to ethanol at 10 ton per day scale. This demo plant is expected to commence operation by 2019 at new R&D campus of IOC and the data generated shall be used to set up a commercial plant based on indigenous technology. The technology will be bench marked with best available in terms of cost of delivered ethanol and both on Capex / Opex and thereafter 100-250 TPD plants will be set up. As a research outcome 11 publications obtained with two processes patented.

DBT-ICGEB Centre for Advanced Bioenergy Research, ICGEB

DBT-ICGEB is the third Bioenergy Center of DBT set up at International Centre for Genetic Engineering and Biotechnology, New Delhi. The research focus of this Center is on use of molecular tools to engineer microbes, Cellulytic enzymes, algae for enhanced biofuel production. Recently the center has developed capabilities in Systems biology. The major achievements in this year are as below.

Cellulase enzyme composition identified giving efficiency equivalent to best commercial enzyme. Complete application and PCT filed in July 2016.

Fungal genome engineering tools including CRISPR/ Cas9 developed. A repressor deleted in the fungal genome to improve enzyme titer by two fold.

Technology for C5 fermentation developed using non-foreign gene approach; engineered strain may be considered non-GMO. US Patent US2014424037A granted on 16th Dec 2016.

New pathway discovered in bacteria for long chain alcohol production, complete patent application filed on Dec 2016 (ref no. 4260/DEL/2015).

Genetic modification tools for algal strains developed and high lipid and biomass producing marine algal strain engineered. Patent filed.

Total 23 papers published from this Center during year 2015-16 and filed 05 patents applications on various aspects of bio-energy production

DBT-Pan IIT Center for Bioenergy:

This is the largest virtual Bioenergy Center established by DBT in 2015 comprising 22 sub projects and 32 project investigators under 5 Thematic areas and 7 Research groups. Laboratories at various IITs facilitated with the infrastructure for molecular biology, fermentors and LCMS experiments. The achievements are briefed below.

Algal Bio-energy Process Engineering: Novel reactor design was developed and patented. Bio-hydrogen is produced from harvested algae at concentrations of 1-8g/L with fatty acids, acetate and butyrate.

Strategies for Enzyme & Strain Improvement: α-glucosidase enzyme was expressed and purified. Glucose-glycerol (60:40) substrate combination mixture resulted in maximum butanol and ethanol titer 11.2 and 11.7 g/L respectively. Bioprocess strategy, coupling media optimization increased the butanol titer to 13.1 g/L with an overall productivity of 0.55 g/L/h.

Bioreactor Design: A mixed pretreatment strategy was developed which removed lignin and loosened bagasse compared to individual pretreatments. An adaptive MPC was developed for the output error (OE) models parameterized using generalized orthonormal basis filters (GOBF).

International Collaboration in Clean Energy:

Indo-US Joint Clean Energy Research and Development Centre: Indo-US Joint Clean Energy Research and Development Centre (JCERDC) is being coordinated by Department in collaboration with DST. The Biofuel consortium is supported by Department while consortium for Solar and Energy Efficiency of Buildings are funded by DST. Last year new research track has been launched for Smart Grid and Energy Storage and funding announcement was made by both countries. Proposals received jointly are being peer reviewed.

The Biofuel consortium is co-led by the Indian Institute of Chemical Technology-Hyderabad and the University of Florida-Gainesville. The U.S.-India Consortium for development of Sustainable Advanced Lignocellulosic Biofuel Systems emphasizes on sustainable feedstock cultivation and supply, biochemical conversion technologies for production of second generation biofuels with minimal environmental impact, and analysis of overall sustainability and supply chain of feedstock.

Capacity Building: Energy Biosciences Overseas Fellowship is a re-entry scheme for scientists of Indian origin who are working outside the country in the field of Energy Biosciences. Since 2009, ten awardees with diverse expertise have returned to India and are working with the DBT Bioenergy Centers IISER, IITs and other institutes. An Energy Bioscience Chair was awarded to a senior scientist who is currently working at DBT-IOC Center and

leading a team of researchers in the area of Biomass characterization.

Recently, Bioenergy Awards for Cutting Edge Research 'B-ACER' well launched for Ph.D. students and young scientists from India to interact with American peers and helping build long term R&D linkages. The purpose of this award is to nurture future innovators and thought leaders in Biofuel and Bioenergy. More than 50 applications received from young scientist and students.

R&D Projects supported to various institutes :

Pretreatment of cellulosic biomass for ethanol production: Microwave based pretreatment: An integrated approach for the development of microwave systems for pretreatment of lignocellulosic biomass was conducted at Central University of Rajasthan and optimization of microwave assisted pretreatment of rice straw with ferric chloride in combination with orthophosphoric acid was performed successfully.

Virtual Enzyme Center: This is a network project involving 6 partner institutes JNU, South Campus Delhi University, DBT-IOC Centre Faridabad, IIT Madras, Anna University, IIT Bombay. The aim is to develop robust and cost effective indigenous enzyme for cellulosic ethanol production. So far fungal strains isolated showing enhanced cellulase activity in SSF. Improved saccharification efficiency obtained in packed bed reactors in comparison to slurry reactors.

Ethanol from food waste: At Punjab University a complete technology has been developed for the bioconversion of Biodegradable municipal solid waste residues into ethanol involving the processes for the production of a cocktail of multiple carbohydrases, enzymatic hydrolysis of biodegradable municipal solid waste, followed by fermentation of released sugars into ethanol.



Facility developed at Punjab University, Chandigarh under DBT project 'Biorefinery for cost effective bioethanol production from biodegradable municipal solid waste: technology development and its validation at pilot scale'

Ethanol from textile mill waste: Enzymatic hydrolysis of pretreated cotton waste with fungus (*Trichoderma reesei*) at optimum conditions released sugar was higher in treated cotton waste (Chemical followed by enzymatic hydrolysis) and the amount of 62% of free sugar was converted from complex form. The fermentation of the treated cotton wastes was performed using immobilized cells of *Zymomonas mobilis*. The estimation of the ethanol production was unerringly 0.48 % in 1 ml of treated cotton sample.

Computational Fluid Dynamic (CFD) Modeling of Algal Photobioreactors for CO₂ sequestration and Conversion to Value Added Products: CFD model of 1000L capacity outdoor open raceway pond operating at CFTRI was developed by IISc Bangalore which predicts the effect of hydrodynamics and pond geometry on velocity distribution profile and mixing. Further many multi-optional closed photo bioreactor system was indigenously designed and fabricated by CFTRI to study of effect of mixing and light on photo bioreactor performance.

Algae production in industrial waste water: Rubber waste water collected by TERI Guwahati was tested for the fungal consortium 3a (*Chlorella*, *Chlamydomonas*, *Chlorococcum*, *Volvox*) found best w.r.t. biomass and chlorophyll a & b production.

Another study has been supported to TERI New Delhi where microbial based bioprocess developed

for hydrogen production by *Enterobacter cloacae* strain DT-1 from baggase and what straw. *Enterobacter cloacae* DT-1 could utilize vegetable market waste treated leachate and sugar industry distillery effluent as substrate to produce hydrogen through dark fermentation route.

B. Bioresource Development & Utilization

Overall aim of the bioresource development & utilization programme is to support research and development activities on inventorisation, characterisation, evaluation and value addition of novel bioresources leading to their conservation and sustainable utilization, biotechnological interventions for improving the availability, productivity and quality of important bioresources, value-addition and industrial utilization, the latter preferably in collaboration with appropriate industry partner and capacity development and public outreach on bioresources importance, diversity & conservation. During the year, some notable scientific leads have been obtained which are being pursued further. New projects on green synthesis of iron nanoparticles from manglicolous fungi of Indian Sundarban and their application in sequestration of heavy metals from contaminated water, assessing the genome sequences of *Termitomyces clypeatus* for novel metabolic discovery, bioprospecting of anti-microbial peptides from Hymenopteran etc. have been initiated.

Following are some of the salient achievements made in the programme.

A Microbial Repository Centre (MRC) has been established at IBSD, Imphal with an aim to act as the nodal centre for deposit, preservation, maintenance and supply of microbial resources originated from the rich and unique ecological niches of North East (NE) India. A total of 21,631 cultures (18777 bacteria, 739 probable actinobacteria, 1881 filamentous fungi and 234 yeasts) collected from various ecological niches of

NE India, including cultures available from and deposited by the microbiologists of NE institutes and universities, have been accessioned and preserved. A total of 20,000 cultures have been characterized using different methods such as MALDI-TOF MS, DNA sequencing and phenotypic characterization.

In the project on bioresource inventorization with a focus on bioprospecting of *Pteridophytes* of Western Himalaya, isolation and identification of the major molecules present in *Adiantum*, *Diplazium* and *Pteridium species* has been carried out at IHBT, Palampur. Pesticidal activity and wound healing properties of extracts prepared was also evaluated. Natural color and dyes from pteridophytes was assessed and was found in between 1.0-5.0%. It was observed that *Diplazium maximum* and *Diplazium esculentum* are very potent source of natural carotenoid Lutein. The different extracts and fractions of *Diplazium maximum* and *Diplazium esculentum* have excellent nutritional profile and displayed potential antioxidant activity. A simple new technique called ETAF (Extra Thin Alginate Film technique) has been developed to track individual spores of fern and fern allies. A total of 388 fern samples comprising 53 species were collected from 22 locations of Western Himalaya and preserved for creation of DNA bank.

In the network project on plant chromosome database for Spermatophytes and Archegoniate, collation of cytogenetical data for 2474 Species, 401 Genera, 65 families of Spermatophytes and Archegoniate have been completed. Cytogenetical account of 401 genera have been compiled and finalized on the basis of information collated for species under each genus. Taxonomic verification/ validation/ editing/ for 8 genera and 155 species is in progress. Improved data entry software and advanced search software according to data entry format for a comprehensive Chromosome and Genome size database have been developed. The plant Chromosome Databases available till date in

the world, report merely somatic and gametic chromosome numbers. The present unique Database of all the higher plants (Spermatophyta and Archegoniatae) reports all information w.r.t. Molecular and Cellular Cytogenetics, including Nuclear DNA content and Nomenclature Intrigues.

In the network on Morphometry and Phylogeography of honey bees and stingless bees, 120 grids were identified for sampling and collection. Samples of *Apis cerana*, *A. dorsata*, *A. florea* and *Tetragonula sp.* have been received from 16, 15, 14 and 12 grids respectively and added to the repository. Morphometric studies of *A. cerana*, *A. florea* and *A. dorsata* has been accomplished from 6, 3 and 1 grids respectively. DNA isolation and quantification completed for samples received. Of 20 microsatellite primer pairs, 10 showed good amplification. Additional SSR markers for *Apis spp* identified.

In the Network project on biotechnological interventions for pharmaceutically valuable compounds from forest resins detailed survey resulted in the identification of a few natural habitats of the targeted plant species *Commiphora mukul* and *Boswellia serrata* for further utilization of these species. Some of the bioactive compounds obtained from these plants seem to be novel in respect of their structure and pharmacological activities.

In the project on chemical profiling of turmeric from different agro-climatic regions and optimization of environmental parameters for high curcumin yield at SOAU, Bhubaneswar, turmeric rhizomes have been collected from 10 agro-climatic zones and analyzed for their curcumin content. The artificial neural network based prediction model for optimization of curcumin content has been developed based on environment parameters and soil sample. The experimental value of Curcumin and the predicted values were generally found to be closer and hence can be employed for enhancing the curcumin yield. Multilocational trial of selected

elite accessions of turmeric for analysis of curcumin content at different agro-climatic regions of Odisha is underway.

A study of the biodiversity and bioactive natural products of non-sporulating fungi associated with mangroves and sponges of Andaman Islands is being jointly conducted at VITM, Chennai and IITM, Chennai in collaboration with ICGEB, New Delhi. Leaves, stems and roots of seven mangroves were collected from Burmanallah of Andaman Islands and screened for the presence of endophytic fungi. Analysis has yielded some significant indications, overall progress has set the stage for identification of novel antimicrobial and antimalarial compounds from the fungal secretome.

Studies on isolation and characterization of xanthine oxidase inhibitors from endophytic fungi for treatment of Hyperurecemia and Gout are being jointly carried out at Thapar University, Patiala and NIPER, Mohali. Investigators have screened 120 endophytic fungi using *in vitro* qualitative and quantitative Xanthine oxidase (XO) inhibitory assays. From the primary and secondary screening, six fungal isolates were found to be true XO inhibitors (> 70%).

Characterization and consolidation of *Hippophae* genetic resources and propagation of elite genotypes for varietal evaluation is being done in network mode. 380 accessions collected by the five network centres are at different stages of gene banking, nursery conservation and propagation. Field nurseries have been established. Chemical and molecular characterization work is underway.

Under Programme Support on biotechnology approach for conservation and sustainable utilization of plant wealth of Western Ghats being implemented by JNTBGRI, Thiruvananthapuram in collaboration with six institutions, elite genotypes have been identified in high-value medicinal plants – *Bacopa monnieri* and *Centella asiatica* along with

developing and validating novel EST-SSR markers in *C. asiatica*. Plant-pollinator studies have been carried out in the context of habitat modification in Western Ghats.

Bioresource: Conservation and Digitized inventorization:

Microbial Culture Collection Centre (MCC) set up at NCCS, Pune: Microbial Culture Collection (MCC) was established in 2008 and since then it is preserving nations precious microbial resources. This is the largest such facility in the country which has IDA recognition under the Budapest Treaty and also acquired the status of 'Designated Repository' under the BD Act, 2002. It receives and distributes cultures to researchers and also offers variety of identification services. Considering its role as a supply centre of microbial cultures for high throughput screening programs, MCC is developing new methods for long term preservation of microbes, thereby strengthening the services section. In addition, the scientists are also actively involved in the research in the area of microbial ecology and taxonomy. As a part of these efforts, in the last year MCC described eight novel taxa from diverse ecological habitats.

The status of Microbial Repository at NCCS, Pune as an IDA makes it mandatory for it to have a continuous existence. Efforts are underway towards upgradation of existing Microbial Collection Culture (MCC) to a National Centre for Microbial Resources. The main goal of the proposed center is to establish world class infrastructure with the aim to preserve India's rich microbial resource and to make them available for long term sustainable use through an organizational structure equipped with state of the art facilities backed by expertise for conservation of and research on microbial diversity. Strong research and service components that are interlinked will form backbone of this activity. This would be crucial and critical to achieve India's Road Map on bio-economy.

Indian Bioresource Information Network: Indian Bioresource Information Network has been launched towards developing a single window gateway to access distributed bioresource database. It is the largest de-centralized bio-resource database including information on Data on 39,000 species of Plants, animals, marine organisms and microbes including the spatial database based on distributed architecture. It works on the principle of spatial data infrastructure wherein distributed databases available across the country are accessed through single window gateway. It provides spatial datasets on biodiversity and species datasets as core data nodes of IBIN. The end-user can also input the data through the crowdsourced mobile application. All the distributed data providers are retrievable through a single window (www.ibin.gov.in).

The IBIN data standards is developed by reviewing globally recognized data standards such as Darwin Core, Ecological Metadata Language, Plinian Core, Species Profile Model, and Access to Biological Collections Data to design the standard schema for the exchange of information about the species between multiple parties. The IBIN mobile app is designed and developed based on crowdsourcing approach. IBIN server is configured as a core data node to visualize the field data sent by the clients using mobile application.

The IBIN portal has a very strong biodiversity and bioinformatics component which needs to be expanded further. Efforts are underway for expansion of Indian Bioresource Information Network towards enriching species and spatial databases on Bioresources and Biodiversity of the country, promoting utilisation of IBIN for conservation, bioprospecting and bioresource education and integration of IBIN data on Bhuvan Geo-portal.

C. National Certification System for Tissue Culture Raised Plants (NCS- TCP)

DBT has established the “National Certification

System for Tissue Culture Raised Plants” (NCS-TCP) vide Gazette of India Notification No. F. No. 18-28/202-SD.IV dated March 10, 2006 under the Section 8 of the Seeds Act, 1966 to provide support to the tissue culture industry for propagation and distribution of virus-free and quality tissue culture raised planting materials. It is a dynamic and comprehensive system intended for facilitating production of quality tissue culture plants and providing mechanisms for certification of quality tissue culture plants. Since the implementation of the system in year 2006, it has been instrumental in building capacities for production and distribution of quality planting material.

At present, this certification system has standards for 8 crops, 5 Accredited Test Laboratories for testing of tissue culture plants and two referral centres for developing standards, referral testing and imparting training to Accredited Test laboratories. A comprehensive NCS-TCP guidelines and SOPs covering all the aspects of commercial tissue culture plant production have been developed for ensuring Quality Management System. A website (<http://www.dbtncstcp.nic.in>) has been developed. 96 companies have been recognized and 5 test laboratories and two referral centres have been accredited under this system. This year 87.46 million tissue culture plants have been certified by ATLS and 73,820 labels were issued. So far total 168.03 million of tissue culture raised plants have been certified and 1,58,440 certification labels have been issued.

This system is building capacity of tissue culture industry by increasing their visibility at National and International level. The tissue culture Companies recognized about five years ago have shown nearly two-fold increase in their production capacities. Besides this, there has been a significant improvement in infrastructure facilities of these companies in terms of maintenance of appropriate sterility levels inside the tissue culture laboratories, improvement in quality management of tissue

culture plants, documentation of procedures, etc. This has resulted in supply of virus-free and high quality tissue culture plants to growers/farmers by the companies leading to increase in market demand and visibility of this industry. Number of incidence of virus infection has been significantly reduced and no major virus outbreak has been reported during last few years since implementation of certification programme.

In order to sensitize the stake-holders, DBT has organized series of State level Awareness programmes to create widespread awareness so that the potential of this quality management system is realized and end users are benefitted. In year 2016, awareness programmes on NCS-TCP were organized at Secunderabad and Kolkata on May 10, 2016 and June 10, 2016 respectively. The programme was widely appreciated by State Agriculture and Horticulture Departments. Stakeholders from various segments such as tissue culture companies, State horticulture department officials and progressive farmers attended the programme. Stakeholders Meet on NCS-TCP was also organized at New Delhi on July 04, 2016. Hon'ble Minister of State for Ministry of Science & Technology & Earth Sciences, Government of India Shri Y.S. Chowdary inaugurated the event. 132 participants from various segments such as tissue culture companies, State horticulture department officials and progressive farmers attended the programme.

NON-COMMUNICABLE DISEASE (NCDs)

Cancer Biology: In addition to the R&D projects, DBT has strengthened resources around established Leaders in Cancer Biology in the form of Unit of Excellence. DBT is currently supporting 113 pilot projects for young investigators. Recognizing the importance of collaborative and complimentary research so as to consolidate resources and pool talent, DBT has signed an MoU with upcoming National Cancer Institute (NCI),

AIIMS at Jhajjar campus to co-design and co-develop research labs/facilities at NCI, train manpower, and jointly support and forge partnership with industry for the development and evaluation of products for public health through Public Private Partnership. Department of Biotechnology has initiated a Cancer Diagnostic Research Center in tertiary care hospital, Sher-I-Kashmir Institute of Medical Sciences (SKIMS), for creation of infrastructure for the State of Jammu and Kashmir. Virtual National Cancer Institute on the thematic area of breast cancer has been initiated and this project envisages to identify novel protein kinases that are activated in hormone refractory breast cancer and to identify key pathways and the therapies that target those pathways. Some of the salient achievements are highlighted as follows:

A comprehensive understanding of the Nasopharyngeal Carcinoma (NPC) in the North-Eastern Region of India: Nasopharyngeal carcinoma (NPC) is a malignant tumor of the nasopharynx. It is commonly seen in southern China and South East Asia, but rare in most other parts of the world. In India, NPC is confined mostly to north eastern states of Manipur, Mizoram, and Nagaland. The possible risk factors for the disease include host genetics, inheritance of the human leukocyte antigen (HLA) loci, Epstein–Barr virus (EBV) infection, and other environmental factors such as smoking, alcohol intake, intake of preserved foods and salted fish, etc. Since information on NPC in India is scarce, a multi-centric case control study was undertaken in the States of Arunachal Pradesh, Mizoram, Nagaland, Manipur, and Assam to determine the risk factors involved in development of NPC. Among the environmental risk factors, only use of firewood for cooking was found in a significant higher proportion of families of the NPC cases in comparison to the families of controls, while other factors did not show any significant difference. Using the EBNA-1 gene as a target for identifying EBV, the detection rate was significantly higher in patients with NPC than the control subjects. Further,

majority of NPC patients had EBV type-1 infection. The control samples showed 60.5% in EBV in latency II, which indicated a possible risk for future occurrence of NPC. Polymorphism of P53, metabolic genes, DNA repair genes, mitochondrial genes, and certain unique SNPs were detected in the NPC cases. However, most of these differences were not statistically significant. HLA studies have identified putative class I alleles that are positively or negatively associated with NPC. Association of HLA-B*40 with susceptibility to NPC was a unique observation.

Evaluation of therapeutic potential of glycogen synthase kinase 3 in chewing tobacco mediated oral cancer: Among various types of oral cancers, oral squamous cell carcinoma (OSCC) of the lip and tongue showed elevated expression of Glycogen synthase kinase 3 α /alpha (GSK3 α /alpha). The increased expression of inactive α and β isoforms not only was correlated positively with cyclin D1 and p53 expression in tongue cancer progression but a gradual shift of their expression from the cytoplasmic to the nuclear compartment and overall disease severity was also observed. The interaction of GSK3 β -cyclin D1 and the positive correlation of p53-GSK3 β and the transcription of cyclin D1 were observed. Besides this, the inactivation of GSK3 β and its downstream molecules like c-myc/ β -catenin, was linked to progressive silencing of reversion-inducing cysteine-rich protein with Kazal motifs gene expression. These results demonstrated that inactivation of GSK3 β , are an important event in oral cancer and can be used as a marker for assessing disease severity. Further, hamster buccal pouch (HBP) carcinogenesis model was also used to analyse the stepwise evolution of oral cancer and for chemo-intervention studies with nimbolide, a limonoid isolated from the leaves and flowers of the neem tree (*Azadirachta indica* A.Juss). In HBP carcinomas, activated Akt, in turn, phosphorylates GSK-3 β at Ser⁹, leading to activation of the Wnt signaling pathway. The studies clearly demonstrated that nimbolide exerts

chemotherapeutic effects in the HBP model by modulating GSK-3 β signalling circuits with impact on key molecules involved in cell proliferation and apoptosis.

Global protein profiling of sequential changes during rat lingual carcinogenesis and different stages of tongue cancer in human: Oral cancer is the single largest cancer in India because of habits of chewing tobacco and allied products. Local recurrence and regional lymph node metastasis are the two major hurdles in the management of this cancer. Despite advances in surgery, chemotherapy and radiotherapy, the average five year survival rate for oral cancer has not changed. At present there is dearth of sensitive and specific early diagnostic and prognostic markers. In human system it is not possible to get all the stages of oral carcinogenesis and tissue size is also another major limitation. An experimental rat model was used to develop a battery of markers for human oral cancer. Differential proteomics was carried out on tissues obtained at different stages of experimental rat oral carcinogenesis and the results were compared with the proteomic analysis of tissues obtained from different stages of human tongue cancer. Some of the differentially expressed proteins were shortlisted for further analysis. Expression of these proteins is known to be altered in cancers other than human oral cancer (Fig. 1)

Molecular analysis of cytogenetically normal acute myeloid leukemia: Acute myeloid leukemia (AML), a cytogenetically and molecularly heterogeneous disease, constitutes 15–20% of childhood leukemia and approximately 35% of adult leukemia. Karyotype at the time of diagnosis provides the most important prognostic information in adults with AML. However, 40 to 50% of patients do not have clonal chromosomal aberrations. This karyotypically normal group, CN-AML, which is less well understood biologically and clinically, has been shown to have mutations and altered gene expression profiles. In a two year study, 163 samples

were collected, out of which 121 were newly diagnosed CN AML patients. The prevalence of Nucleophosmin 1 (NPM1), FMS-like tyrosine kinase-3 (FLT3-ITD) and CCAAT/Enhancer Binding Protein (CEBPA) mutations was 54%, 27% and 9% respectively in CN-AML cases. Over expression of Brain and Acute Leukemia, Cytoplasmic (BAALC) was found in 79% cases of CN-AML. Risk stratification of AML cases is being done based on these studies.

Validation of the Cancer-Testis Biomarker Calcium Binding Tyrosine Phosphorylation Regulated (CABYR) gene in Cervical Squamous Cell Carcinomas: Cervical cancer remains a major public health problem for women in developing countries like India. About 90% of cervical cancers are squamous cell carcinomas and a considerable proportion of patients are diagnosed only at the advanced stages of the cancer. Therefore, there is an urgent need of potent biomarkers for early detection of this medical problem. The expression of specific CABYR isoforms in early stages and various grades of cervical cancer were investigated. CABYR is a calcium-binding tyrosine phosphorylation regulated protein which was initially reported to be testis specific. Studies revealed that CABYR isoforms particularly CABYR c expression is significantly associated with various cervical cancer and precancerous stages. The mRNA expression of specific spliced variant CABYR 3 was found in 80% of the cervical cancer stages and 60% of the precancerous stages through RT PCR. Whereas protein expression of CABYR c isoform was observed in 100% of cervical cancer and cervical intraepithelial neoplasia (CIN) stage samples through western blotting, as well as immunohistochemistry analysis. Moreover pap smear of cancer and CIN bearing patients also showed CABYR c positive tumor cells through immunofluorescence studies. Furthermore, this CABYR isoform was also detected in the protein isolated from the urine of the cancer and CIN

patients through western blotting. In cervical cancer cell line HeLa, CABYR c was observed to be located in the cytoplasm of these cells. Therefore, a novel biomarker, CABYR has been identified in cervical cancer which can be explored for early diagnosis and prognostics of cervical cancer and its management.

Diagnosis of Cancer using Fluorescence Lifetime Imaging: Cancer of the cervix is the fourth most common cancer in women worldwide, with about 5,28,000 new cases and 2,66,000 deaths each year, as per WHO reports of 2012. Conventional screening techniques for cervical cancer like pap smear, colposcopy and biopsy are time consuming, expensive and limited in specificity or sensitivity. A cost-effective indigenous technology for early stage detection that minimizes mortality due to cancer is hence imperative. Fluorescence spectroscopy offers exciting possibilities for novel diagnostics being highly sensitive to biochemical changes and may be an effective tool in detecting human cervical dysplasia. The abnormal cells are morphologically and biochemically different from normal cells and these manifest optically through scattering and fluorescence. A combination of fluorescence life time imaging (FLIM) and static autofluorescence measurements were carried for improved tissue diagnosis which can lead to development of a non-invasive functional / diagnostic modality for early diagnosis of cervical cancer. A wide-field fluorescence lifetime imaging system has been developed. FLIM in combination with static autofluorescence measurements has been used to enhance contrast between cancerous and normal sites of resected human breast tissues and uterine cervix samples. These two techniques were used in combination so as to obtain both morphological as well as functional information from normal and pathological tissues. Wide-field fluorescence lifetime images were recorded from 1 cm² area of the epithelium of the cervical tissue sample. A whole cervix sample containing both normal and

precancerous regions was tested for delineation of abnormal region using fluorescence lifetime images. The time-resolved fluorescence images at different delays were subjected to principal component analysis (PCA). The demarcation between normal and abnormal regions was seen to be better resolved compared to the static, while a significant enhancement was achieved in the constructed image as shown in (Fig.2). A combination of FLIM and PCA differentiates normal and abnormal regions and precisely has the potential to be used in real time diagnostics.

Plakophilin3 functions required for tumor progression and metastasis in colon cancer: Colorectal cancer is one of the most common tumors worldwide. The incidence of colorectal cancer is the third of all malignant tumors. While some progress has been made in the treatment of colorectal cancer, about 50% of patients relapse after treatment and up to one third of patients with localized tumor in the bowel will develop liver metastases, indicating that improving the treatment of colorectal cancer is still necessary. Therefore, identifying novel therapeutic targets for metastatic disease is crucial to improved patient survival. The generation of animal models that parallel human disease is important both from the point of view of understanding mechanisms and for testing of new drugs in preclinical settings. Plakophilin3 (PKP3) is a desmosomal plaque protein required for desmosome formation and whose expression is decreased at the invasive front in tumors of the colon. Results from Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Mumbai have demonstrated that PKP3 loss leads to the increased transformation and metastasis in a colon cancer cell line. It was further demonstrated that K8 protein levels were increased upon PKP3 loss and that the expression of Lipocalin 2 (LCN2) and Matrix Metalloprotease 7 (MMP7) are increased upon PKP3 loss. Loss of K8 and LCN2 in the PKP3 knockdown clones lead to a decrease in

the transformation. Studies are ongoing to generate a colon specific knockdown of PKP3 in the mouse to determine whether this leads to increased tumor progression.

Role of metadherin in breast cancer metastasis and its molecular regulation: Recent studies have highlighted the involvement of metadherin (MTDH), an oncogenic protein in promoting cancer progression, metastasis and chemoresistance in many cancers including mammary carcinomas. However, the molecular regulation of MTDH is still poorly understood. 5-Aminoimidazole-4-carboxamide ribonucleotide (AICAR), an 5' AMP-activated protein kinase (AMPK) activator, imposed a significant growth arrest, inhibition of migration and invasion of TNBC cells. Intriguingly, AICAR or metformin treatment resulted in significant down-regulation of MTDH expression via inhibiting c-Myc expression. In contrast, treatment of cells with compound C, an inhibitor of AMPK, increased both c-Myc and MTDH expressions in triple negative breast cancer (TNBC) cells. Also, AMPK activation caused increased GSK3 α activity by inhibiting the inactive phosphorylation at Ser-9 on one hand, and activation of Sirtuin 1 (SIRT1) by inhibiting Ser-47 phosphorylation, as evidenced by deacetylation of p53 on the other hand. It was shown that AMPK activation by inducing GSK3 α and SIRT1, down regulates MTDH expression via inhibiting c-Myc in TNBC cells.

Isolation and characterization of Epithelial cell adhesion molecule + (EpCAM+) cell populations in Cirrhosis and Hepatocellular Carcinoma (HCC) to target cancer stem cells: Despite the current progress in understanding the contribution of cancer stem cells (CSCs) to the generation of heterogeneity of tumors, the molecular complexity and exact regulation of CSCs is poorly understood almost in all cancers and especially in hepatocellular carcinoma. Notably, liver tumors with progenitor cell characteristics have been found to be particularly aggressive and related to poor patient survival. The

identification of liver CSC markers and their related pathways has hence become one of the most important goals of present-day cancer research, and working towards this goal would first require an intricate knowledge of the biological characteristics of these cells. Hepatocellular carcinoma (HCC) which originates from cancer stem cells (CSCs), mostly develops on a cirrhotic background. Through mRNA and miRNA profiling, molecular similarity between EpCAM+ cirrhotic cells and EpCAM+ CSCs was established (Fig. 3). *In vitro* and *in vivo* functional studies have also shown similarities between the two populations.

Understanding the role of tumor derived glycosphingolipids in carcinogenesis: An *in vivo* approach : The role of tumor derived ganglioside, GM2 in the impairment of host immune response in different cancer types, primarily by rendering the immune cells dysfunctional, has been very well documented. On the other hand, very little data actually exists on the role of GM2 in mediating tumor progression and growth. Studies were designed to define the precise role of tumor derived glycosphingolipid, GM2 in mediating tumor growth, progression and metastasis in experimentally feasible animal models. A stable GM2-synthase knockout mouse tumor cell line, Renca-vGM2-syn-KO was successfully established using targeted genome editing technology, TALEN (Transcription activator like effector nuclease) and characterized. The Renca-vGM2-syn-KO cell line displayed significant reduction in anchorage independent growth owing to anoikis sensitivity, thereby indicating that GM2 has a definitive role in imparting anoikis resistance, anchorage-independent growth and EMT (Epithelial-mesenchymal transition). Mice injected with Wild type cells showed significantly reduced tumor volume compared to those injected with Renca-vGM2-syn-KO cells.

Elucidating the role of p53 and DNA damage response pathway in anti-cancer activity of a novel coumarin-chalcone hybrid: A coumarin-chalcone hybrid synthesised inhouse in CDRI showed potent *in vitro* anti-tumor activity. The compound (S009-131) was most found to be the most potent molecule among 21 compounds of this class. The compound (S009-131) had also been found active in repressing xeno graft tumor (induced with human cervical cancer cells) in severe immunodeficiency (SCID) mice. Oral administration of this compound was more effective than intravenous treatment of adriamycin in regressing tumor xenografts. S009-131 causes DNA damage by binding to the minor groove which triggers phosphorylation and activation of serine threonine protein kinase and DNA-dependent protein kinase (DNA-PK), but not ataxia telangiectasia and Rad3-related protein (ATR). Pharmacological inhibition of Phosphatidylinositol 3-kinase-related kinases (PIKKs) abrogated S009-131 induced phosphorylation of p53. Additionally, docking studies revealed that S009-131 might also contribute to increased cellular p53 level by occupying p53 binding pocket of MDM2. Posttranslational modifications of p53 upon S009-131 treatment led to enhanced affinity of p53 towards responsive elements (p53-RE) in the promoter regions of target genes and increased transcriptional efficiency. Together, the results suggest that S009-131 cleaves DNA through minor groove binding and eventually activates PIKKs and associated DNA damage response signalling to promote stabilization and enhanced transcriptional activity of p53 through posttranslational modifications at key residues.

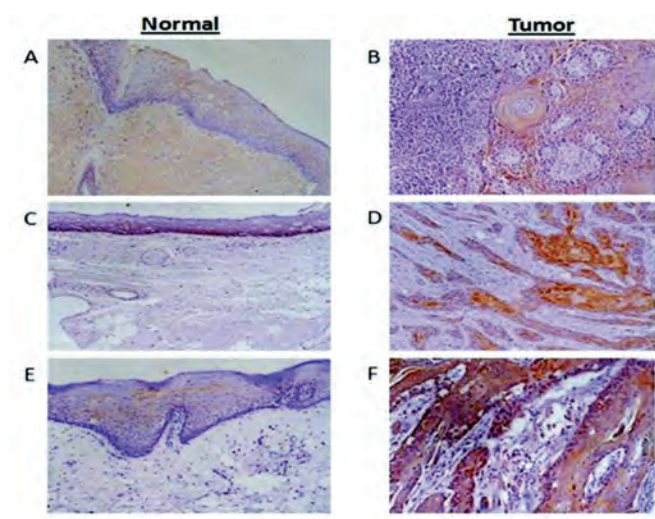


Fig.1 Sequential increase in NDRG1 expression across the stages of human tongue cancer using Immunohistochemistry

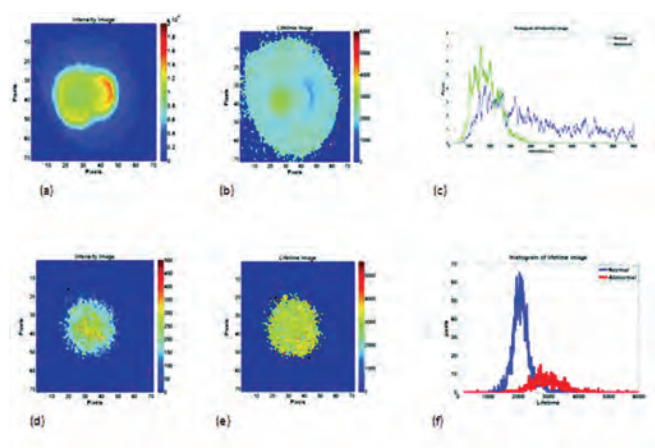


Fig.2 (a) and (b) are fluorescence (static and lifetime) images of normal cervical samples respectively, (d) and (e): of precancerous cervical samples respectively. Histogram plots of (c) static and (f) lifetime images over the 1cm² area displays the overlap and decoupling of normal and precancerous areas respectively

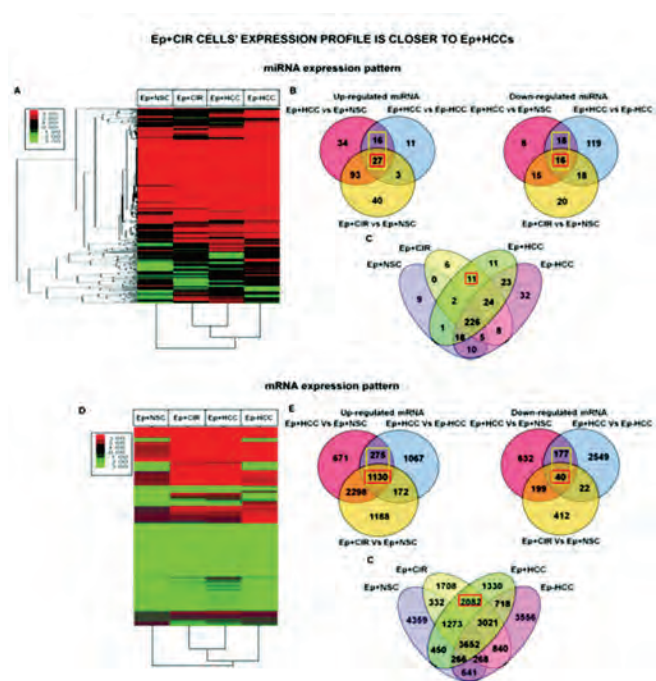


Fig.3 miRNome and transcriptome analysis showing close association between EpCAM+ cells from both advanced cirrhosis and HCC

Metabolic Disorders/ Diseases: The Department is supporting competitive R&D programme on identified non-infectious disease conditions, genetic/epigenetic mechanisms, development of affordable and non-invasive diagnostics/imaging for early diagnosis and optimal management, point-of-care interventions and development of personalized medicine approach etc. The salient achievements in some of the ongoing programs are:

Two major networks have been supported on kidney diseases. One of these programme has been initiated with the aim of conducting research on pediatric nephrotic syndrome, the chief chronic kidney disease in children across 15 centers in the country. Objectives of the project include the setting up of a nationwide, longitudinal prospective cohort of patients with nephrotic syndrome linked to a biospecimen repository that can be used for future studies into disease pathogenesis. The project will also examine focused questions related to the

genetics of nephrotic syndrome, pathogenesis of C3 glomerulopathy, corticosteroid therapy and effect of pharmacogenetic factors on response and cardiovascular outcomes. The research will allow to characterize the burden of monogenic nephrotic syndrome in India including discovery of new genetic variants that cause the condition or act as disease modifiers. Information on genetic mutations will help to develop an appropriate and rational genetic screening algorithm that is cost effective and also provide molecular drug target for therapeutic interventions. In addition, a bioinformatics platform will be used to establish links between working groups on nephrotic syndrome within the country to enable integration of disease cohorts followed prospectively at individual centers into an anonymized national disease registry for pediatric nephrotic syndrome. Work on the main proposal has been initiated as planned. Longitudinal patient registries are recruiting patients at two centres (AIIMS, St. John's) on an electronic database linked to a biospecimen repository. Simultaneously, patient recruitment and assay standardization for next gen-sequencing (main proposal) and two sub-proposals, is ongoing. As originally proposed, three subproposals will commence patient enrolment by mid-2017. Twelve other centers across India, currently awaiting IRB approvals, are expected to join the registry and biorepository beginning early 2017.

Another large observational cohort is being established for the Indian population with CKD at 8 centers nationwide in order to assess risk factors for the progression of CKD, assess gender related differences in the risk for CKD and CVD progression. Identification of yet unknown risk factors and biomarkers related to the progression of CKD will help identify new and improved strategies for diagnosis, therapies and preventions. A total of 343 patients have been enrolled in year 1 along with establishment of logistics for the study. One of the earlier findings in the project has been that cholecalciferol supplementation improves CVD risk

factor profile through positive impact on vascular function in non-diabetic subjects with early CKD, likely due to improvement in both endothelial and vascular smooth muscle cell function. In another important study on Kidney disorders, the results indicated that the disruption of the *thyA* and *alr* genes in *L. plantarum* provide a new strategy for improved method of group II intron technology. The comprising advantages of this technology including site specificity, relatively high frequency of insertion and without introduction of antibiotic resistance gene into the chromosome, could facilitate construction of biologically contained *L. plantarum* mutant, persistent to expression of oxalate decarboxylase protein for the prevention and treatment of hyperoxaluria.

In order to unravel the sexual dimorphism of vitamin A metabolic pathway, its role in region-specific adipose tissue development and their relevance to insulin resistance, the data from a study showed that vitamin A accumulation does not follow dimorphism under control diet-feeding condition between male and female rats. However, the diabetogenic diet feeding increased the vitamin A levels in visceral white adipose tissue of males, while subcutaneous white adipose tissue in females, without altering the expression of various vitamin A metabolic pathways genes. Among various pathways analyzed, lipid-droplet associated genes and proteins, namely such as lipocalin-2 and perilipins were affected by both sex and dietary treatment, which corroborate with increased adiposity observed in these rats.

In a study for improving autophagy in Failing Hearts by Activating Sirtuin 6, SIRT6 deficiency impaired the lysosomal functions and thus caused defective autophagy. SIRT6 transcriptionally control the lysosomal biogenesis in cardiomyocytes. Interestingly, it was found that overexpression of SIRT6 corrects lysosomal problems, promote the autophagy and restores the homeostasis in cardiomyocytes. In addition, it has also been found

that SIRT6 deficiency also leads to the defects in protein synthesis in heart.

Neuro Disease Biology: The Department has created a niche of well-defined researchers in the area of neuroscience due to its persistent efforts over several years. Over 192 projects were implemented since 2010 covering – degenerative disorders, drug development, neuro inflammatory disease, neuro-infections, epilepsy, stroke etc, besides the multi-centric Glial project and two HR initiatives viz. Initiative on the Neuro-Clinical Research Education (INCRE) and Initiative on Neuro-informatics and Computational Neuroscience Education (INCNE) instituted for facilitating hypothesis- driven research by clinicians and to inspire young scientists and engineers to work in Neuro –informatics and Computational Neuroscience. 152 projects have been closed after due process of review. A major focus area identified by the Task force i.e. Hypoxic ischemic brain injury has undergone two rounds of deliberations and brain storming sessions and this resulted in generation of 12 proposals that are under consideration for financial support by the Department. Yet another critical area “Glial Cell Biology” that has successfully completed its first round of implementation is under consideration for review and deciphering the future road map to take the findings of first phase to a logical conclusion. A Brainstorming was held in Jiwaji University, Gwalior on 2-3rd Feb, 2017 that witnessed the participation of around 50 groups as compared to the 12 groups that had initiated the programme in 2013. The 12 groups from NBRC, Manesar; NIMHANS, Bangalore; CDRI, Lucknow; JNU, Delhi gave brief presentations and future road-maps for prospective proposals. There was a vibrant cross-talk among the groups and the meeting witnessed the prospective networking among researchers.

Two Task Force meetings were organized to review new projects in Delhi, and 15 are in the process of implementation.

DBT's Autonomous institute i.e. NBRC organized IBRO-APRC school on “Development and Functions of Brain Circuit: From Molecules to Behaviour” on March 15th – 30th, 2016.

The Department supported the 34th Annual Meeting of Indian Academy of Neurosciences (IAN- 2016) on “Molecules to Mind” at National Brain Research Center, Manesar during October 19th -21st, 2016. This was a mingling ground and for researchers in the area that leads to exchange of novel ideas and forges collaborations.

A very interesting study supported at UDSC, Delhi has demonstrated for the first time that *dmyc* (a *Drosophila* homologue of human *cmyc* proto-oncogene) could be utilized as an efficient drug target to restrict the pathogenesis of human neurodegenerative disorders such as Huntington's, Alzheimer's, and Parkinson's disease etc. It has been seen that tissue specific upregulation of *dmyc* suppresses the polyglutamine[poly(Q)] mediated neurodegenerative phenotypes by alleviating the cellular level of CREB binding proteins (CBP) and improved histone acetylation, resulting in restoration of transcriptional machinery which is otherwise abbreviated due to poly(Q) disease conditions. Subsequently, studies have demonstrated that the inherent chromatin remodeling ability of *cmyc* proto-oncogene could be exploited to restrict the pathogenesis of human neuronal tauopathies such as Alzheimer's and Parkinson's disease. Interestingly, recent reports on successful uses of some anti-cancer drugs against neuronal tauopathies in clinical trials and animal models strongly support the results. In brief, the research findings provide very critical and novel insights about pathogenesis of human neurodegenerative disorders, and the generated information would potentially facilitate in designing of novel therapeutic strategies to combat the devastating human neurodegenerative disorders.

Centre of Excellence for Epilepsy (CoE) is collaborative project between National Brain

Research Centre (NBRC) and All India Institute of Medical Sciences (AIIMS) established under the aegis of DBT. The main aim of the centre is to develop a cure for Drug resistant Epilepsy (DRE) by bridging the gap between clinical and basic research which is mediated by the close coordination between NBRC and AIIMS. A screening tool has been developed to identify surgical candidates with DRE in a resource limited settings. Endoscopy-assisted interhemispheric trans callosal-hemispherotomy and endoscopic-assisted (through a mini craniotomy) Corpus Callosotomy combined with anterior, hippocampal, and posterior commissurotomy in Lennox-Gastaut syndrome has been developed. It has been shown that magnetoencephalography (ictal-MEG) source localization added information towards delineating the ictal-onset zone and helped final decision-making in epilepsy surgery. RNAseq analysis of HS patient samples revealed novel genes that are significantly regulated in HS. Cellular electrophysiological studies in slice preparations of resected brain samples of patients with HS indicated differential increase in glutamatergic activity in the hippocampus and anterior temporal lobe. This provided the first direct evidence of two distinct resting state networks at cellular level in patients with HS. GABAergic activity in patients with FCD is shown to be enhanced and the magnitude of alteration was different in paediatric patients compared to that in adult patients with FCD. A commendable out-come is that over ten peer reviewed research articles have been published in the past one year and over fifty papers in the past five years. Recently a collaboration with Institute for Plasma Research (IPR), Gandhinagar has been done to develop a deep-learning based software for analysis of MRI and EEG data of patients with DRE. The 2nd NBRC-AIIMS Epilepsy Surgery & Neurobiology Workshop in September, 2017 was organized. The major future goal of the CoE will be to comprehensively study the molecular mechanisms associated with DRE and to extend the

studies to identify novel biomarkers and validate them.

The Neuroimaging and Neurospectroscopy laboratory of NBRC has developed complete and integrated software that could help early diagnosis of mental health problems. Developed by a team of neuroscientists, the software can quantify a brain neurochemical called γ -Aminobutyric Acid (GABA) through neuroimaging of brain metabolites using Magnetic resonance spectroscopy (MRS). Titled KALPANA, the software allows visualization and single-click processing of MRS data acquired using a variety of methods. With the incorporation of premade end-to-end processing workflows for a variety of data and use of algorithms that enable accurate estimation of chemical concentrations from the signal and a graphical interphase for its easy interpretation, the software offers distinct clinical scope.

While several signal processing packages do already exist, KALAPNA offers a distinct advantage in three aspects. It can handle a variety of signal types and processing algorithms, it offers versatility for both in-depth interactive use for research purposes and one-click processing for diagnostic purposes and utilizes an adapted algorithm to improve the accuracy of quantification thereby, increasing clinical value of the package. The package has been made free for academic use. GABA has been well known to be central to the pathology of several neuropsychiatric disorders like depression, schizophrenia and bipolar disorder. DBT has supported mapping of GABA for Alzheimer's diseases which laid the base for this new technology. Quantification of this chemical can help early diagnosis of these conditions and for understanding the patho-physiology of these disorders by evaluating treatment responses. Given the immense clinical scope of GABA as a potential quantifiable indicator of increased risk for mental health disorders as well as of both disease progression and effectiveness of therapeutics, the

scientists decided to develop an easy method of quantifying it and creating a graphical user interface that allows the processing of any MRS signal rapidly and accurately. MRS can provide a range of indicators like concentrations of brain chemicals, to pH and temperature to the biochemist or radiologist non-invasively, from any well-defined region in the ever elusive brain.

SILK BIOTECHNOLOGY

The programme on application of biotechnology towards developing newer and emerging technologies in silk and its applications in biomaterials continued during the year.

A “Brainstorming Session on Biotechnology Applications in Tasar Culture” were jointly organized by DBT and Central Silk Board (CSB) on June 08, 2016 at Central Tasar Research and Training Institute (CTRTI), Ranchi with a view to develop a well-focused network programme on technology development in tasar silk. Significant achievements are summarized below:

Development of improved races of silkworm for enhanced productivity: The proteo-genomic studies of silk glands of the two strains – Pure Mysore and CSR2 of the mulberry silkworm (*Bombyx mori*) was carried out at R. V. College of Engineering, Bangalore to determine the novel genes and the gene products expressed by the cells of the middle and posterior silk gland (transcriptome) at developmental different stages of the silkworm to find the mechanism behind the regulation of silk proteins (fibroin and sericin) production and the roles of genes and gene products in the regulation of silkworm developmental pathways.

Efforts are in progress to introduce sex-limited foundation crosses for cocoon colour as a male component for the production of commercial cross breed at APSSRDI, Hindupur. The aim is to introduce such sex-limited foundation crosses which are easy to multiply at farmers’ level. This will enable for

easy sex separation of pupae at grainage and to reel all the yellow cocoons and the males (100%) can be utilized for the preparation of cross breed. Presently, ten sex-limited breeding lines are in the process of establishment at F-12 level. Further, inbreeding and selection is under progress, so as to adjudicate foundation crosses in the production of commercial hybrids.

A Network Programme on use and validation of DNA markers in silkworm breeding programme for NPV resistance along with large-scale field trials at different locations has been initiated at Seribiotech Research Laboratory (SBRL), Bangalore; Central Sericultural Research & Training Institute (CSR&TI), Mysore; CSR&TI, Berhampore and CSR&TI, Pampore, J&K.

Development of Disease and Pests Control Measures: Reserach of SBRL, Bangalore on Uzifly (*Exorista bombycis*) infestation has shown the increase in Reactive oxygen species which induce cytotoxicity in haemocytes of the silkworm, *Bombyx mori* and suppress immune responses enabling the parasitic survival. After infection with microsporidian (*Nosema bombycis*) spores in *B. mori* larva, Toll pathway activation is delayed, probably due to requirement of a threshold level of spores to activate toll pathway which enabled initial survival and multiplication of the spores. Utilizing the information generated, immunocompetent strains of the silkworm, *Bombyx mori* will be identified from the germplasm and will be utilized for breeding programs to synthesize new immunocompetent and high yielding strains.

Work on developing a diagnostic kit for early detection of baculovirus causing tiger band disease in *Antheraea proylei* (oak tasar silkworm) has been initiated jointly at SBRL, Bangalore and Regional Tasar Research Station (RTRS), Imphal, Manipur.

Improvement of Host Plants: Stable transgenic mulberry plants expressing *HVA1*, *Osmotin* and *bch1* (â-carotene hydroxylase) genes developed at UDSC,

New Delhi have been evaluated at transgenic containment facility of University of Agricultural Sciences, Bangalore. Work has been carried out on multiplication of transgenic lines, characterization of events for root growth, evaluating the selected lines under stressful conditions and examine their suitability for silkworm rearing. The stress screening assays indicated improvement in cellular level tolerance in all the transgenic lines tested. Grafting experiments indicated good graft compatibility in the transgenic plants. Large scale silkworm rearing bioassay conducted using select transgenic lines indicated no deleterious effects on silk worm growth, cocoon yield and productivity, when fed to multivoltine hybrid PM X CSR2 fifth instar silkworms. Overexpression of beta-carotene hydroxylase, an enzyme in the carotenoid biosynthetic pathway, showed higher levels of carotenoids and improved oxidative stress tolerance as compared with the untransformed wild type under non-stressed and stressed conditions. Enhanced tolerance to high light, heat and UV irradiation was also achieved in *Morus indica* cv. K2 indicating the potential of this gene to suit the changing climatic conditions.

Genetic variability and diversity among fungal pathogens (*viz.*, *Macrophomina phaseolina*, *Fusarium* spp. and *Botrydipodium theobromae*) associated with root rot disease in mulberry has been assessed using morphological, cultural and molecular markers at Central Sericultural Research & Training Institute (CSRTI), Mysore. Among the 95 fungal isolates, the root rot infection on V-1 mulberry has been categorized into pathogenic (30), moderately pathogenic (43) and non-pathogenic (22). A total of 211 mulberry diverse germplasm were screened for root rot and based on the disease reaction, the diverse germplasm were categorised into resistant (20), moderately resistant (51), susceptible (41) and highly susceptible (99). Microsatellite markers were used to assess the genetic divergence among the mulberry germplasm screened for root rot resistance. Divergent

contrasting lines for disease resistance *viz.*, *Morus multicaulis*, ME-0006 (R) x Thailand Male (S); *M. multicaulis*, E-0168 (R) x Thailand Male (S) and Punjab Local (S) x *M. cathayana* hybrid (R) were utilized for crossing and three mapping populations for root rot resistance trait were developed by pseudo-test cross strategy. These mapping populations will be utilized in locating QTLs controlling the trait by linkage analysis and designing disease tolerant variety through Marker Assisted Breeding.

Silk Proteins as Potential Biomaterials: Under a Network Project being implemented at West Bengal University of Animal and Fishery Sciences, Kolkata, IICB, Kolkata and IIT, Kharagpur, the *Antheraea mylitta* (Am) silk films were found to support corneal cell attachment and proliferation. The cells maintain their normal characteristics i.e. epithelial, keratocytes, and corneal stem cells. The support for cellular growth is comparable to scaffold currently in clinical use i.e. amniotic membrane. Extensive biocompatibility studies conducted in rabbit eye showed these films are safe for use in cornea. Studies conducted in two different model of corneal surface disorder demonstrated Am silk films as appropriate scaffold for corneal regeneration. The results of the study have been published in Scientific Reports (Nature Group) 2016. Patent has been filed in India.

Utilization of By-Products: Work on characterization of silkworm pupal bioprotein and processing for value-addition through microbial interventions has been undertaken at UAS, Bangalore. Efficient bacterial isolates were screened for decomposition of silkworm pupal residue (SWPR) *viz.*, *Pseudomonas* sp., *Stenotrophomonas maltophilia*, *Sphingomonas wittichii*. Effect of environmental factors on evolution of volatile organic compounds during silkworm pupal residue (SWPR) degradation was determined. The SWPR compost as plant nutrient source was evaluated on growth and yield of French

bean. Alpha-linolenic acid was isolated from silkworm pupal residue. The silkworm pupal residue samples collected from four silk reeling units (Vijayapura, Ramanagara, Channapatna and Shidlaghatta) were subjected for amino acid profiling. Different delicious value added products were developed such as chocolate, masala cookies and tamarind balls.

Work has been initiated on isolation and characterization of sericin from tasar silk fibre waste at CTR&TI, Ranchi. Lipid peroxidation assay has been standardized and hydrogen peroxide scavenging assay has been estimated.

Centre of Excellence on Genetics and Genomics of Silkmooths: Under the Centre of Excellence on Genetics and Genomics of Silkmooths at Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad, SBRL, Bangalore, CSRTI, Mysore and APSSRDI, Hindupur, baculovirus-resistant transgenic silkworm hybrids have been generated by crossing genetically engineered BmNPV resistant silkworm (*Bombyx mori*) transgenic lines of Nistari and CSR2 with various commercial silkworm breeds. The hybrids are being tested for their efficacy at multiple locations i.e. at APSSRDI, Hindupur and at three institutions of Central Silk Board namely CSR&TI, Mysore, CSR&TI, Berhampore, CSR&TI, Pampore under Contract Research Scheme with appropriate regulatory approvals.

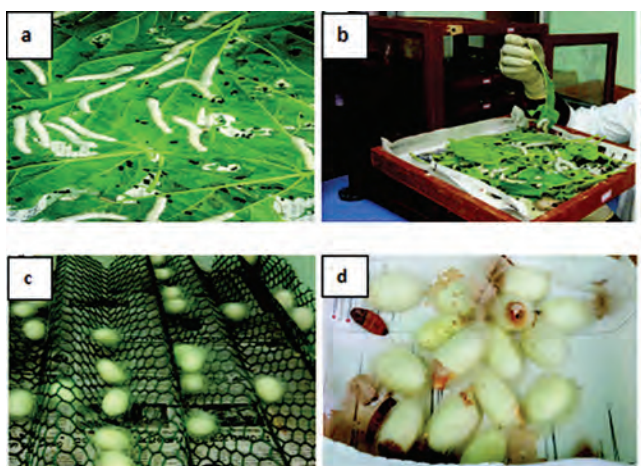


Figure: Representative photograph showing the rearing of silkworms. The performance of wild type and transgenic mulberry plants was assessed by silkworm feeding at 5th instar stage. Silkworms were fed with the leaves collected from either transgenic or wild type plants (a, & b). The worms were left for spinning on rotary mountages and the cocoons spun were assessed for pupation efficiency (c) and subsequently tested for fecundity (d).

STEM CELLS AND REGENERATIVE MEDICINE

Stem Cells and Regenerative Medicine has been identified as one of the thrust areas under biomedical research of the Department. The objective is to promote basic, early and late translational research and formulation of regulatory framework for stem cell research in India.

During the year, a number of projects have been implemented on various aspects of embryonic, adult and induced pluripotent stem cells. A number of studies aimed at developing improved methods and techniques for isolating and culturing stem cells from different origin and also ability to create induced pluripotent stem cells from various somatic/adult tissues. A study was undertaken to reprogram buffalo fetal fibroblasts into pluripotent stem cells by non-viral method, employing the piggyBac transposon system encoding the reprogramming factors OCT-4, SOX-2, KLF-4, C-MYC, LIN-28 and NANOG, each separated by self-cleaving peptide sequences and driven by the chimeric promoter. The derived buffalo iPS cells displayed typical morphological characteristics of pluripotent stem cells. This study provided insights into viral-free iPS cell culture technology and will facilitate genetic modification of the buffalo genome, and be helpful for production of transgenic animals using genetically modified iPS cells in future. Another study to evaluate wound healing properties of ischemic WJ-MSCs was supported where gene expression profile between control and ischemic WJ-MSCs was compared by PCR array and the result showed upregulation of many ECM and adhesion molecules, cytokines and trophic factors in the ischemic population. The study suggested

that WJ-MSCs might be therapeutically beneficial and effective in treating ischemic diseases. In another project, an *in vitro* model that could recapitulate retinoblastoma tumorigenesis is being attempted. Here, the cells from orbital adipose tissue of the patients undergoing therapeutic enucleation will be assessed for generating patient derived iPSCs that can be further developed as *in vitro* model and would aid in understanding mechanism of RB tumorigenesis and formulating therapies. In a study supported at CMC Vellore, a total of five children with large segmental bone defects have received tissue engineered bone transplant (custom made triphasic hydroxyapatite scaffolds loaded with mesenchymal stem cells) with no serious adverse effects. This confirms the safety of the autologous stem cell directed into osteoblastic lineage on HASi scaffolds with success in union so far suggesting that this cell scaffold product can be taken further for the phase 2 trial to assess efficacy commercialization process. In yet another project, stem cell intervention along with transient-modulation of PTEN gene in injured spinal cord in mice model have shown augmented functional recovery from spinal cord injury compared to the other control cohorts. Gliomas are the most common tumors of the Central Nervous System and glioblastoma multiforme (GBM) are the most malignant tumors of the brain. A study has been supported to gain better understanding of Cancer stem cells (CSCs) in primary and secondary gliomas for devising better treatment strategies. For this primary & secondary neurosphere culture from surgically removed primary glioma tissues and cell lines is being standardized.

The Department implemented a programme titled '*Accelerating the application of stem cell technology in human disease (ASHD)*' as Indo-Japan collaborative programme with four participating institutions from India, namely: inStem, Bangalore; NCBS, Bangalore; NIMHANS Bangalore; CSCR, CMC Vellore; & CiRA, Kyoto University, Japan as international partner. It has two broad research

components dealing with human diseases of national importance, namely "Accelerator program for discovery in brain disorders using stem cells (ADBS)" and "Novel approaches to hematological disorders (NAHD)".

Under ADBS component, so far forty-six subjects from 18 families of 1134 screened families have been recruited with brief assessment of putative endophenotypes in a subset of this cohort. Deep phenotype assessments are planned along with neuroimaging and electrophysiological studies. The process and protocols for generating and banking hiPSC's as well as characterizing these has been set up and over the last year the target of 50 iPSC lines has been achieved. A basic genomics pipeline has been put in place and cellular assays are also being made operational. Processes for distributing material from the bio repository have been approved by statutory bodies such as the IC-SCRT and initial requests for control lines have been processed. Training programs in stem cell technology have been initiated both within ADBS as well as in collaboration with CiRA, Japan.

Under the NAHD component, there are three major programmes, (i) a gene therapy program capitalizing on the developments in vector based gene therapy for haematological diseases in the world both as a clinical trial for haemophilia and preclinical research for the major hemoglobin disorders, (ii) a haplobanking program exploiting the iPSC technology to develop a bank of pluripotent cells lines from HLA homozygous individuals and (iii) a community based control program for the major haemoglobin disorders. Activities under all these three programmes have been initiated.

Centre of Excellence for Stem Cell Research: Basic and Translational: DBT had supported Centre of Excellence for Stem Cell Research at AIIMS, Delhi in 2008. It has now completed its Phase I and has accomplished the construction of basic research lab, animal housing facility and cGMP Lab. Standardized SOPs for more than 25 techniques and

more than 08 techniques under cGMP conditions has been achieved including procedures for isolation and expansion of stem cells under cGMP conditions for clinical research. So far more than 12 clinical studies involving various departments of AIIMS have been completed and results of few have been published in peer reviewed journals. This Centre has been providing amniotic membrane within as well as outside AIIMS and has been providing training to more than 10 students every year in the field of stem cell research. It has also initiated public private partnership in area of stem cell banking and drug testing. So far two patents have been filed for the technologies developed/ designed during these years. At present the Centre is fully functional with cGMP laboratory to carry out basic as well as clinical research.



Figure: cGMP Facility and Cryopreservation Facility

Guidelines for Stem Cell Research: A regulatory framework and the guidelines for stem cell research have been formulated jointly by DBT and ICMR have been revised based on the feedback from all the stakeholders. The government has also constituted a National Apex Committee for Stem Cell Research and Therapy (NAC-SCRT), for effectively reviewing and monitoring the stem cell research in the country. As per the guidelines it is mandatory that any institution/organization involved in stem cell

research should be registered with the NAC-SCRT through Institutional Committee for Stem Cell Research (IC-SCR).

Centre for Chemical Biology and Therapeutics (CCBT): The Centre for Chemical Biology and Therapeutics (CCBT) has been established as an integrated programme with a close-knit team effort that combines biophysics, structural biology, computational chemistry, medicinal chemistry and cell biology.

Selective modulation of intracellular signaling pathways is a major challenge impeding deeper understanding of the biology of human diseases, as well as their therapy using small-molecule drugs. Thus far, efforts in academia and the pharmaceutical industry have focused largely on the inhibition of enzymes such as protein kinases using ATP-competitive inhibitors. These approaches suffer from the lack of chemical and biological selectivity. Biologically, inhibition of proximal catalytic steps in signal transduction can lead to a wide variety of phenotypic effects. Alternately, signal propagation in pathways initiated by enzymes like protein kinases or ubiquitin ligases occurs through the molecular recognition of site-specific post-translational modifications by distinct protein domains.

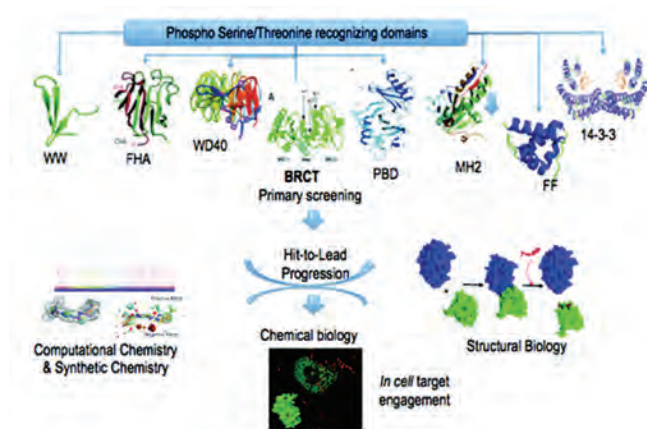
The creation of small-molecule chemical tools that target the molecular recognition of site-specific post-translational modifications offers a potentially attractive new approach for the selective modulation of intracellular signaling pathways, which could markedly extend the reach of chemical biology and seed therapeutics development.

The centre aims to explore this concept, with the first objective of creating a palette of selective chemical tools that modulate the recognition of site-specific protein phosphorylation by specific domains. This is a challenging goal, beset with many underlying technical as well as conceptual hurdles. Therefore, this programme takes a stepwise

approach that aims to provide deeper scientific insight into the structural mechanism of phosphosite recognition, as well as innovative new approaches to develop chemical tools that selectively target it.

High-throughput primary screening assays for three hitherto “undrugged” molecular targets representing distinct structural mechanisms for phosphopeptide recognition have been conducted, followed by hit identification and confirmation. The computational chemistry and medicinal chemistry teams have cooperatively optimized the confirmed hits in an iterative manner based on the understanding of the structural basis of molecular recognition of protein-peptide complexes and the formulation of binding-mode hypotheses, validated by directed synthesis. The structural biology team has focused on co-crystallization of potent compounds with protein targets, while the cell biology team has developed a cascade of biological assays suitable for determining target engagement and compound selectivity in the cellular milieu using genetic approaches to benchmark each assay.

Outline of CCBT Scientific Workflow



Small-molecule inhibitors have been developed that selectively target conformers of the tandem BRCT domain to disrupt its interaction with phosphopeptide substrates. Confirmed primary hits from a biophysical screen were clustered/analogue based on structural/field similarity and based on

the physicochemical properties versus synthetic feasibility, a chemotype series was prioritized. The binding mode of the confirmed chemotype was validated by generating synthetic analogs that challenge the crucial interactions, and their potency tested through a series of biochemical assays involving both competitive and direct binding to the target domains. A clear structure activity relationship (SAR) was established based on the 100+ synthesized compounds, which has led to the next generation of compounds with apparent K_d ~75nM to their target, about an order of magnitude greater than their endogenous ligands. The selectivity of the compounds has been determined against other structurally varied BRCT domains.

One example compound, CCBT2008, exhibits an apparent potency of ~75nM in vitro, and exhibits selectivity against between different BRCT domains. While co-crystallography is ongoing, STD NMR experiments have already demonstrated that CCBT2008 binds to the target protein. CCBT2008 has shown promising activity in cells. An in-cell FRET assay has also been developed that determines target engagement and show that CCBT2008 but not a structurally related control compound decreases the binding of the target BRCT domain to its peptide substrate in the cellular setting. It has been demonstrated that CCBT2008 but not the control compound exhibit selective biological activity in cellular assays of the DNA damage response. Thus, the results exemplify a strategy to interrupt intracellular signaling via the molecular recognition of PTMs, with implications for chemical biology.

Collaborations: With the Medical Research Council Cancer Unit, University of Cambridge - Joint Centre Award from the DBT and UK Medical Research Council.

Measurable outcomes: Manuscripts in preparation: (1) Interrupting intracellular signaling by inhibiting the molecular recognition of post-translational modifications by BRCT domains (2)

Analysis of the structural determinants of substrate recognition by tandem BRCT domains

Patent document in preparation: Benzoimidazole compounds and uses thereof.

The Department has formulated the draft bill on “The Use and Regulation of DNA-Based Technology in Civil and Criminal Proceedings, Identification of Missing Persons and Human Remains Bill” (earlier named as “The DNA Identification Bill”). The proposed Bill aims to regulate the use of DNA-based technology in civil and criminal proceedings, identification of missing persons and human remains; to establish the DNA Profiling Board for laying down the standards for laboratories, collection of human body substances, custody trail from collection to reporting; and also to establish a National DNA Data Bank. Draft Bill is under consideration by the Government.

TRANSLATIONAL RESEARCH ON MEDICINAL AND AROMATIC PLANTS

Programme on translational research for developing products and processes from medicinal and aromatic plants following multi-disciplinary approach continued during the year. A Brainstorming Session-cum-Stakeholders Meeting on Aroma Crops and Technologies for North East Region was organized on March 10-11, 2016 at Institute of Advanced Study in Science and Technology (IASST), Guwahati, Assam to develop a well-focused translational programme on technology development in aromatic crops along with formulating some end-to-end demonstration projects in network mode for aroma cultivation in NE Region with an aim to develop aroma based future start-ups in NE Region. A Brainstorming-cum-Interactive meeting on Herbal Drug Pipeline Project was held on May 18, 2016 to initiate a herbal drug pipeline project based on the research leads already available. A technology transfer agreement has been signed between ICGEB, New Delhi and Sun Pharmaceutical Industries Ltd., Gurugram for clinical

development of most bioactive fraction (*CiPa*) from *Cissampelos pareira* towards developing a phytopharmaceutical drug for dengue infection. The salient achievements of the programme during the year are as follows:

Characterization, Multiplication and Agrotechnology: SSR and AFLP markers revealed the existence of very narrow genetic base among seven populations of *Symplocos racemosa*, 12 populations of *Pterocarpus marsupium* and seven populations of *Saraca asoca* in Eastern Ghats at Sikha-O-Anusandhan (SOA) University, Bhubaneswar. Vegetative propagation of *S. racemosa* and seed propagation of *P. marsupium* and *S. asoca* is in progress. Seed germination rate in *P. marsupium* was very low (25.5% with cow-dung slurry treatment and 3.83% with cold-water treatment) whereas in case of *S. asoca*, it is moderate (55.3%).

Kewda male flowers have been collected from 17 patches covering three districts of Odisha jointly by SOA University, Bhubaneswar and FFDC Extension Unit, Berhampore. Extraction of essential oil has been completed from 110 flower samples followed by the GC MS analysis and their constituent identification. Phenyl ethyl methyl ether (PEME), the major constituent of kewda oil varied from 68-82% among all the zones. Eighty-five leaf samples have been collected from all the patches. Molecular characterization of all the leaf samples is in progress with sixty designed SSR primers. Based on essential oil yield and quality analysis, elite lines of Kewda have been identified and maintained for further multiplication.

Phenotypic and chemotypic characterization of *Andrographis paniculata* and *Rauwolfia serpentina* have been undertaken jointly at Centre for Biotechnology, Hisar and CIAB, Mohali. Huge chemotypic variations was noted in 80 accessions of *A. paniculata* with respect to andrographaloids, neo-andrographaloids and 14-deoxy-andrographaloids. An enormous chemotypic

variation in 60 accessions of *R. serpentina* has been observed with respect to seven major constituents – ajmalicine, vomilenine, ajmaline, yohimbine, serpentine / alstonine, serpentine and reserpine.

Work has been recently initiated to develop microbial inoculants for high-value agarwood oil production in *Aquilaria* tree at Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow.

A total of 62 germplasm accessions of *Zingiber zerumbet*, 55 accessions of *Hedychium coronarium* and 40 accessions of *Curcuma caesia* have been collected from different ecoregions of Eastern India jointly at SOA University, Bhubaneswar and RKMU Centenary College, Kolkata. Four new chemotypes have been identified in *Hedychium coronarium* i.e eucalyptol rich (eucalyptol>32.07), α -pinene rich (α -pinene>29.27), linalool rich (linalool>45.11) and coronarin-E rich (coronarin-E>39.57) chemotypes. Fingerprint profile of *H. coronarium* essential oil has been developed through GCxGC-TOFMS. GC-MS analysis of extract of 25 representative samples of *H. coronarium* revealed the presence of α -Levantenolide, 9-cis-Retinal, Valeric anhydride, Glycerol trihexanoate, Methenolone and Agathic acid as major constituents from different ecoregions of Eastern India. A total of 6 elite chemotypes in *Z. zerumbet*, 4 elite chemotypes in *H. coronarium* and 3 elite chemotypes in *C. caesia* which have high drug yielding potential have been identified and conserved in field gene bank.

An end-to-end demonstration project on field evaluation of *Cymbopogon flexuosus* (lemongrass), *Cymbopogon winterianus* (citronella) and *Cymbopogon martinii* (palmarosa) covering an area of 53.5 acre in the farmers' fields involving 10 villages of Dhar block (Kandi area) in Punjab was completed. Three farm distillation units were installed and made operational in adopted village clusters. The marketing of essential oil has been provided through linkage organizations. The capacity building of farmers was carried out on cultivation, harvesting and processing operations

through 59 on-farm contact programmes, 25 awareness programmes and six exposure visits. Further, a District level workshop was organized to motivate other farmers of region to adopt aromatic crop cultivation. The Memorandums of Understanding (MoU) have been signed by Kelkar's Scientific Research Centre, Mumbai and Unati Co-Operative Marketing-Cum-Processing Society Limited, Hoshiarpur, Punjab with individual farmers adopted under the project for complete buy back of essential oil generated under the project.

Novel Bioactive Agents and Herbal Formulation:

Standardized aqueous extract of *Tribulus terrestris* was found to be effective in inhibiting crystallization *in vitro* and proved protective towards oxalate induced renal tubular epithelial cell injury in various animal cell lines at Amity University, Noida. Prophylactic and curative property of statistically optimized aqueous extract of *T. terrestris* against experimentally induced nephrolithiasis showed concurrent reduction in the nephrolithiatic symptoms in Wistar rats. Pre-clinical acute toxicity studies in Wistar rats showed no toxicity and in the chronic toxicity studies no pathological changes were observed. This study provides the therapeutic potential of *T. terrestris* which may lead to the development of single plant based herbal formulation against urolithiasis.

Six medicinal plants (*Agave americana*, *Piper nigrum*, *Chenopodium ambrosioides*, *Piper longum*, *Cedrus deodara* and *Trachyspermum ammi*) from folklore claims were evaluated for their anti-leishmanial properties jointly at Jadavpur University, Kolkata and Balaji Utthan Sansthan, Patna. Ethyl acetate fraction of *A. americana* and benzene fractions of other plant extracts showed significant antileishmanial activity. The isolated lead molecules (Hecogenin, Piperin, Linalool and Thymol) of most active extract is being tested for safety measurement.

Studies were undertaken to scientifically validate the use of *Asparagus racemosus* (Shatavari) as

substitute for rare and rejuvenatic plant drugs *Meda-Mahameda* – the members of *Ashtavarga* group of Ayurvedic drugs at Foundation for Revitalisation of Local Health Traditions (FRLHT), Bangalore. HPTLC and LC-MS analysis of *Asparagus racemosus*, *Polygonatum cirrhifolium* and *P. verticillatum* quantified Shatavarin I and IV present in *A. racemosus* as 0.67%w/w and 0.59%w/w, respectively. *Drosophila melanogaster* model based life-span enhancing (*Vayasthapana*) and fecundity (*Vrshya*) assays showed similar bioactivity profile for the authentic and substitute drugs. A similar trend in the muscle building activity (*Balya*) of the drugs was demonstrated by the semi-quantitative expression profile of *Drosophila myo* gene. The observations indicate the legitimacy of the use of shatavari as a substitute for *Meda-Mahameda*.

Methanolic and aqueous extracts of *T. arjuna* bark and leaf extract standardized by HPLC, promoted osteoblastogenesis by decreasing osteoclastogenesis and simultaneously mitigated adipogenesis *in vitro* at Mahatma Gandhi Medical College and Research Institute, Puducherry. Oxidative stress-induced osteoblastogenesis as a possible mechanism was investigated. The extract of *T. arjuna* has a potential to be developed as a nutritional supplement for human consumption to prevent osteoporosis.

Piparine and piperonol – the major phytoconstituents of black pepper (*Piper nigrum*) have shown promising anti-obesity and anti-hyperglycemic activities at SV University, Tirupati. Piperine and piperonol showed anti-lipase activity and also regulated various parameters such as lipid metabolizing enzymes, leptin and adiponectin levels and expression adipogenesis related genes such as PPAR genes, FAS, SREBP-1c, ACC, HMG-CoAR, Fab-4 and UCP-2.

Three selected phytochemicals viz. FG-3 (3',5-dihydroxyflavone-7-O- β -D-Galacturonide-4'-O- β -D-glucopyranoside), Piperine and Quercetin when co-administered with three anti-HIV drugs namely

Tenofovir (TNV), Zidovudine (ZDV) and Nelfinavir (NFV), enhanced the oral bioavailability of respective drugs at Ambedkar Marathwada University, Aurangabad. These phytochemicals inhibited the CYP450 enzymes responsible for the metabolism of these drugs and or inhibited the p-glycoprotein based efflux of these drugs which in turn enhanced the oral bioavailability.

Aqueous extracts of *Solanum xanthocarpum* and *Albizia lebbbeck* have shown significant reversal of markers of inflammation and oxidative stress in experimental model of bronchial asthma at V. P. Chest Institute, University of Delhi, Delhi. Significant improvement in goblet cell hyperplastic and thickness of bronchial epithelial layer, smooth muscle later and total wall was recorded in different doses of extract.

Combination therapy of Risperidone and *Withania somnifera* extracts were able to reverse the changes in memory, learning and anxiety in experimental animal model of autism at PGIMER, Chandigarh.

An anti-dermetophytic topical formulation using essential oil of *Trachyspermum ammi* (Ajwain) as main ingredient has been developed jointly at Dolphin Institute of Biomedical and Natural Sciences, Dehradun and Centre for Aromatic Plants (CAP), Dehradun. The tested formulation showed better efficacy as compared to some popular antimycotic ointments and antifungal drugs already available in the market.

Genomics and biosynthetic pathways: Key regulatory genes named farnesyl diphosphate synthase and santalene synthase involved in downstream terpenoid pathway towards santalol synthesis were functionally characterized from sandalwood at Vittal Mallya Scientific Research Foundation, Bangalore. Two gene cassettes containing 35S promoter – SaFDS and EntCUP-SaSS were constructed in p-Bluescript – KS vector (PBS) for over expression in sandalwood cell suppression

culture to achieve santalol synthesis. A method of *Agrobacterium* mediated transformation of sandalwood embryos was optimized as confirmed through GUS assay and PCR of the transformed callus.

Under a Programme Support being implemented jointly by Jaypee University of Information Technology (JUIT), Solan and Himalayan Forest Research Institute (HFRI), Shimla, work on functional analysis and validation of *Picrosides* biosynthetic pathway and development of gene markers for elite chemotypes of *Picrorhiza kurrooa* has been undertaken. The biosynthetic pathway of Picrosides-I production has been validated through feeding different concentrations of cenicamic acid (CA) and catalpol (CAT) alone and in combination, which revealed that both CA and CAT must exist for maximum production of Picrosides-I in *P. kurrooa*. Biosynthetic route for Picrosides-II production has been deciphered by utilizing natural variation for Picrosides-II content in different *P. kurrooa* chemotypes and established that Picrosides-II is biosynthesized via degradation of ferulic acid (FA) to produce vanillic acid (VA) which acts as its immediate biosynthetic precursor. The association of picrosides contents with allelic variations in biosynthetic pathway genes, reflected as SNPs in coding regions, is being pursued towards developing molecular markers for authentication of elite chemotypes.



Figure 1: Mass propagation of *Pterocarpus marsupium* at SOA University, Bhubaneswar

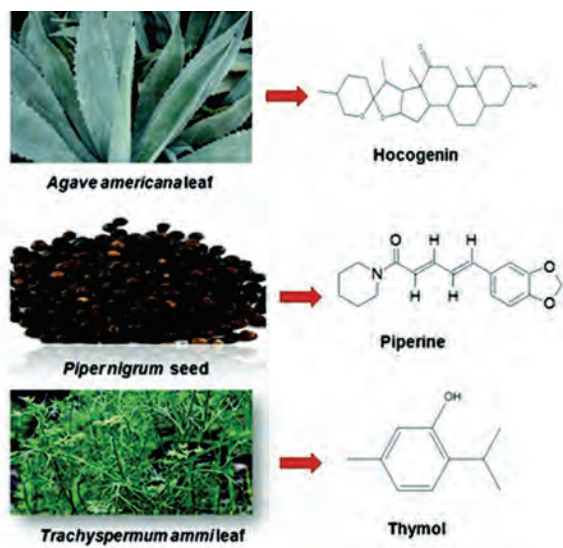


Figure 2: Medicinal Plants having potential anti-leishmanial activity



Figure 3: Collection of Kewda flowers in Ganjam area of Odisha

Vaccine Research & Development Programmes

Vaccines remain the most effective public health tool that provide safe, cost effective and efficient means of preventing morbidity and mortality and constitute critical component of a national health security. Department of Biotechnology (DBT) has made concerted efforts in strengthening vaccine research and development since its inception in 1986-87 through: Task Force on Medical

Biotechnology, National technology Mission on Immunization and National Jai-Vigyan Mission on S&T for the generation of new and improved vaccines. In the last plan, vaccine research and development efforts have been implemented through Vaccine Grand Challenge Programme (VGCP) and Indo-US Vaccine Action Programme (VAP) with major objective to accelerate development of candidate vaccines for which earlier leads are available and to take them through pre-clinical, clinical development and commercialization.

VACCINE GRAND CHALLENGE PROGRAMME :

VGCP was implemented to encourage novel and innovative vaccine related discoveries, accelerated development of candidate vaccines for which earlier leads are available, research of basic & applied nature to improvise current understanding of vaccine science and to strengthen the scientific basis for future vaccine design. The programme is under implementation since 2009-10, through an EFC of DBT. Support has been provided to R&D projects through VGCP focusing on:

Development of candidate vaccines such as: Recombinant combination blood stage vaccines for *P. falciparum* malaria (JAIVAC-2 & JAIVAC-3), rBCG85C -a candidate TB vaccine, Dengue Virus-like particle (VLP) vaccine candidates, BAC-EBV vector-based vaccine approach for Hepatitis C, novel candidate vaccines against *Salmonella enterica* serovar *Typhi* and *Paratyphi*.

Development of vaccine related technologies such as: Novel Adjuvants for Mucosal Priming, adenovirus based novel viral vector for vaccine delivery, Vitamin D supplementation to improve immune responses to vaccines, Mycobacterium indicus pranii (MIP) as a booster to BCG, Chemo enzymatic assembly of defined protein dendrimers for vaccine use.

INDO-US VACCINE ACTION PROGRAMME (VAP) :

The VAP is a bilateral Indo-US program, which

supports a broad spectrum of activities relating to new and improved vaccines. The program was designed to encompass laboratory-based research, evaluation of candidate vaccine development, testing for clinical development, vaccine quality control, delivery of vaccines etc. Itich supports a broad spectrum of activities relating to new and improved vaccines. The oversight to the program is provided by the VAP Joint Working Group (JWG) which is comprised of eminent scientists and policymakers from both countries. The programme is under implementation since 1987. The 28th Meeting of JWG was held in Jan 2016, in New Delhi.

VAP-supported research projects have directly addressed critical health problems relevant to both countries.

PROGRESS OF MAJOR VACCINE DEVELOPMENT PROJECTS

Rotavirus Vaccine: ROTAVIRUS VACCINE- (ROTAVAC®) is the first indigenous rotavirus vaccine, developed from an Indian strain- by an Indian company, and tested by Indian investigators in an effort led by the Indian government and supported by several national and global partners. The vaccine has been developed by a unique social innovation of public-private sectors along with institutional collaboration.

Department supported the development of first rotaviral diarrhoea vaccine 116E in India at All India Institute of Medical Sciences (AIIMS), New Delhi in collaboration with Centers for Disease Control and Prevention (CDC), USA. With continued financial support from DBT, National Institute of Health (NIH) & Programme for Appropriate Technology in Health (PATH), the vaccine completed Phase III clinical trials at three sites: Society for Applied Studies (SAS), Delhi (ii) Christian Medical College (CMC), Vellore and (iii) KEM Hospital, Pune. Data from the trial, showed ROTAVAC® to have an excellent safety and efficacy profile. The clinical study demonstrated for the first time that the India-developed rotavirus vaccine is efficacious in preventing severe rotavirus diarrhoea in low-resource settings in India.

The vaccine is manufactured in India by M/s Bharat Biotech International Limited, Hyderabad under cGMP conditions. Bharat Biotech announced a price of US\$ 1.00/dose (or approximately INR 54/dose) for and will soon file for registration of the vaccine in India. It is licensed by the Drugs Controller General of India (DCGI) and is a more affordable alternative to the rotavirus vaccines already on the market. The vaccine has been commercialized and based on the recommendations of NTAGI; ROTAVAC® has been introduced in the EPI programme of Haryana, Himachal Pradesh, Andhra Pradesh, and Orissa.

Malaria Vaccines: To promote the development of vaccines against *P. falciparum* and *P. vivax* malaria, Department has provided continued support to MVDP (Malaria Vaccine Development programme)- A consortium of DBT, ICGEB, Malaria Vaccine Initiative (MVI), PATH, EMVI and WHO-TDR. MVDP was established as an independent society in July 2010. It takes vaccine projects up to proof of concept and efficacy studies (Phase II) and turns them over to companies for Phase III trial and commercialization.

Currently MVDP is involved with developmental activities of following vaccine candidates being developed at ICGB:

1. Development of a recombinant combination blood stage vaccine for *Plasmodium falciparum* malaria: JAIVAC 2. The study aims to study combination of fusion chimera (PfMSPFu24), PfF2 (EBA175) and PfRH2/PfAARP in JAIVAC-2 that will target and inhibit parasite growth by two independent mechanisms, namely by inhibiting erythrocyte invasion and by antibody dependent cellular inhibition (ADCI) mechanisms to provide protection against malaria.
2. Develop a receptor blocking malaria vaccine against *Plasmodium falciparum* based on a novel combination of three blood stage antigens (PfAARP + PfRH2 + PfF2): JAIVAC 3.

The development of blood-stage malaria vaccines in the past has focussed primarily on two essential antigens, MSP-142 and AMA-1, which both play a crucial role in red cell invasion but are under immense immune pressure. As a result, these antigens exhibit a high degree of polymorphism such that their respective antibodies exhibit neutralizing activity only against homologous *P. falciparum* strains and not against the heterologous strains, thus impeding their potential as vaccine targets. Hence, the primary goal in the development of efficacious blood-stage malaria vaccines has been the identification of essential target antigens that conserved and can elicit strain-transcending neutralizing antibodies. In this regard, the group at ICGB and JNU has identified essential novel antigens (PfRH5, CyRPA) and produced them in recombinant form that elicits potent strain-transcending invasion inhibitory antibodies. These target antigens hold great promise as efficacious blood-stage vaccine candidates. The team is working on developing the antigen combination PfMSPFu24+PfRH5+PfRH2/PfAARP/PfF2 as a candidate blood stage vaccine.

Dengue Vaccine: Department has been supporting the group at ICGB, for the development of safe, efficacious and inexpensive tetravalent dengue vaccine. The ICGB has developed a tetravalent **Dengue Subunit VLP (DSV⁴)** based vaccine candidate, expressed using the methylotrophic yeast *Pichia pastoris*. This candidate is based on EDIII. Unlike domains EDI and EDII, which elicit largely flavivirus cross-reactive and weakly-neutralizing or non-neutralizing antibodies, EDIII elicits potent serotype-specific virus-neutralizing antibodies. The ICGB's 'four-in-one', tetravalent vaccine candidate incorporates the EDIIIs of all four DENVs spliced together through flexible linkers in a single translational reading frame. Further, it is genetically fused with Hepatitis-B surface antigen (HBsAg) and co-expressed with four expression cassettes of HBsAg in order to display EDIIIs on the surface of HBsAg virus-like-particles (VLPs). It is

immunogenic in mice and macaques and it elicits serotype-specific neutralizing antibodies against all four DENVs in mice. These antibodies exhibit breadth of neutralization against various genotypes of each serotype. Additionally, these antibodies are protective in dengue sensitive AG129 mice.

The Wellcome Trust wrote an international patent, which is now online. ICGEB has identified a pharmaceutical company to license the vaccine.

MAJOR INITIATIVES IMPLEMENTED UNDER INDO-US VAP : REGIONAL PROSPECTIVE OBSERVATIONAL RESEARCH FOR TUBERCULOSIS : RePORT India

Initiative: RePORT India is a bi-lateral multi-organizational collaborative effort designed to advance regional basic and clinical tuberculosis (TB) science in India. The goal of this program is to establish long term longitudinal cohorts of TB patients in India to strengthen TB research capacity and infrastructure, and foster research collaboration within India and with other countries. The RePORT Consortium is comprised of research organizations in India with their U.S.-based partners. The primary funding for Consortium research activities comes from the Indian Department of Biotechnology (DBT), Ministry of Science and Technology, U.S. National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS), U.S. National Institutes of Health (NIH), and Office of AIDS Research (OAR).

The RePORT India Consortium consists of five distinct TB cohorts mainly in Southern India working in collaboration to address a wide array of scientific objectives and to institute a unified common prospective observational research protocol (Common Protocol) that is supported by a central biorepository, a central data management centre. It aims at the utilization of harmonized data elements and specimen collection standard operating procedures (SOPs).

In 2016, the CRUs initiated concurrent enrollments into the RePORT India Common Protocol. Biospecimens will be “banked” over time from two

prospective, observational cohorts, one with participants who have active pulmonary TB (Cohort A) and the second with participants who are household contacts (HHCs) to an active case of TB and who have latent TB infection (LTBI) (Cohort B). The National Institute for Research in Tuberculosis (NIRT) in Chennai, India will serve as the specimen bio-repository. The primary objective is to provide specimens to Indian biomarker researchers and their collaborators to better understand the pathogenesis of progression from LTBI to active disease, and to better understand the prognosis of TB disease.

RePORT India Leadership Meetings: The leadership to the RePORT Consortium is provided by the governing committee comprising of principal investigators (PIs) from CRUs and their US partner organization, representatives from the funding organizations. The face-to-face meetings and interactions were held with various stakeholders during the meeting that help in (i) Approval of the policies and overall procedures of the Consortium (ii) Review and prioritization of study concepts (iii) Monitoring the performance of the CRUs (iv) Cross-study coordination of timelines, standardization of procedures, means for resource sharing, and other broad operational issues for effective implementation of the research agenda across all study sites.

The Fifth RePORT India Leadership Group (LG) Meeting in CMC, Vellore: This RePORT India LG Meeting took place on March 03-05, 2015 Vellore, India. The Christian Medical College (BJMC) hosted the event and the meeting was well-attended by representatives from the DBT, NIH, U.S. Embassy, and investigators, scientists, and other participants from India. The meeting covered a wide breadth of scientific, programmatic and operational topics. Also a Symposium on “Update in TB Research” was hosted at CMC for young faculties and students.

Human Immune Phenotyping and Infectious Disease Initiative: The goal of this funding program is to promote U.S.-India collaborative research on human

immune-phenotyping in the context of infectious disease and vaccine development, and in collaboration with investigators of the HIPC (Human Immunology Project Consortium). Both NIAID (through HIPC) and DBT have allocated funds to support joint activities pursued under this program.

Meeting of the Candidate Vaccine Advisory Committee, May 29 – MAY 30, 2016 in New Delhi

The 28th meeting of the Joint Working Group (JWG) of Indo—US Vaccine Action Programme (VAP) was held on January 27-28, 2016 at New Delhi. The JWG was attended by the Indian and US members and the investigators of various vaccine programmes both from India and US. The JWG discussed the progress of various initiatives being implemented under Indo-US VAP and also discussed the development of affordable vaccines for Dengue, RSV, Malaria etc. At VAP JWG 2016, JWG members agreed to establish an expert Advisory Committee that would guide Indo-US researchers regarding next steps in the decision-

making process pertaining to VAP priority areas. Accordingly, Candidate Vaccine Advisory Committee (CVAC) for advice on future VAP projects: candidate vaccines, has been constituted.

The Indo-U.S. Vaccine Action Program (VAP), Meeting of the Candidate Vaccine Advisory Committee (CVAC) took place from May 29 – May 30, 2016 in New Delhi, India. Participants included people from Bharat Biotech, the Department of Biotechnology (DBT), Gennova Scientific, the International Center for Genetic Engineering and Biotechnology (ICGEB), the India Council of Medical Research (ICMR), the Infectious Disease Research Institute (IDRI), the National Institute of Allergy and Infectious Diseases, and the Serum Institute of India (SI). A total of seven candidate vaccines were presented to CVAC for review: two dengue candidates, two TB candidates, and one candidate each for chikungunya, RSV, and Zika.



05

BIOTECHNOLOGY BASED PROGRAMMES FOR SOCIETAL DEVELOPMENT

Department has been supporting projects aiming to promote use of biotechnological processes and tools for the benefit of the disadvantaged section of the society comprising women, rural population and SC/STs in ecologically compatible manner. The programme aims to create platform for self-employment generation among the target population by diffusion of proven and field-tested technologies through demonstration, training and extension activities. The projects are supported in agriculture and animal husbandry including fish farming, poultry farming, pig production, goat farming, value added products, floriculture, hybrid seed production, integrated farming system, entrepreneurship development, bio-resource utilization, women and child health, hygiene and nutrition. Large number of rural, SC/ST and women population including youth have been benefited through implementation of these projects. A programme for the rehabilitation of Flash Flood affected area in Uttarakhand is being continued to extend the benefit to flood affected people of Uttarakhand. Some of the salient achievements of the programme are as follows:

Biotechnology Based Programme for Rural Development

Fish Farming: A project on fish seed production technology for sustainable livelihood in Udham Singh Nagar, Uttarakhand was implemented at College of Fisheries, Pantnagar. Hands-on-training provided on fish seed production to 55 beneficiaries. Beneficiaries have adopted pond based practical method for seed production technology including

identification and selection of brooders. In-house field trainings were organized at different places in seven rural clusters in which 237 beneficiaries participated. A technical booklet on “Carp Matsya Beez Utpaan evam Palan” has been published and distributed amongst stake holders. 32 fish farmers have produced fish seed of carp for stocking in their own ponds. Adoption of fish farming has increased the income of the farmers.

Pig Farming: A project on capacity building and awareness generation and enhanced productivity of pig through assisted reproductive biotechnology and conservation of biodiversity was taken up with community participation at College of Veterinary Science, Assam Agricultural University, Khanapara, Guwahati. Awareness cum training programmes were conducted in Hajo, Kamalpur, Bezara, Sonapur, Malibari, Bangsar, Bonda, Chandrapur, Maloibari, Karara, Nalbari and Sipajhar areas. Vaccination camp has been in selected areas. Training programmes conducted on various aspects of scientific pig rearing and artificial insemination. Workshops organized on capacity building on artificial insemination in pig. A leaflet in local language (Assamese) has been prepared on scientific pig farming and distributed to the rural farmers cum breeders.. Farmers adopted pig farming for their livelihood generation earning good income.

Goat and backyard poultry farming: A project on empowerment of rural farmer and youths through improved livestock breeding, feeding, goatery and backyard poultry farming was implemented in

Sitapur district at Krishi Vigyan Kendra, Sitapur 200 and rural families unemployed rural youth from 10 villages of Sidhauili Block and 10 villages of Godlamau Block were trained on scientific rearing of goat and poultry. 30 does and 06 bucks were distributed to 15 beneficiaries along with 1250 birds were given to 25 beneficiaries. Awareness and motivation programme organized on different aspects of scientific feeding and management of goat and backyard poultry. Pamphlets have been published in local language and distributed the farmers. Adoption of goater and backyard poultry farming has helped in creation of self employment opportunities for youth and farmers.

Turkey Farming: A Project on poverty alleviation through scientific turkey farming was implemented in selected rural areas of Trichy District of Tamil Nadu by Asirwad Trust. 33 training programmes on capacity building, re-orientation programs and health care camps were organized for SHG members. 200 turkey poult have been distributed to the SHG farmers for adoption of turkey farming. Farmers adopted turkey farming for livelihood generation.

Value added Milk products: A project on production and marketing of fermented dairy products was implemented at Gulbarga University, 50 women have been given hands-on-training for production of value added milk products like cheese, buttermilk, yoghurt and khawa. These products were marketed during seasonal functions like marriage parties, festivals. Trained women beneficiaries have been successfully established small milk parlours for income generation on commercial scale. The beneficiaries have got employed in different milk vendors and small industries.

Agri-biotechnologies: A Project on agri-biotechnologies for livelihood enhancement of farmers of Dhari and Ramgarh blocks of Nainital District, Uttarakhand was implemented by the Energy and Resources Institute (TERI), Seth New

Delhi. 1032 farmers in eight villages of Dhari and Ramgarh blocks of Nainital district have been benefited through various project activities. 25 hectares of land brought under cultivation up-scaling of garlic production. Farmers adopted started earning good amount of income. Cultivation of aromatic herbs also helped the farmers to earn additional income. 4470 farmers were trained on agri-biotechnologies for livelihood generation.

Another project on socio-economic and technological empowerment of pulse growers of Jalaun and Ramabai nagar district of Uttar Pradesh was implemented by Indian Institute Kanpur. 113 complete package technology demonstrations on pulse production were conducted in 52 hectares of area in four project villages of Kanpur dehat and Jalaun district. Two registered seed societies were formed for strengthening the formal and informal seed system of pulses in the selected districts to encourage the youth for agriprenuership. Capacity building programme on pulse production technologies were organized in which 400 farmers participated.

Cultivation of Flowers and Vegetables: A project on protected cultivation of flowers and vegetables to improve livelihood security of rural people was implemented at University of Agriculture Sciences, Dharwad. 10 farmers from 03 villages of Dharwad district were selected based on the resource available. Field programme was organized for farmers. Training conducted on protected cultivation on flowers and vegetables in which 60 growers participated. 06 farmers have established polyhouse of 2000 m² each with the support of National Horticulture Mission and growing capsicum. Adoption of this practice has helped for self employment opportunities of farmers.

Another project on in-vitro propagation and bio-farming of Anthurium (*Anthurium andreanum*) and Gerbera (*Gerbera jamesonii*) and transfer of technology in Terai-Dooars region of West Bengal was implemented by Uttar Banga Krishi

Viswavidyalaya. The mother plant blocks of Gerbera and Anthurium have been established and tissue culture protocol of Anthurium and Gerbera were standardized including surface sterilization and acclimatization techniques in the plant tissue culture. The demonstration plot of bio-farming of Anthurium and Gerbera under protected conditions were established. Demonstration at farmer's fields conducted and training programmes were organized in which 140 farmers participated.

Rural Bio-Resources: A Project on rural bio-resources innovation application to uplift the Socio Economic status of farmers and entrepreneurs from Uttar Pradesh was implemented at Amity University Uttar Pradesh, Noida. Farmers, predominantly females and entrepreneurs were provided hands-on training and demonstration at 3 fully equipped Common Facility Centres (CFCs) established at Gayatri Suman Farm (Bulandshahr), Krishi Vgyan Kenda, Muradnagar (Ghaziabad) and Krishi Vigyan Kendra, Dadri (Gautam Budha Nagar). Beneficiaries trained on post harvest management of fruits and vegetables, bio-control of crop diseases and pests including root-knot nematode, planting of nutritious grass spp. and cultivation of *Azolla pinnata* as green animal feed. Demonstration conducted on making pits for cultivation of *Azolla pinnata* for use as animal feed. Starter cultures were provided to farmers for cultivating *Azolla*. 15 trainings of 5-days duration in Uttar Pradesh. Trainings also conducted on post harvest and value addition of fruits and vegetables in which 1876 persons participated and 237 farmers directly benefited.

Another on establishment of rural bio-resource complex for Bio-Entrepreneurship development at Latur district was implemented Krishi Vigyan Kendra, Latur, Village Knowledge Center (VKC) was established at KVK campus where Bio-fertilizer production cum supply unit, poultry nursery shed, shed net for vegetable cultivation, vermin-compost demonstration unit and mini dal mill unit were established. 4145 farmers, 580 farm women/SHGs, 770 rural youths and 275 extension functionaries

visited the centre. The selected beneficiaries were given hands-on-training at VKC. Soybean seed production programme was conducted by forming 12 farmers groups in two tehsils of the district. Grampriya and Vanaraja improved birds were supplied to the 123 rural beneficiary farmers in 29 villages of district. 30 farmers were trained on vegetable production. Liquid bio-fertilizer microbial strains like Azotobacter, Acetobacter, Rhizobium and PSB were mass multiplied at laboratory and supplied to 1802 farmers in demonstrations of soybean, pigeon pea, bengal gram and sugarcane. 30 vermicompost units of size 120 sq. ft. have been established at farmer's field. Farmers are benefitted by adopting these activities for their livelihood generation.

Biotechnology Based Programme for SC/ST Population:

Fish Farming: A Project on Economic development of SC and ST community of mid hill region of Pithoragarh district through Aquaculture intervention was implemented at DCFR, Bhimtal, Uttarakhand. 25 farmers were trained adopted aquaculture intervention for socio economic development. Several training programmes were conducted on fish culture. Polythene lined ponds were created for temperature maintenance for stocking with exotic carps i.e., *Cyprinus carpio* (normal common carp and Hungarian carp), *Hypophthalmichthys molitrix* (Silver carp) *Ctenopharyngodon idella* (Grass carp). Training programmes conducted on fish culture helped the farmers to earn additional income.

Another project on sustainable fish seed production in eco-hatchery and multi-species fish rearing for livelihood security of tribal youths in Manipur was implemented at Democratic Community Development Organization, Leikai, Manipur. Training cum demonstration programme conducted on various aspects of fish seed production including induced breeding, nursery rearing, fingerlings and yearlings. 150 SC/ST farmers were trained in various

aspects of fish production. 10 SHGs have been formed during the project period. Adoption of fish farming practice has increased the additional income of the beneficiaries.

Pig Farming: A Project on Socio-economic upliftment of SC/ST population through adoption of piggery farming for sustainable development in five villages of Churachandpur District, Manipur was implemented with the help of the Department of Veterinary & Animal Husbandry Services, Manipur. Project was implemented in 05 villages from which 05 SHG groups were formed and training cum demonstration programmes were conducted on scientific rearing of pig. Piglets with inputs of feeds, medicines were also distributed to the target beneficiaries. Regular project monitoring activities helped the farmers in adoption of pig farming for their livelihood generation.

Goat Farming: A Project on Economic empowerment of rural goat farmers through scientific intervention In Block was implemented at Sher-E-Kashmir University of Agricultural Sciences & Technology in R.S. Pura, Jammu. Benchmark survey for the selection of beneficiaries was conducted in three villages namely Qutab Nizam, Chohala and Bagga Channa of Tehsil R.S. Pura, Distt. Jammu of J&K. Seven families from the village Qutab Nizam were selected and trained on goat farming. Each family was given two goats of beetal breed between age group of 1-2.5 years along with one adult buck in each village for breeding purpose. 30 female goats and two male goats (bucks) were distributed to the beneficiaries. Regular health monitoring has been provided to the beneficiaries alongwith proper deworming and vaccinations. Beneficiaries were given exposure in Kissan Mela organized by the Directorate of Extension, SKUAST-Jammu. Farmers adopted goat farming for livelihood generation.

Promotion of Black Pepper and Ginger Crops: A Project on Production Enhancement and Market Promotion of Black Pepper and Ginger Crops among

the tribal population in Wayanad District of Kerala was implemented by M.S. Swaminathan Research Foundation, Kalpetta, Kerala. Baseline survey on socio-economic status and agronomic practices on pepper and ginger have been done. 170 soil samples have been collected from pepper gardens and analysis have been done. 03 decentralized pepper nursery units at three intervention sites with a total capacity of 50,000 plants for two improved varieties and 9 traditional varieties have been established. 05 women groups identified for bio-inputs production and in engaging in maintaining nursery units. Ginger cultivation through mini rhizome technique started at five tribal villages. Training and capacity building programmes on various techniques in sustainable pepper and ginger cultivation have been done for 190 farmers. Novel strains of *Trichoderma*, *Pseudomonas fluorescens*, *Beauveria bassiana* isolated. Linkages established with various State and Central Govt. institutions. Adoption of this activity benefited the farmers.

Vegetable Production: A Project on Socio-Economic Upliftment Of The Rural And Peri Urban SC/ST Population Of Srikakulam District was implemented through Agri Biotech Foundation. 03 units in vegetable seedling production were established in (Kothavalasa, Chintalapeta and Mandawakuriti) are progressing successfully. Vermicompost units established helped in distributing the produced vermicompost to the surrounding farmers for income generation. 105 farmers benefited through vegetable seedlings and vermicompost and adoption of Agri biotechnologies practice for income generation by the beneficiaries.

Another Project on Empowerment of ST-Women SHGs through organic cultivation of seasonal vegetables plantation was implemented by Central Agricultural University, Nagaland. Awareness created in Women Self Help Groups on seasonable vegetable production and marketing. The cultivation of vegetable is providing supplementary diets as well as income generation for rural women. Rural women benefitted through training and

demonstration activities their socio-economic status. The project helped in eliminating food insecurity in their households.

Cut Flower Production Technology: A Project on formulation of cut flower production technology by demonstration and training programme of SC/ST population was implemented at Sam Higginbottom Institute of Agriculture, Technology 400 SC/ST farmers have been trained in the project through training programmes conducted in the Department of Horticulture. Training on tuberose, gerbera and gladiolus cultivation were also given including field demonstration on various aspects of cut flower production technology. Planting materials of gladiolus and tuberose were distributed to the farmers for cultivation in their fields. Regular field visits were arranged with on-site training, monitoring. Two naturally ventilated polyhouses, each of 200m² area were established in the Department of Horticulture, SHIATS, Allahabad for conducting regular training and multiplication of planting materials of cut flowers like gladiolus and gerbera. Farmers benefited through training programmes for livelihood generation.

Health & Nutrition: A Project on nutritional security in tribal areas of East Godavari District, Andhra Pradesh through community based approaches was implemented at Central Tobacco Research Institute (ICAR), Rajahmundry. Various awareness and capacity building programmes and extension activities have been conducted for the benefit of 1000 tribal families. The important nutri-preneurial income generation homestead units viz., adda leaf plate making, soya milk processing, soya milk products, solar dried food products and millet based bakery units were established in the villages. Value added products with minor forest produce viz amla powder, amla candy, amla supari, desiccated coconut powder, vegetables chips, fruit jellies, aamchur, herbal powder, etc., were promoted through Self Help Groups (SHGs). Millet based food products viz., ragi biscuits, jowar biscuits, tadi biscuits, cakes and buns were promoted among the

women groups. Adda leaf cups and plates, bamboo sheath cups, teak leaf cups were also promoted as homestead units with the help of the adda leaf plate making unit. The SHGs trained in this project are earning good income by selling their finished products to different agencies.

Biotechnology Based Programme for Women:

Health and Hygiene: A project on prevention of genetic and congenital disorders, awareness, counseling, screening and genetic education programme was implemented at West Bengal University of Technology, Kolkata 395 individuals have been screened for genetic disorders of which 142 children diagnosed as Down Syndrome (DS), 40 mosaics down syndrome, 21 turner syndrome, 7 with hereditary gingival fibromatosis, 84 with ambiguous genitalia and 101 with miscellaneous genetic disorders. 15.49%, 4.93% and 39.44% of typical DS patients are suffering from congenital heart disease, intestinal obstruction and respiratory distress respectively. Seven cases of hereditary dental abnormalities were also analyzed. Chromosome analysis has also been carried out in 101 individuals suffering from gynecological problems such as primary amenorrhea, infertility etc. To create awareness on genetic disorders and their management, a book has been published in local language and distributed among the parents/guardians of the affected children and in different hospitals. A web based portal on genetics has been developed and is being aired for the benefit of medical students and practicing physicians.

Another project on women breast cancer screening is being continued in four districts of North East India namely Manipur, Meghalaya, Mizoram & Tripura through coordinating agency Cancer Foundation of India, Kolkata. Public health nurse visited the field and door to door to generate awareness and brought the suspected women for screening mammography. 3099 women were performed mammography during 3 years.

Ultrasound in dense breasts and characterization was performed by sonography and elastography. All women with suspicious lesions (32 in number) were biopsied, out of which 14 found to be benign and 18 were malignant in nature. The project has not only benefitted the women by early diagnosis and treatment of breast cancer, but also educated the women on early symptoms of breast cancer, methods of breast self examination as well as importance of regular mammography and clinical breast examination.

A project on setting up of a multi-purpose behavior therapy (MPBT)/health promotion room for women attending gynecology OPD in an apex level hospital of north India was implemented at PGIMER, Chandigarh. 6500 patients have been counseled on various disease problems and MPBT facility has been established in Obstetrics and Gynecology OPD, PGIMER, Chandigarh. Booklets on urinary incontinence, prolapse uterus, dysmenorrhoea, menopause and care of pregnant / lactating women have been published in hindi. Patients family members were involved during the counseling as an integrated part of MPBT. The implementation of the project helped women understand the behavioral therapy along with counseling, exercises and lifestyle changes.

Entrepreneurship Development: A project on socio economic empowerment of rural women through bakery entrepreneurship was implemented at University of Agricultural Sciences, GKVK Bangalore. 50 women were trained on various aspects of bakery products for 15 days. The trainees have been imparted knowledge on bakery raw materials used and the product development, food safety and personal hygiene including knowledge on product promotion. Trainees were also educated on different channels of marketing conditions prevailing in the existing bakery units and consumer preferences in the area. Adoption of this practice has increased additional income of the trained women.

Livelihood Generation and Skill Development: A project on development of bio-agent and mycorrhiza colonized seedlings of horticultural crops by rural women, dissemination of technology in PPP mode was implemented at Indian Institute of Horticultural Research (IIHR), Bangalore. Training on Production of bio-agent and mycorrhiza colonized seedlings of horticultural crops were conducted at different villages of Karnataka and Tamilnadu. 1240 rural women and men were trained to produce bio-agent colonized seedlings by using a combination of bio-agents (*Pseudomonas fluorescens*, *Paecilomyces lilacinus*, *Glomus fasciculatum* and *Glomus mosseae*) for raising the seedlings of the horticultural crops in the shade net, nursery beds and in the open field conditions. Awareness was created among the farmers on bio-management of disease of horticultural crops using bio-agents including use of micro-nutrients in production of vegetable crops. Linkages developed between IIHR and CNBRCD Bengaluru and other NGOs including KVKs, with the local target groups for effective dissemination of the technology of bio-agent to the farmers. Adoption of skill development programme has helped in livelihood generation.

Another project on improved livelihoods through conservation and cultivation of near extinct banana landraces of Kolli Hills of Tamilnadu was implemented at NRC for Banana, Tiruchirapally. 13500 *in vitro* tissue culture raised plantlets of cv. Manoranjitham and 10000 plantlets of cv. Numaran were distributed to 550 beneficiaries along with bio-fertilizer kits and protocol details on plant production and protection techniques. Various training programmes on macro-propagation for the production of low cost planting material in their backyards, visual diagnostics, identification and differentiation of various banana pests and diseases of plant were conducted. 269 farmers have been benefited through cultivation of extinct banana varieties. 2100 plantlets of variant Manoranjitham were produced distributed to farmers of Kolli Hills for livelihood generation.

A project on preserving future genetic resources through capacity building of women farmer and utilization for livelihood improvement was implemented at Assam Agricultural University, Jorhat, Assam,. Two community seed banks at Jorhat and Golaghat districts have been established. Documentation of local germplasm has been done and farmer's varieties were sent to PVPFR (Plant Variety Protection and Farmer's right) Authority of India for registration and protection of farmer's right. Awareness camps on conservations of local genetic resources have been conducted in Jorhat and Golaghat district. A state level one day workshop on Market Linkage for commercial promotion of Indigenous specialty rice of Assam was organized. Rice Diversity fair and mela organized for displaying more than 300 varieties of rice. Market linkage and entrepreneurial skill development workshop on commercial prospect of indigenous rice of Assam in which large number of farmers participated.

A project on mushroom spawn production for the entrepreneurship of Kashmir valley was implemented at University of Kashmir, Srinagar. 90 rural and 90 urban educated women were trained on mushroom cultivation at different demonstration unit. Women were fully trained on the spawn production at spawn production unit of Kashmir University. They were given trainings for production of pure and disease free spawn. Farmers including entrepreneurs from different districts were provided with quality spawn from spawn production laboratory at Kashmir University helped beneficiaries to increase mushroom production among the rural as well as in commercial urban growers. Trainings were also helped to develop proper market linkages for selling the mushrooms and its products.

A project on plant tissue culture programme for women and rural development was implemented at College of Agriculture Biotechnology, Marathwada University, Latur, Maharashtra. Nine

hands on training programmes of 10 to 15 days duration were conducted in which 287 women, rural youths and students participated. Post-evaluation of these trainings have revealed high level of adoption. 30 women and 26 trainee participants have established their own acclimatization nursery, vermicomposting and Azolla production units. Adoption of practices have increased the income of the beneficiaries.

A project on biotechnology led socio-economic empowerment of farm women was implemented at IARI, Pusa New Delhi. 542 beneficiaries have been selected from 5 villages and 35 SHGs have been formed. Several trainings programmes have been conducted on use and maintenance of drudgery reducing equipments, preparation of mineral mixtures for animals, mushroom production, improved cropping, seed production, vegetable production, goats rearing and poultry. Women were motivated for enhancing entrepreneurship in preparing chips of potato and golden sweet potato. They were also given improved varieties of rice, wheat, mustard lentil, onion, pea, fodder crops and vegetables, fruits and tree crops, subabul, drumstick and forage grasses. Barbari and Black Bengal goats, Kuroiler chicken, and mushroom were also introduced for income generation. Adoption of this practice has increased additional income of the beneficiaries.

Poultry Farming: A project on sustainable livelihood generation for rural women through improved backyard poultry farming was continued at College of Veterinary Science and Animal Husbandry, Central Agricultural University, Mizoram. Parent Vanaraja chicks have been purchased from Project Directorate of Poultry, Hyderabad and they are being reared in deep litter system of management in the instructional poultry farm complex of the College. Ten women were imparted training on scientific poultry management to enhance their skill to serve as local service providers in their respective villages. Rural poultry

resource centre has been established in the villages. Vanaraja chicks have been distributed to the beneficiaries for establishing poultry farming (Fig1).

Adoption of backyard poultry farming helped in increased additional income of the beneficiaries.



Fig.1: Distribution of Vanaraja Chicks to the women beneficiaries



06

BIOTECH PRODUCT AND PROCESS DEVELOPMENT

BIOSYSTEMS AND BIOPROCESS ENGINEERING (BBE)

Biosystems and bioprocess engineering program supports interdisciplinary approaches towards analysis and synthesis of complex cellular systems based on the hierarchical structure and decomposability of bio-systems. Further, towards achieving efficient bioprocess, research on recombinant technology integrated to process design and in silico modeling and process systems engineering are being encouraged. During the period, projects have been supported in the areas of host and metabolic engineering, biotransformation and bio-systems engineering. A call for proposal for development of an indigenous expression platform was issued to address the challenges faced in producing recombinant proteins in soluble and/or fractional form and for expressing enzymes and metabolites. A total of 85 proposals were received and after initial short listing and technical assessment, 20 proposals have been recommended for support. Some of the major achievements of the projects supported are as follows:

Metabolic Engineering of bio-system for propionic Acid production: Acrylate pathway is of vital importance since it can produce an array of green chemicals with propionic acid being the primary product which is widely used as food and feed preservative. In a collaborative work, IIT Madras and Anna University, Scientists have successfully cloned and expressed all the genes of the acrylate pathway from *clostridium propionicum*

along with genomic integration of D-lactate dehydrogenase in *L. lactis*. They have identified the bottleneck in the pathway and it is found to be due to inhibition of propionyl CoA transferase enzyme by lactate and propionate. The reason for low pathway flux has been identified and construction of retro synthetic pathway has been found to circumvent this.

Engineering fungal strains for enzyme production: Expressing useful enzymes in fungal cells minimizes downstream processing due to extracellular secretion of the desired product. Scientists at IIT Bombay and Guru Nanak Dev University, Amritsar achieved expression of *P. citrinum* b-glucosidase in *A. niger*. The *citA* promoter used to achieve the fungal expression has been patented.

Pre-evaporative stripping of acetone, butanol and ethanol (ABE) for improved ABE fermentation: Separation of ethanol from fermentation broth is not possible by the conventional high temperature distillation. Thus, separation of ethanol-water mixtures by a membrane process, i.e., pervaporation where heating of the liquid mixture is not required and the ethanol-water mixture is separated at low temperature (~30°C) by applying low pressure on the downstream side of the membrane with a vacuum pump was attempted by researchers at University of Calcutta, Kolkata. However, the membrane used should be mechanically stable and highly selective to ethanol, i.e., organophilic when low concentration of ethanol is to be separated from

water or highly hydrophilic when high concentration of ethanol is to be dehydrated by pervaporative membrane process. Accordingly, both organophilic and hydrophilic membranes were synthesized and separation potential of the membranes was studied under varied process conditions. In the present work several mixed matrix type hydrophilic membranes were prepared by incorporating nano sized bentonite clay in the copolymer of acrylonitrile (AN) and acrylic acid (AA). The novelty of the work is that instead of physical mixing, the nano sized clay was introduced in the membrane by an in-situ method, i.e., during polymerization reaction so that no agglomeration of the nano clay occur within the membrane matrix.

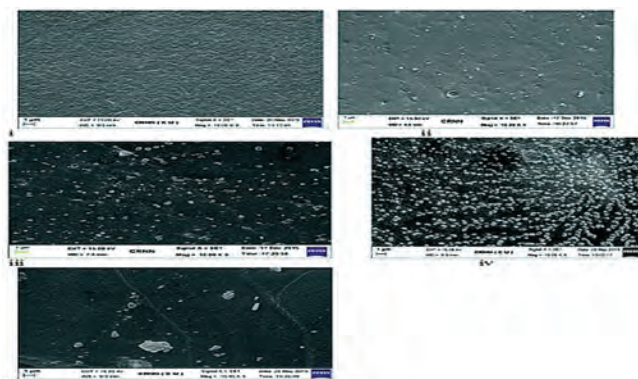


Fig. SEM of the i) unfilled PAN5, ii) F0.5 iii) F1 iv) FL5 and v) F2 filled copolymer

Formate as an alternative to methanol for inducing production of recombinant proteins :

The yeast *Pichia pastoris* is a popular host for production of recombinant proteins by the Indian biotechnology industry. At present, synthesis of these proteins is induced (i.e., stimulated) by exposing the cells to methanol. To reduce methanol consumption, researchers at IIT, Delhi developed modified strains of *P. pastoris* (called Mut^s and Mut) which metabolize less methanol than the wild-type parent strain (called Mut⁺). However, it is not known if the lower consumption of methanol by Mut^s and Mut compromises their ability to synthesize the proteins. The rates of recombinant protein synthesis

in all three strains was compared by the protein expression rate in Mut⁺ and was found to be approximately 10 times the rate observed in Mut^s and Mut suggesting that methanol may not be the real inducer of protein expression. Interestingly, it was found that formate, a product of methanol metabolism, induced protein production as well as methanol. Since it is not flammable either, formate is much better than methanol for inducing large-scale production of proteins.

Tuberculosis therapeutics by manipulation of Rifamycin Polyketide Synthase Gene Cluster for Rifamycin B analogs:

The purpose of generating one or more analogs of the Rifamycin B by modification of the polyketide synthase gene cluster of the multi-drug resistant of strain *M. tuberculosis* by the manipulation of Rifamycin Polyketide Synthase (*Rif* PKS) gene cluster of *Amycolatopsis mediterranei* S699 is being taken up at UDSC and IGIB. Proof of concept for the development of an effective analog of rifamycin B: 24 desmethylrifamycin B was developed by genetic modification of *rif*PKS in *A. mediterranei* S699. The analog thus produced showed about 30 times better activity than normal rifamycin B derivatives against various drug sensitive and resistant strains of *M. tuberculosis*. Construction of plasmid clones has been done. Acyl transferase (AT) domain coding genes of the rifamycin biosynthesis gene cluster are taken for the genetic transformation of *A. Mediterranei* S699 and plasmids has been constructed. These plasmids now contain a malonate specific acyl transferase coding gene (*rapAT2* from rapamycin producer *Streptomyces hygroscopicus*) sandwiched between the flanking regions of the AT's that are targeted for swapping. They have five plasmid constructs specifically capable of swapping either of the three AT's viz. AT5, AT7 or AT8. These plasmids are being electro-transformed into *A. mediterranei* S699 for carrying out the genetic manipulation.

Bioprocess development for caffeine

degradation: The 5 genes involved in caffeine degradation by *Pseudomonas sp.*, NdmA and NdmD were cloned into pET28a expression vector. Cloning was confirmed by Sanger sequencing and insert release by double digestion. Over-expression of NdmA in *E. coli* BL21 and *E. coli* Rosetta by induction using 0.3 mM IPTG results in the formation of inclusion bodies. Post induction temperatures were varied and found that at 22 °C nearly 40% of protein was in soluble form. Further attempts are being made to increase the solubility of over-expressed NdmA. Attempts made to increase theobromine production revealed that varying Co₂ concentration had no significant effect on theobromine production. It was also found that when induced cells produced from caffeine media with galactose was used in resting cell experiments, theobromine production was increased from $1.08 \pm 0.1 \text{ g/l}$ to $1.38 \pm 0.06 \text{ g/l}$.

Fabricating microchip for in-situ product monitoring in bioreactors:

Scientists at IIT Delhi have developed amperometric detector microchip for in-situ product monitoring in bioreactors. The strategy is to fabricate microfluidic devices compatible to capillary electrophoresis amperometric detector (CE-AD). CE-AD devices developed based on micro patterned indiumtin oxide (ITO) and polydimethylsiloxane (PDMS) and testing the separation and analysis of flavor enhancing components of Beer and Wine (fermentation products) was carried out. Microchip fabrication using conventional photolithography has been carried out based on Au-microelectrodes fabricated on glass substrate and PDMS based microchannel. Off-chip analysis of selected group of analytes in beer has also been completed. Validation of the microchip was completed by obtaining electropherograms using well-known electro active compounds.

Three projects under the DBT-COE scheme is being

implemented under this taskforce. The salient achievements in COE are as follows:

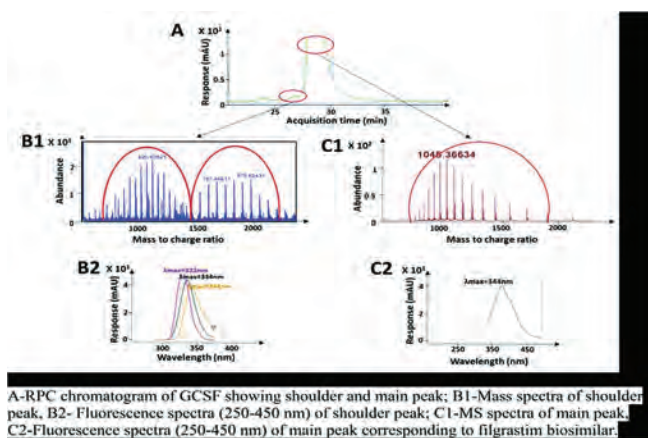
Programme Support for Microbial Production of Designer Bio-Polymers from Renewable

Resources: Scientists at IIT Delhi are working on Microbial Production of Designer Bio-Polymers from Renewable Resources. In-depth Biopolymer production experiments were conducted in the newly developed laboratory with sucrose as raw material and *Azohydromonas australica* (gram negative bacteria) in 7-liter bioreactor. Batch growth and Polyhydroxybutyrate production kinetics was established. *A. australica* cultivation has reached to the stage of 300 liter bioreactor. Copolymer production protocols using *A. latus*, *C. necator* and *W. eutrophas* has been optimized and validated up to 3.5 liter bioreactor. This is being scaled up to 70 liter bioreactor. *Bacillus thuringiensis* IAM 12077 batch cultivation has been scaled up-to 70 liter bioreactor. Model based optimization studies have been done for *Bacillus thuringiensis* IAM 12077 to produce medical grade polymer. This is being scaled up to 70 liter bioreactor configuration. PHB production using the most promising culture and well-optimized fermentation conditions is being attempted for obtaining medical grade polymer.

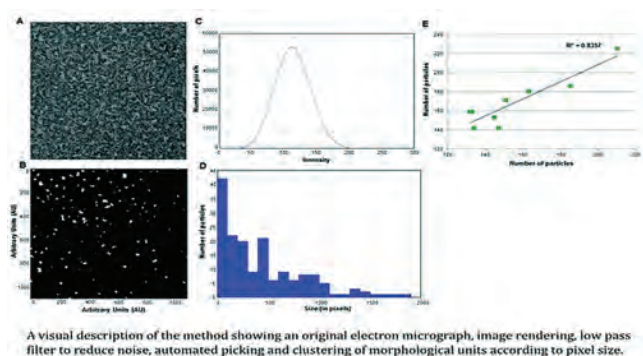
Centre of Excellence for Biopharmaceutical Technology :

The DBT COE for Biopharmaceutical Technology is being implemented at IIT Delhi. The major research highlights are:

Analytical comparability was proved among five approved Granulocyte Colony Stimulating Factor (GCSF) bio-similars marketed in India to innovator product. ESI-MS together with RPC-FLD was proposed as a tool to monitor occurrence of conformational variants of GCSF. This was demonstrated by the presence of double charge envelope by ESI-MS and multiple fluorescence peaks measured by RPC-FLD for the peak eluting earlier than the peak corresponding to the main product.



A novel, automated method for characterization of morphological patterns in therapeutic protein formulations using electron microscopy has been developed. The quantitative rendering of electron micrographs is expected to fill the gap between non-visual, indirect techniques and direct, high-resolution structure determination by providing the means to obtain a signature distribution of structural and morphological units present in protein-based drugs, and provide requisite information to reduce aggregation under various conditions of manufacture and storage. Routes for the catalytic transformation of 6-amyl- α -pyrone (6PP) to produce long chain hydrocarbons were explored for the first time. 6PP was established as a potential biomass-derived platform molecule to produce precursors for fuels, chemicals, polymers and pharmaceuticals



Centre of Excellence in Vaccine Delivery using Biodegradable Polymeric Particles: Scientists at NII are working on pneumococcal polysaccharides

vaccine formulation and its delivery as micro-particles. Sterile polymeric particle formulation setup is being established at NII. Production of polymeric microparticles in gram scale is being optimized by using spray drying. Four pneumococcal capsular polysaccharides used for formulation from serotypes 1, 5, 6B and 19F and are being tested for the immunogenicity through immunization experiments. Pneumococcal proteins such as PsaA and SP0845 have been expressed in *E. coli*. Purification of these proteins is in progress.

PUBLIC HEALTH FOOD AND NUTRITION BIOLOGY

Research and Development endeavors were continued in food biotechnology and nutrition biology, addressal of micro & macro nutrient deficiencies through development of fortified foods with generation of clinical evidence, health care products/nutraceuticals/dietary food supplements; pro-biotics for holistic health; addressal of celiac diseases; addressal of vitamin B₁₂ deficiency; nutriepigenomics; postharvest processing and value addition; food safety & allergenicity, shelf life extension of perishable foods etc. Projects were funded in two new areas: (i) Food to Food Fortification and (ii) Addressal of Food Allergy. A programme for strengthening research in the area of Food sciences through an integrated M.Sc-Ph.D programme in Gauhati University was initiated. Research leads in major thematic areas are given below:

Public Health: Demonstration Unit for Production of Iron Fortified Rice Premix: Iron deficiency is the most common cause of anaemia in India. Being a staple diet for most of India, rice can become a vehicle to carry the required micronutrient to the affected group. To address this problem, IIT Kharagpur team developed the process technology & machinery for the production of iron fortified rice premix from the broken rice and an iron fortificant. The broken rice is first grounded into flour, and then desired amounts of water and iron fortificant are

uniformly mixed and then fed into a twin-screw extruder for the production of the extrudate of a rice-like shape. The iron fortified rice premix, thus produced, is mixed with normal rice in the ratio of 1:100 and packaged. The developed iron fortified rice premix has iron content 600-800 mg per 100 g; the iron fortified & normal rice blend has 6-8 mg Fe per 100 g. (Fig 1). A pilot scale demonstration facility (Fig. 2) with a production capacity of 100 kg/day iron fortified rice premix has been established at IIT Kharagpur. This technology is ready for commercialization.

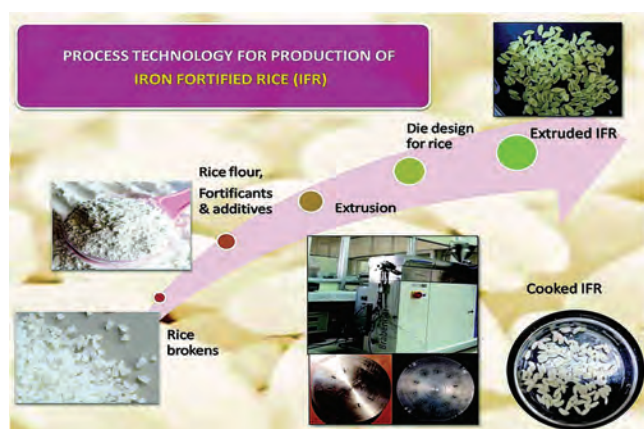


Fig.1 Process flow for Iron Fortified Rice Technology

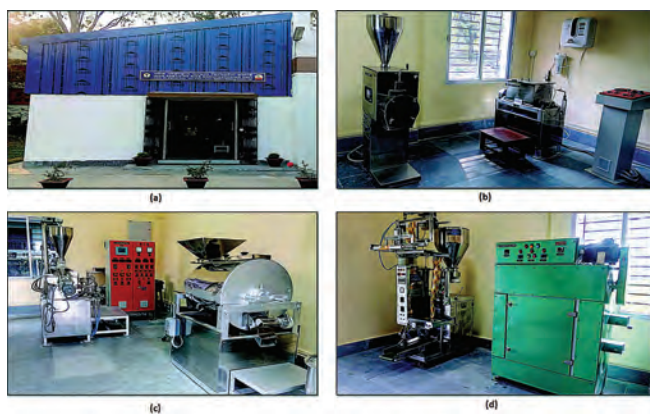


Fig 2: Pilot Scale unit for Manufacture of Iron Fortified Rice (a) Front view of Iron Fortified Rice Manufacturing Unit (b) Micro Pulveriser, Blender & Conditioner (c) Twin Screw extruder and Polisher (d) Re-circulatory Tray Dryer and Packaging Machine

Nutrition Biology:

Estimation of body cell mass using potassium counter in pregnant women and neonates: Low

Birth Weight (LBW) prevalence is high in India (~30%) and is has a multiple etiology. One of the causes is low quality and quantity of maternal protein intakes in Indian women, which may be especially relevant in anthropometrically undernourished women, or adolescent mothers whose body protein (muscle) stores are as yet underdeveloped, subsisting on vegetarian diets with sub-optimal protein quantity and quality. Furthermore, the diets of Indian pregnant women do not meet their increased gestational protein requirement, with the protein quality being low, and from a predominantly cereal based diet. Since body composition measurements in pregnancy are limited due to factors such as hydration status and safety issues related to radiation exposure, there is a need for a safe, accurate and non-invasive method to measure body composition in pregnant women. A state of art whole body potassium counter to accurately estimate the body cell mass (lean body mass) has been built at St John's Research Institute. This newly built whole body counter is being utilized to answer research questions related to protein requirements in pregnancy, measuring the impact of diet on gestational weight gain and fetal growth, particularly of fetal body cell mass. About 50 women have been recruited and are being followed throughout their pregnancy and the final measurement will be carried out at the time of birth of the baby along with measurements of the baby.

Association of Vitamin D and Calcium with Development of Breast Cancer: In India, breast cancer is the most common cancer with an estimated 115,251 new cases being diagnosed every year and the second most common cause of cancer-related deaths with an estimated 53,592 breast cancer deaths in 2008. Vitamin D is a secondary-steroid hormone that has been associated with health outcomes ranging from bone health to cancer. Vitamin D and Calcium are suspected of independently possessing anti carcinogenic properties effective in protecting

against breast cancer. The results of a study conducted by AIIMS, New Delhi revealed a significant difference in the serum 25(OH) D and calcium levels between patients with breast cancer and controls.

Effect of finger millet (*Eleusine coracana*) and kodo millet (*Paspalum scrobiculatum*) arabinoxylans on adipogenesis and associated inflammatory markers: Whole grain consumption has been suggested to modulate metabolic complications such as obesity. Millets play an important role in human nutrition. Several animal based studies and certain human studies suggested that finger millet and kodo millet and their polyphenols confer hypoglycemic effect. Arabinoxylans are non-starch polysaccharides present in all cereal grains including wheat, finger millet, kodo millet and other millets. Arabinoxylans from wheat has been seen to alleviate high fat diet induced alterations. However the nutritional benefits of finger millet and kodo millets and their dietary constituents, mainly arabinoxylan (AX), in protecting from high fat diet induced metabolic alterations are yet to be elucidated. A study conducted by National Agri-Food Biotechnology Institute, Mohali suggested that both finger millet and kodo millet whole grain and bran beneficially modulate the host physiology under high fat diet conditions. Finger millet arabinoxylan supplementation prevented high fat diet induced weight gain and improved oral glucose tolerance and prevented abdominal fat accumulation.

Enhancing Research Capacity and initiating Integrated M.Sc &Ph.D Programme in the area of Nutrition Biology in CFTRI Mysore: The main objectives of this programme are twofold: (i) Initiating Integrated M.Sc and Ph.D programme in the area of Nutrition Biology in CFTRI Mysore and (ii) Enhancing Research capacity; Nutrigenomic approach to study type 2 diabetes mellitus. Students were selected through an all India advertisement hosted by AcSIR and the process included initial

screening based on percentage of marks obtained, subjects studies followed by two rounds of interview. Research has also been initiated to study the early molecular signatures of Type 2 Diabetes mellitus, selection of potential biomarkers for the different stages of Type 2 Diabetes mellitus, designing of tailored diet formulations to enable personalized intervention and use of food technological approaches for scale up production of anti- Type 2 Diabetes mellitus dietary sources/ components/formulations.

Impact of B12 deficiency and hyperhomocystenemia on BMD, osteoporotic fractures and bone turnover in postmenopausal women: The relationship of homocysteine (Hcy), folate and vitamin B12 with bone mineral density (BMD) has been studied in various populations. A study conducted in urban community dwelling postmenopausal women in SGPGI, Lucknow for their clinical, nutritional, life style, vitamin D, B12, homocysteine, oxidative stress, cytokines, vitamin D binding protein, bone mineral density status, body composition and hip geometry. A high prevalence of osteoporosis (42%) was seen in women aged 50 and above. On the other hand, a high prevalence of vitamin D deficiency (52%) was seen majority of the subjects. It was further observed that serum free vitamin D, and bioavailable vitamin D correlated with serum total 25(OH)D levels and there was no correlation of total vitamin D with homocysteine. Serum glutathione levels showed a trend of negative correlation with bioavailable Vitamin D, while total vitamin D has significant positive correlation with total antioxidant levels.

Food Biotechnology: Development of indigenous hypoimmunogenic wheat based food products targeting Celiacs: Gluten allergy in individuals causes inflammatory bowel disease. Avoidance of wheat related products is one of the preventive strategy. The other approach is to reduce the immunogenicity of wheat using food

biotechnological approaches. At CFTRI Mysore indigenous wheat milled products (Whole wheat flour, Refined Wheat Flour, Semolina, Durum and Dicocum) modified by enzymatic hydrolysis using food grade fungal protease and chemical deamidation at alkaline (Sodium bicarbonate) & acidic (lactic acid) condition to reduce immunogenicity against gliadin antibodies. Based on experimental studies, Whole Wheat Flour and Refined Wheat Flour are found to be best hypo immunogenic flours with enzymatic hydrolysis and chemical deamidation (alkaline condition) respectively. Five types of hypo immunogenic products, namely hypo immunogenic muffins, hypo immunogenic bread, hypo immunogenic biscuits, hypo immunogenic chapatti and hypo immunogenic spinach pasta were developed.

Engineering Microorganisms for production of metabolites used in food industries: D-Tagatose is a ketohexose and is a rarely occurring natural sugar. D-Tagatose is an odorless, white crystal, which has almost same sweetness as sucrose. D-Tagatose is stable in the foods to which it is added during the processing and storage of food. The chemical process of Tagatose production is inefficient and involves toxic reagents and solvents. Tagatose production can be carried out using the enzyme L-arabinose isomerase which mainly catalyses L-arabinose to L- ribulose and D-galactose to D-Tagatose. This enzymatic reaction requires temperatures higher than 50°C which is energy inefficient and may lead to Mallards reaction or caramelisation. A recombinant L- Arabinose isomerase was synthesized by gene cloning technique. This enzyme showed maximum activity at 65°C and retained almost 70% of its activity at 15°C.

Investigation on nigerloxin, an aldose reductase inhibitor from *A. niger* in the treatment of Diabetic complications: Nigerloxin, an inhibitor of lipoxygenase, aldose reductase with free radical scavenging activity could be a useful molecule for

the treatment of diabetic complications. A rapid reverse phase HPLC method was developed for the detection and quantitation of Nigerloxin, an aldose reductase inhibitor. Safety studies confirmed that Nigerloxin is non toxic.

Reverse Transcriptase PCR (RT-PCR) technique for detection of meat borne pathogens: Real time PCR based technologies emerging as the leading methods for rapid identification of pathogens due to their speed and high degree of sensitivity and specificity. This limitation is overcome by using Reverse Transcriptase (RT-PCR) which is dependent on mRNA. A new PCR technique was standardized using *iroB* gene of *Salmonella enterica* (MTCC 3223 and MTCC 9844), *ystB* gene of *Yersinia enterocolitica* (MTCC 3238) and *hly* gene of *Listeria monocytogenes* (MTCC 657). The technique was standardized using chicken samples artificially contaminated with *Salmonella enterica*. This could detect a DNA concentration of up to 1 ng/ µl for *Salmonella* and *Yersinia* sp., and 0.0025 ng/µl for *Listeria* sp.

Pro-biotics of Non-Dairy Origin from Northeast India: An attempt was made to study the bacteriocin and probiotic properties of *Lactobacillus* associated with traditionally fermented foods of North-East India. *Enterococcus* spp. recovered from fermented food samples were also characterised, focusing on the incidence of virulent factors and presence of antibiotic resistance that may represent a transmission route for enterococci to healthy humans. *Lactobacillus*, *Vagococcus*, *Lactococcus*, *Enterococcus*, *Bacillus*, *Staphylococcus* spp., and *Enterobacter* spp. were characterized from the fermented products of non-dairy origin from Northeast India based on biochemical profiling. The *Lactobacillus* community involved in the fermented foods, *Tungtap* and *Tungrymbai* traditional foods of North East revealed high percentage of cell surface hydrophobicity and anti-oxidant activity when compared to other non-lactic acid bacteria. Antagonistic activity of five *Lactobacillus pobuzihii*

against some indicator bacteria such as *Klebsiella pneumoniae*, *Bacillus licheniformis*, *Bacillus cereus*, *Salmonella typhi* and *Escherichia coli* was also observed. High level resistance of the *E. faecalis* to the aminoglycosides, kanamycin and gentamycin was observed in the study. A high percentage of *E. faecalis* isolates showed resistance to vancomycin. The occurrence of *gelE*(gelatinase), *efaAfs* (cell wall adhesins expressed in *E. faecalis*), *esp* (extracellular surface protein), *agg* (aggregation substance), *cylA* (activation of cytolysin, bacterial toxin) and *cpd* (sex pheromone) genes in the enterococci isolates from fermented food was also reported.

Molecular detection and quantification of shiga-like toxin producing *Escherichia coli* in fresh vegetables: The persistence of Shiga-like toxin producing *E. coli* (STEC) strains in the agricultural soil creates serious threat to human health through contamination of fresh vegetables. An attempt was made to assess the possible contamination of STEC in the fresh vegetables through PCR-based molecular methods, to identify the source of contamination in the production chain and to develop some simple controlling measures to avoid the pathogen in the fresh raw eaten vegetables. Among the raw eaten vegetables collected from the markets, cucumber, lettuce, coriander and carrot were found to be highly contaminated followed by cabbage, radish, mentha and broccoli with *E. coli*. The mean occurrence of *E. coli* in those contaminated vegetables ranged from 2.0 to 4.0 log₁₀ cfu per g of vegetable. Through the source tracking experiment, the partially decomposed manure applied soil for coriander and processing water for washing the carrot and soil were identified as major source for *E. coli* contamination in those vegetables. The screening of *E. coli* for O157 by shiga-toxin specific primers confirmed that about 5-15% of them are possible O157 strains.

Vitamin A and Oxidative stress on foetal growth, placental function and low birth weight: The theme of the Center of Excellence sanctioned to St. John's National Academy of Medical Sciences is 'Low

Birth weight and Nutrition' with an aim to generate sustainable nutrition strategies targeted at Indian pregnancies. Under the CoE evidence based research into nutritional strategies for healthy pregnancy were carried out. Studies to examine the constant environmental exposures during pregnancy, document their nutritional lifestyle and environmental exposures during pregnancy, and phenotype the women during pregnancy, and their infants at birth, and through childhood were pursued.

BIOSAFETY RESEARCH

The programme emphasizes implementation of bio-safety procedures, rules and guidelines to ensure safety from the use of high risk group microorganisms, genetically engineered (GE) Organisms and products thereof in research and application to the users as well as to the environment. The Review Committee on Genetic Manipulation (RCGM) functioning from the Department of Biotechnology; and the Genetic Engineering Appraisal Committee (GEAC) in the Ministry of Environment, Forest and Climate Change, has been established for evaluation, approval and monitoring of safety aspects associated with handling of recombinant DNA (rDNA) products in healthcare and agricultural sectors leading to their commercial/ environmental release.

During the year, the RCGM evaluated about 498 applications in its 6 meetings in the areas of agriculture, healthcare and industrial products. The applications were for import/exchange of high risk group microorganisms and recombinant research related materials including seeds, gene constructs, plasmids, vectors, genetically modified organisms (GMOs) & living modified organisms (LMOs); for conduct of pre-clinical toxicity studies; and evaluation of pre-clinical study data. 14 applications for conduct of event selection trials (ESTs)/ Biosafety Research Level 1 (BRL1) trials in confined conditions for seven transgenic crops under development viz. cotton, corn, rice, chickpea,

pigeonpea, brinjal, and okra were also considered from 8 public/private organizations for generation of biosafety data.

Five Central Compliance Committee (CCC) teams with more than 20 experts with expertise in plant breeding, physiology, plant biotechnology, entomology, pathology, silkworm biology etc., along with agriculture and silkworm experts from the states and members of state agricultural universities (SAUs) were constituted and visited the containment and biosafety research trial sites to interact with the in-charges of the trials and the Directors of Research of the respective SAUs and silkworm rearing facilities for monitoring the compliance of biosafety rules and regulations while conducting the trials on GE crops and silkworm as stipulated in relevant Guidelines.

In the pharmaceutical sector, 25 rDNA products were permitted for conducting pre-clinical toxicity studies by 16 private/public institutions & companies. Based on the evaluation of pre-clinical study reports, 11 rDNA products developed by 9 private/public institutions & companies were recommended by RCGM to Drug Controller General of India (DCG (I)) for appropriate phase of clinical trials.

The Department has also been entrusted by GEAC, Ministry of Environment, Forests & Climate Change (MoEF&CC) with the responsibility of reviewing applications for commercial release of Bt cotton hybrids expressing approved events through 'Event Based Approval Mechanism (EBAM)', since 2009. The Standing Committee, serviced by the Department considered more than 400 applications from 32 applicants for commercialization of Bt Cotton hybrids in its two meetings. Based on desirable characteristics, superiority attributes, and agronomic performance submitted through SAU/ AICCIP-ICAR reports, the Committee recommended qualified Bt cotton hybrids for commercial cultivation in respective States in North, Central & South Zones in India

The Department has undertaken several reforms in biotechnology regulatory system including the Establishment of Bio-safety Support Unit (BSU) in partnership with Regional Centre for Biotechnology (RCB). The unit has ensured the preparation of draft guidelines on Bio-containment, Stacked GE crop events, Molecular characterization of GE crops, GE microbes etc. The unit has streamlined the process of techno-scientific scrutiny of field trial applications for the development of Risk Assessment and Risk Management Plans (RARMPs), and became a cornerstone for several RARMP documents. The unit has extended logistic and technical support for scrutiny of applications considered during RCGM and GEAC meetings round the year. One of the significant achievements was the development of draft 'Assessment of Food and Environmental Safety (AFES)' of GM Mustard.

BSU has also provided logistics and financial support for conducting training programs/ workshops like Scientific/ Strategic Research on Biosafety & Biosecurity; Risk Assessment and Risk Management (RARM) workshop for GE plants; Current Developments in GE Crops and Food & Environmental Safety to bring awareness about existing laws, rules and guidelines governing bio-safety regulation of GMOs among various stakeholders as well as for in-house capacity building.

The Department in collaboration with *Central Drugs Standard Control Organization (CDSCO)*, Ministry of Health & Family Welfare has successfully accomplished revision of 'Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India' and formally adopted it on 15.08.2016. The revised guidelines further streamlined data requirements for quality attributes, non-clinical and clinical studies.

Establishment of Indian Biosafety Knowledge Portal (IBKP) gained significant momentum and would commence soon. The portal would ensure biosafety compliance at the organizational level along with

online submission-tracking-review-processing & monitoring of the applications submitted by the organizations to RCGM and ensure easy access of database resources and information related to trends in biosafety & biosafety regulation of GMOs worldwide.

As a measure to observe strict compliance of biosafety guidelines for rDNA activities by various colleges, universities, institutions, laboratories, and industry through their Institutional Biosafety Committees (IBSCs), during the period under report, 31 new IBSCs have been constituted, while 67 old IBSCs were renewed.

Foreign Trade, In-House R&D recognition and other issues: Trade plays an indispensable role and always been a decisive parameter for the growth of country's economy. The Department had fixed and communicated Input/output norms for 03 biotechnological products. Comments on export/import of 04 restricted items were also shared with Directorate General of Foreign Trade (DGFT) to facilitate trade in biotechnology.

Incentivize the core research & developmental

capabilities of various public and private establishments' remains a major boost for innovation driven industrial growth in the country. Keeping in view of the technical expertise, relevancy & essentiality of the projects, resources & manpower established, intellectual property (IP) generated, the Department had recommended 20 R&D units of biotechnology firms under in-house R&D unit scheme to Department of Scientific & Industrial Research.

Patent facilitation and Capacity Building: The Biotechnology Patent Facilitating Cell (BPFC) provides single window awareness-cum-Patent facilitation (examination, filing, maintenance and follow-ups) to scientists and researchers on request for filing of Patent Co-operation Treaty (PCT) and National phase applications on inventions pertaining to Life Sciences and Biotechnology through empanelled IPR firms.

The Department through BPFC filed 04 Indian patent applications and 01 foreign patent application during the year. Following patents have been granted during 2016-2017:

S. No.	Country & Patent No.	Name of the Inventor(s)/ Applicants	Title
1	KOREA Patent No. - 10-1598876 Dated-24.02.2016	Dr. Sarman Singh, AIIMS, New Delhi AND Department of Biotechnology, New Delhi	Chimeric DNA Vaccine Construct against Tuberculosis and Leishmaniasis
2	Vietnam Patent No. 15219 Dated- 29.02.2016	Dr. Nripendranath Mandal, Bose Institute, Kolkata AND Department of Biotechnology, New Delhi	Development of Microsatellite DNA marker to identify disease resistant populations of <i>Penaeus monodon</i> (Giant black tiger shrimp)
3	European Patent No.-2 250 198 Dated- 09.03.2016	Prof. Subrata Sinha, NBRC, Manesar AND Department of Biotechnology, New Delhi	A humanized of high affinity recombinant mouse antibody against Hepatitis B surface antigen
4	European Patent No.- 2483418 Dated- 03.08.2016	Dr. Hari Mohan Saxena, Guru Angad Dev Veterinary & Animal Sciences University, Ludhiana AND Department of Biotechnology, New Delhi	Superagglutination Test



07

BIOTECHNOLOGY INFORMATION SYSTEM NETWORK (BTISNET)

The Biotechnology Information System Network (BTISnet) of the Department of Biotechnology established in the year 1986 is now spread across the country with 170 centres. Based on the infrastructure, developments and capabilities the network centres are in various levels and include Centres of Excellence (CoEs), Distributed Information Centres (DICs), Distributed Information Sub-Centres (DISCs) and Bioinformatics Infrastructure Facilities (BIFs). The network houses one Supercomputer Facility for Bioinformatics and six Interactive Graphics Facilities. Large numbers of R&D projects in bioinformatics are also being supported through bioinformatics programme. The network supports teaching program in M.Sc., M.Tech. and Ph.D. in Bioinformatics and Computational Biology to generate skilled manpower in Bioinformatics. Further, the BTISnet centres are conducting short term trainings/workshops for the benefit of research community including experimental biologists. Large numbers of peer-reviewed publications have been emerged during this year. These publications are being compiled into a compendium. These centres also provide services to the scientific community. These activities are being coordinated by the Apex Biotechnology Information Centre (BTIC) which is located at the Bioinformatics division of Department of biotechnology (DBT).



Location of BTISnet Centres on India Map

Centres of Excellence (CoE):

Six Centre of Excellence (CoE) in Bioinformatics, Computational and Systems Biology have been established as part of BTISnet. These Centres are well equipped with State of Art Bioinformatics infrastructure to support research within the Institute as well as neighbouring institutions. The focus of these centres is high quality research, education and services.

Supercomputing facility for bioinformatics & computational biology (scfbio), has been established at IIT-Delhi with a vision to develop personalized medicine using Gene to Drug (Dhanvantari) pathway. Their efforts have resulted in a whole genome analysis methodology and software based on DNA energetics (ChemGenome), an all atom

energy based computational protocol for protein tertiary structure prediction (Bhageerath-H), and a binding free energy based methodology for protein/DNA targeted lead molecule design (Sanjeevini). These softwares are web-enabled and made freely accessible from the SCFBio site (www.scfbio-iitd.res.in) to the entire global community of interested scientists and students. With the help of these softwares one can design a lead molecule which could be improved iteratively in combination with experiment to yield personalized medicine. This Gene to Drug pathway is a major step towards finding the right medicine for the right disease for the right person in an automated way with a potential to help the society in a big way. Leadinvent (www.leadinvent.com) incubated at IIT-Delhi from 2006 to 2009 and Novoinformatics (www.novoinformatics.com) under incubation at IIT-Delhi since April 2011 are two start-up companies created by the students and staff of SCFBio based on the Gene to Drug innovations at SCFBio, IIT Delhi. The centre developed software called Distance to native - D2N for to calculate a score for a given protein structure based on the physico chemical properties of the known structures, to make prediction in unknown cases. The centre has also developed a meta server for protein tertiary structure analysis and validation. The centre has published seven papers in the peer reviewed international journals of high impact.

The research focus of the CoE at JNU, New Delhi has been on comparative genomics, structural biology, in-silico drug design, biological evolution, biomolecular simulation, data-mining, analysis of large scale data, systems biology, complex systems and artificial intelligence. A new program on complex systems has been initiated in this year. The facility is ably supported by excellent computational and communication infrastructure, computer clusters, multiprocessors nodes, large memory nodes and GPUs to facilitate specialized research. Four book chapters and 33 publications have emerged from

the centre during the year.

The thrust areas of research for the CoE at IISc, Bangalore are genome analysis, development of new algorithms, internet computing, structural analysis of biological macromolecule, structural pharmacology, computational immunology. The centre has developed software packages for structural biology such as CSSP, MIPS, FAIR and SSMBS. The centre supports the Interactive graphics facilities. Twenty four research papers in high impact journals have emerged from the centre.

The CoE in Bose Institute, Kolkata is undertaking research in the area of genome analysis, molecular evolution, genetic engineering, regulatory RNA, stem cell & oncogenomics, structural bioinformatics, ligand-design and network biology. The centre has developed two web servers: PVT (pipeline version of TopHat); PVT Cloud for implementing PVT pipeline in cloud computing systems and has published 21 high impact papers in the current year. The centre also offers webservices in the six selected areas.

The main activity of the centre at MKU, Madurai has been on structural genomics of prophage proteins, structural bioinformatics of membrane proteins, studies on protein aggregation in human diseases. The centre also coordinates the network teaching programme involving MKU, Anna University and Pondicherry University. The centre has published eight research papers

The CoE at Pune University focuses on genomics, proteomics and phylogenetic analysis of infectious viruses such mumps, rhinovirus, Dengue etc. The centre has developed a number of databases and server viz. RTD – phylogeny server, HRV typer – Human rhinovirus server, BDE – Bio Db extractor, IRESPred server for cellular and viral internal ribosome entry sites prediction, AEROMONAS ML styper to identify the Aeromonas sp. and has published about 16 papers and three book chapter during the year.

Distributed Information Centres (DICs)

As part of BTISnet eleven Distributed Information Centres (DICs) in Bioinformatics have been established. The focus of these centres, like CoEs is high quality research, education and services. The DIC at CCMB has developed a database on miRNAs and their targets in breast cancer, sequenced four bacterial genomes including of *Psychrophilic bacterium*, *Sphingomonas antarcticum*. They have published 21 research papers. CCMB has also developed a tool for identification of histone free regions (HFRS) at HOX loci. The DIC at IARI, New Delhi has divided the research activities in three areas of genomics, proteomics and chemo-informatics.

The IMTECH Chandigarh, DIC has developed 6 webserver and 9 databases including t-RNAmod for prediction of t-RNA modifications, HLP for prediction of half life of peptide in intestine like environment, ntEGFR – open source web server for predicting inhibitory activities of molecules. The centre has published 22 peer reviewed publications. The most notable achievements by the researchers working at the NII, New Delhi centre is the development of Ten Web Servers including Substrates of PDZ domains, Analysis of miRNA-mRNA base-pairing, Analysis of PKS/NRPS, Motif Discovery, Analysis of enzymes catalyzing novel PTMs, Substrates for MHCs & Kinases. The centre has published 6 research papers. The DIC at Kerala Agriculture University, Thrissur has created to new databases DIACAN (Antidiabetic and Anticancer Medicinal Plants Databases) and MangoDB a complete web source for varieties of mango cultivated in Kerala. The DIC M.S. University, Baroda has divided the research activities in Five areas of Genetics, Molecular Biology, Immunology, Industrial Fermentation and Biophysics. The centre's two Bioinformatics publications got the status of "highly accessed" papers in peer reviewed journals. The researchers working at the University of Calcutta, Kolkata centre has carried out the bacterial clade,

Hadobacteria which is famous for the high resistance to gamma & UV radiation as well as their ability to survive in high extreme environment. The centre has also developed novel & simple quantitative measure for automatically evaluating the biological relevance of one or more clusters of genes. The centre has published 18 research papers & two Book-Chapters.

Sub-Distributed Information Centres (DISCs)

Fifty Sub-DICs are functional as part of BTISnet at various Institutions/ Universities. These centres were mainly established with the aim to provide service to the research community. However these centres are now also imparting training in bioinformatics through workshops. Many centres have now ventured in bioinformatics related R&D activities and have also developed information resources in the form of Databases.

ACTREC, Mumbai has developed a Histone database and a webserver namely PNAS (Predict Putative Substrates of Proteases). At BHU, Varanasi centre has developed *Akriti v1.0* tool for physico-chemical properties calculation for multi FASTA proteins. They have also published nine peer reviewed research papers. The DISC at Bharathidaran University, Tiruchirappalli focuses on Cynobacterial-Bioinformatics. The centre has also developed two important tools namely CKB (Cyanobacterial Knowledge Base) and Syn-R-io, is an interactive R application based on the shiny package for visual exploration of Synechocystis 6803 chromosome with simple data extraction. CARL, Port Blair has developed database for corals, horticulture crops, and butterflies in the Andaman and Nicobar island. Central Plantation Crops Research Institute, Kasargod has developed databases and software packages like (a) COCMAP-Pred: a tool to predict sequences with MAP Kinase domains from coconut transcriptome data. (b) SmiRNA: A ready-made software package for the large-scale of discovery,

annotation and prediction of miRNAs in plants. (c) A transcriptome database was created from RNA-Seq of coconut leaves and embryogenic calli on an Illumina Hi Seq 2000 platform. The major thrust areas of the centre at CSTRI, Mysore is Seri-biotechnology and Seri-bioinformatics. A number of databases for silkworm and mulberry have been developed. These include SILKPORT (an annotated protein database for silkworm and Mulberry), SilkTF (for silkworm specific transcription factors), Mulberry genome database, The Silk e-lab (on silkworm genome and proteome) and Soilinfo (providing information on type of soil, its physio-chemical characteristics, nutrient composition etc). IIIM, Jammu has developed theoretical models for the screening of *Escherichia Coli* (Ec) GlmU protein inhibitors. The centre has also created MedchemDBportal, a compilation of various pathways, crystal structures and target details related to stem cell research. IISR, Calicut has developed Sequence Repository of IISR database, designed to store the sequence information from the projects carried out at IISR and updated Ginger transcriptome database, and Phytophthoragenome database. The major activities at IIT, Kharagpur include microRNA analysis in *Cajanus cajan*, structural analysis of intrinsically unstructured protein, macromolecular assembly in ribosome, cDNA-microarray analysis of *Entamoeba* genome, protein-RNA interactions, Metagenomics, Immunoinformatics. A Biomaterial database: Biomat_database has been developed by the centre and published in a reputed journal. The National Institute of Oceanography, Goa has developed databases on "Fungi associated with marine sponges of India" and *Mangroves of India*. The centre has also developed computer aided taxonomic identification system for class: *Bivalvia*. NIPGR, New Delhi has developed NEXCADE: an online webserver for Perturbation analysis of complex networks, PLecDom: Plant lectin Domain Analysis & ESSOILDB: The essential oil database. NBRI, Lucknow centre has developed databases for Legumes of South East Asia (2030 unique legumes), and plants of India (covering 19000 taxa). The centre

has published 27 research papers. TNAU, Coimbatore has established millet and pulses database and *ProDisC* a stand alone tool to predict the inter atomic distance of proteins. The TBGRI, Thiruvananthapuram has created a database for scanned images of 5000 herbarium specimens of JNTBGRI. Phytochemicals from *Mimosa pudica*, *Phyllanthus amarus*, *Hemidesmus indicus* and *Tamarindus indica* which were docked with Russell's viper venom proteins and have identified lead molecules having inhibitory effect on the activities of named toxic proteins.

Bioinformatics Infrastructure Facilities (BIFs): For Biology Teaching through Bioinformatics (BTBI)

The aim of these centres is biology and biotechnology teaching through bioinformatics. The scheme is designed to expose teachers, scientists and students to the use of bioinformatics in solving hard core biological problems. The centres use lecture materials, video clippings, demonstrations, tutorials and online facilities for teaching. Hundred and one educational institutions have so far been supported under this scheme.

The BIF at Alagappa University, Karaikudi has developed two databases: *Streptococcus pyogenes* enzyme inhibitors using Docking studies (SPEIDS) and Ribosomal database for marine bacteria associated with coral reefs, sponges, marine sediments and sea water. The centre has also published 32 research papers with a good impact factor. The BIF centre at CCS Haryana Agricultural University, Hisar has created a database of pests (plant mites) and found Heterotetramer of AGPase of rice (*Oryza sativa*) having p493A mutant large subunit. The BIF centre at FRI, Dehradun is the National Forest Biodiversity Informatics centre. The centre has developed a web portal of Forest Flora of Manipur: A database of Ligneous Plants of Manipur including plants identification system. The centre has also developed the database of forest pathology herbarium (8600 no. of specimens) and

DNA finger prints database of *Cedrus deodara* species. Maharani Lakshmi Ammanni College for Women, Bangalore has created databases for Phytomellitus, BambooDb, and Ectomycorrhiza. Manonmaniam Sundaranar University, Tirunelveli has sequenced and annotated above 10,000 genes of earthworm, *E. eugeniae* which will be helpful to understand the biology of the agronomically important animal earthworm. The centre at the Presidency College, Chennai has registered for five patents for Novel antiviral combination for treating Asian and East Central South African genotypes of Chikungunya & for treating sensitive, isoniazid resistant strains and Multi Drug Resistant *Mycobacterium*. The centre at Sher-e-Kashmir University of Agricultural Sciences and Technology of Kashmir, Srinagar has developed a pipeline for annotating protein sequences, Transcriptome profiling of double humped camel and Microarray analysis for differential expression of the genes under cold stress in pashmina goat with qPCR for validation of the microarray data. A centre for Venom informatics has been established at the University of Kerala. The University of North Bengal, Siliguri centre has created a database for North Bengal's bamboo's.

North Eastern Bioinformatics Network (NEBInet)

Under the special drive to strengthen the North Eastern States of the Country a Bioinformatics network 'NEBInet' consisting of 29 Bioinformatics centres was established across 8 states. NEBInet comprises of 2 DICs (at NEHU and AAU), 2 DISCs (at IBSD, and Sikkim State Council of Science and Technology) and 25 BIFs (at various universities, colleges and institutions). In order to monitor the progress of these centres the interactive meeting of NEBInet was organised in Tripura University, Tripura on 18th & 19th November, 2015. The Meeting was attended by the Senior dignitaries including university science fraternity, teachers & students pursuing research in the area of Biotechnology and Bioinformatics.

The DIC centre at NEHU, Shillong has specialization in Animal Husbandry & Dairy Technology, Horticulture and Rural Development. The centre is currently working on *Helminth parasite* database. Published two books entitled Dairy and Food Processing Industry-Recent Trends, in Volume –I & II. The DISC at Sikkim State Council of Science and Technology, Gangtok has completed web database of all *Rhododendron* sp. of Sikkim.

The DIC at AAU, Jorhat has done reconstruction of transcription factor-gene regulatory network in rice and miRNA FeedForward Loops. The research work at Assam University, Silchar has developed one database on anti-diabetic phytochemicals and is named as *DiaBank*. The centre has also published 16 papers in indexed journals. The BIF CAU, Tripura has developed database on Fisheries Resources of Tripura. The CVSc& AH, Aizawl centre has prepared database on animal disease prevalence in NE region, and the animal genetic resources of NE region. The BIF at College of Veterinary, AAU, Guwahati has developed a database BABRONE for human resource available in the major institute of north east India. Also a globally accessible online server has been developed on "Serotyping of common clinical isolates of Salmonella by Multiplex PCR" in collaboration with the Vaccine Research Institute of San Diego, USA. The BIF at DM college, Imphal has done Morphometrics and Molecular Phylogenetic Analysis of certain fishes found in Manipur river System and Developed a Database on Ethnozoological resources of Bishnupur District in Manipur. The centre at Gauhati University, Guwahati modelled important proteins from different organisms like *Varanus komodoensis*, *Siluranatropicalis*, Silk Worm, Turtles, Fish & HIV-2 pol-polyprotein. The BIF at Gurucharan College, Silchar has carried out research activities about the Role of heavy metal tolerant rhizobacteria in sustainable cultivation of rice and MicroRNA & its application. Manipur University, Imphal centre is actively engaged in development of a comprehensive database for pollen grains found in

Manipur state. The Mizoram University, Aizawal centre has distributed their research activities in areas of Molecular Phylogeny, Human Genome Analysis, Molecular Modeling and Docking. The centre has also published 10 research papers with an good impact factor. The centre at Nagaland University, Kohima has done Nucleotide compositional analysis and statistical clustering of 90 species of *Paphiopedilum* species. The centre has also launched a quarterly e-Newsletter. The BIF at IBSD, Imphal is creating an 'Application Database' for the anti-tuberculosis properties of plants available in Sikkim Himalayan region. At Rajiv Gandhi University, Itanagar research activities mainly focus on creation of area-specific plant databases having medicinal value.

BTISnet website

The BTISNET programme, envisaged as a National distributed bioinformatics network organization, was launched during 1986-87 and this network is having 170 centres spread all over the country. In order to enhance the information availability a website was designed and hosted at <http://www.btisnet.nic.in> for the dissemination of information. This website contains an over view of the BTISNET programme, its participating institutes, taskforce member details, resources, fellowships etc. This is being updated on a regular basis. The details of each of the individual institute along with their contact details are also given in the website. Number of visitors who have visited this site last year was 123,961 and the average per day is 338.

Coordinator's Meeting of Biotechnology Information System Network (BTISnet):

The 28th BTISnet Annual Coordinators meeting was held on 3rd-4th February, 2017 in ACTREC, Mumbai. The focal theme was on 'Bioinformatics- biological big data: fostering and innovative environment. The Peer reviewed research papers published in last one year by the Centres have been scrutinised and the

incentive awards for the best publishing centres as well as best publications during the year 2015 will be announced in this meeting. This year a special presentation on PFMS has been arranged for awareness creation and for the benefit of the coordinators so that they can update the UCs timely on the PFMS to help the next year release of grant.

BIOINFORMATICS R&D ACTIVITIES

R&D projects supported under competitive grant scheme:

The first R&D proposal in bioinformatics was received by the department in 1999. Since then the department has supported about 130 projects of which 40 are ongoing. The projects have been supported in various areas such as NGS data analysis; Structural Bioinformatics of proteins and nucleic acid; Computational analysis of metabolic pathways; Large scale network analysis; Computational Image analysis; Large scale data-mining, analysis, integration, curation and storage. Some notable achievements of the ongoing projects are as follows:

Establishment of national database on Tuberculosis:

This database is being developed in a multi-centric mode with NJIL&OMID, Agra; NTI, Bangalore; IOB, Bangalore; JNU, New Delhi; IISC, Bangalore and TRC, Chennai as partners. This database is being with the objective to integrate all major aspects of TB infection which allow simple submission of data as well as retrieval for exploratory analysis of information. This website provides links to the participating institutes and the databases/analytical tools developed by them. The whole genome sequences of a *Mycobacterium smegmatis* laboratory wild-type strain (MC(2) 155) and mutants (4XR1, 4XR2) resistant to isoniazid. The data is publicly available through the GEO database with accession number GSE64132. A prototype has also been developed for the Tuberculosis pathway resource, in which we have identified 52 protein-protein interactions including 22 post-translational

modification reactions between 21 unique enzymes in the pathways. Metabolic control analysis and flux balance analysis has been applied to specific and global pathways in *M.Tb* (RV Strain) pathways to assess various search of drug targets.

National Mango Database: Development of National Mango Database for providing information on following aspects:

The improved database schema has been developed for uploading all received data from the partner institutions. The information of GIS based analysis, vector layer and the mantic maps were generated for mango database. 10 *Mangifera* species suitability map was generated for South East Asia including India Five hundred eighty two records updated with the details from different patent offices and 303 research based abstract reprints related to mango is also down loaded and updated on database. Details of 511 phytochemicals, 1200 EST, 10000 Nucleotides and 110 Proteins were updated in database. Also a database (<http://mangifera.res.in>) developed for custodian farmers and district information. For efficient management of mango phenology-data a web-based tool was developed in php. This tool provides an aid to the researchers for arranging the phenological data on timescale by decoding phenophases and depicting as images which helps in summarizing the data by generating frequency tables of different phenophases and thus makes interpretation easy. Mango variety '*Rumani*' showed offseason bearing in Nagapattinam district of Tamilnadu. In Vellore, Kanchipuram districts, non-commercial mango sucking variety called '*Rasalu*' is exclusively used for its juice in these area. Data on status of disease and pest occurrence on mango, production and postharvest technology and the Nutritional & Medicinal values of collected mango varieties was updated in the database from various parts of India. Based on presence on *Mangifera* wild species, Maximum entropy approach (Maxent) was used for producing predictive maps of species occurrences both as image files and as raster output

that can be further manipulated in a GIS. In our database the information included as, Geographical Distribution, Species, Varieties, Botany, Area Production and Productivity, Disease & Pest, IPR Issues and knowledgebase. In knowledgebase - Accession at Gene bank, Accessionbase, Literature base, Chemobase, Genes & Proteins, Technology base, On Farm Conservation, Reprints Paper, and Useful Links. Link for mango database is - <http://www.mangifera.org/litsearch.php>

National Rice Resource Database

Information documentation is key for utilization of genetic resources in crop improvement. The above project is an initiative to generate characterization and evaluation data of selected rice germplasm accessions and develop a user friendly interface to access such information. The project has two components. Component A- Development of database for rice genetic resources for which NBPGR is the lead institute; component B- Development of knowledge based database of rice genome with University of Delhi, South campus as lead institute.

Eight centers viz NBPGR, NRCPB, CRRI Cuttack, DRR Hyderabad, BHU Varanasi, CSSRI Karnal and IGKV Raipur, University of Delhi-South Campus (Text based curation) are partners in the project. So far 15000 accessions (3000 by each center) have been characterized for 30 descriptors (19 qualitative and 11 quantitative) during the last five years. Excellent variability for characters like leaf blade colour, stigma colour, seed coat colour and hull colour awns and panicle has been observed by various centers. From the data on characterization, a core of 1548 accessions has been developed and is being validated at different centers for certain biotic and abiotic traits. Molecular characterization of core is in progress. NRRD database for accessions has been developed and implemented on server. It consists 15,000 records of rice passports, 3000 (Accessions) X 5 (Centers) X 3 (Years) characterization data and circulation data of

accession among centers over the years. An NRRD website has also been developed. A text based database on rice has also been developed by UDSC, South Campus.



HUMAN RESOURCE DEVELOPMENT IN BIOINFORMATICS, COMPUTATIONAL AND SYSTEMS BIOLOGY

As an emerging interdisciplinary area of biotechnology, Bioinformatics is progressively attempting solving of biological research problems through systematic application of IT. Proteomics, genomics, combinatorial chemistry, nanotechnology, spectroscopy and structural and computational biology are having increasing applications of Bioinformatics for data acquisition and analysis. To handle biological research problems, it requires highly trained manpower to deal molecular biology and application of software tools. High priority has been accorded by the Department to this area and has introduced several innovative educational activities to meet the present requirements including several long-term and short-term educational programs to address this gap. The details are as follows:

M. Sc. Network Program, M.Tech, Advanced P.G. Diploma Courses & Ph.D. Program in Bioinformatics:

The M.Sc. in Computational Biology is a two year

Master's programme designed for students who have a good degree in the biological sciences or the physical sciences (computer science, mathematics, physics, engineering). The programme provides specialist skills in core systems biology (such as computing and biology) with a significant focus on the development of computational and mathematical research skills. The programme is ideal for students aiming for careers in industry or academia. This interdisciplinary programme is based in the MKU, Madurai, Pondicherry University, Pondicherry and Anna University, Chennai and has been initiated in a Network mode, on consortium basis two years back. The classes for these courses are being conducted through video conferencing and virtual class room approaches. The objective of the network programme is to share the expertise of teachers as well as the resources which are created by the BTISnet Centres. The program envisages creating of a strong computational and experimental basis to bioinformatics education at the post graduate level.

The other HRD programmes are i) M. Tech in Computational Biology at Centre for Computational Biology and Bioinformatics at JNU, New Delhi ii) M.Sc. in Bioinformatics at Department of Bioinformatics, Pune University, Pune and iii) Post Graduate Diploma course in bioinformatics Calcutta University, Kolkatta, respectively. This year more than 60 students have graduated from these programs this year. The six Centres of Excellence in Bioinformatics of BTISnet including the super-computing facility at IIT, New Delhi are running Ph.D. programs in Bioinformatics to meet the huge requirement for high-end human resource in Bioinformatics and Computational Biology.

Training Calendar of Short Term Training Programs:

Bioinformatics being a multidisciplinary area, hands on experience to the researchers and students working in the areas of Biotechnology and Life

Sciences is provided, by all the BTISnet Centres by conducting one or more short term training programmes each year. A schedule of the important training programmes conducted by BTISNet Centres all over India is published in the form of annual training calendar each year by the Department. This year the training calendar is distributed to all institutes through the btisnet website (http://www.btisnet.gov.in/trainingcalendar/TC_14-15.pdf). The BTISnet centres have organized more than 100 short-term training during the year 2015-16 with focus on a broad spectrum of areas such as knowledge discovery from Data, computational and structural Bioinformatics, network pathways and systems biology, genome and proteome analysis, Bioinformatics with respect to Medical, Agricultural, animal, aqua and Environmental Sciences.

DeLCON Consortium

The DBT's Electronic Library Consortium (DeLCON) is a significant initiative of the Department of Biotechnology (DBT), Govt. of India, to enhance information resources in its research Institution. It was launched in January, 2009 with the ten DBT member-Institutions with large number prominent handpicked online journals. It is a topical endeavor for providing access to scholarly electronic resources including full-text and bibliographic databases in all the life science subject disciplines to the DBT Institutional community across the country. It facilitates access to high quality e-resources to research Institutions to enhance research, teaching and learning.

The access has now been extended to new 17 more DBT Institutions in 2nd phase of extension in this year 2010 and further 07 members added in the 3rd phase of extension in the Year 2011. In the year 2012 there emerged the enlarged DeLCON Consortium with 33 members. In the year 2013 total members of DeLCON Consortium were 33 Institution. Besides the DBT Institutions, an emphasis has been given to incorporate institutions and universities (both in the state and central

government sectors) across the states in North Eastern India. DeLCON provides current as well as archival access to more than 1000+ core peer-reviewed journals and a bibliographic database (SCOPUS) in different disciplines from 22 overseas publishers and aggregators. Presently there are 28 members and 21 publishers in this consortium.

The Faculties, Scientists, Research Scholars, Students and Project Assistants of Institutions covered under DeLCON are the primary beneficiaries. DBT sponsored the entire expenses for DBT organizations for providing e-Journals access through 'DeLCON Consortium'. This consortium has given value addition to the member scientific institutions in terms of access to more number of journals and saving of time as compared to the print version. The consortium has an excellent usage pattern. For more details log on to <http://www.delcon.gov.in>

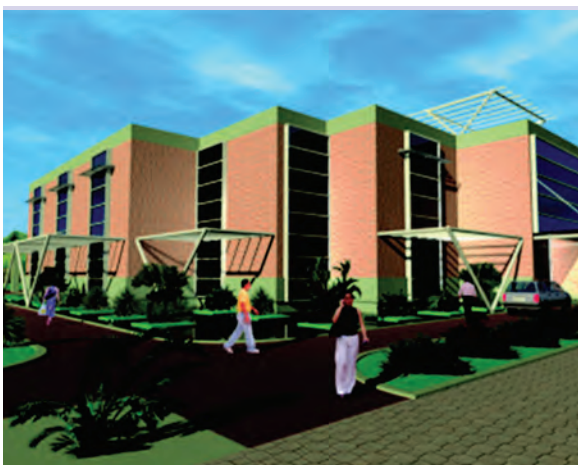
Indo-Japan Collaboration

The Bioinformatics Division is also handling this programme in which four projects were supported in the Bioinformatics area and subsequently four in the Cell Engineering area so far. The bioinformatics projects focus mainly focus on drug development and delivery systems. Four projects supported in the area of Biomedicine and Cell engineering focus mainly on senescence and cell proliferation, with the aim to understand cancers and develop novel ways for intervention using Ashwagandha.

In order to promote close and effective collaboration, AIST and DBT have set up DAILAB [DBT-AIST International Laboratory for Advanced Biomedicine] at the Biomedical Research Institute of AIST in Tsukuba (Japan) on October 3, 2013. In another effort to promote research in the field of biology, life science and materials science, the Ministry of Science & Technology, Govt. of India (DST and DBT) and RIKEN, Japan signed an MoU at NII, New Delhi on 14th Sept, 2013.



Dignitaries releasing the Proceedings of the 26th Annual BTISNet Coordinators Meeting



08

BIOTECHNOLOGY PARKS AND INCUBATORS

The Department of Biotechnology promotes Biotech research and helps to translate research into products and services. One of the means by which development of new commercial products is to be achieved through the setting up the Biotechnology Parks, where facilities for technology incubation, technology demonstration and pilot plant studies are provided for accelerated commercial development of Biotechnology. The Department in partnership with State Governments/ State Government Organisations/Central Government Organisations has established Biotechnology Parks and incubators in different parts of the country to facilitate biotech product development, entrepreneurship, research and innovation.

Following Biotech parks and Incubation Centres have been supported:

Uttar Pradesh: Biotech Park, Lucknow

Kerala: Biotechnology Incubation Centre, Cochin

Andhra Pradesh: Biotech Incubation Centre, Hyderabad

Tamil Nadu: TIDCO Centre for Life Sciences (TICEL) Biotech Park, Siruseri, Chennai

Tamil Nadu: The Golden Jubilee Biotech Park for Women

Assam: Guwahati Biotech Park

Karnataka: Bangalore Biotech Park

i) Biotech Park, Lucknow

Biotech Park, Lucknow is successfully working to develop knowledge based economy in biotechnology, assure benefits of biotechnology to all sections of the society and promote entrepreneurship in biotechnology based industry. The Park is a model of active collaboration between industries, research institutes and academia. This year Biotech Park joined hands with M/s Adhita Biosciences Pvt. Ltd. which is focusing on development of target specific cosmaceuticals / nutraceuticals. The other newly joined company M/s Pirinc Pharmaceuticals Pvt. Ltd. using the Technical Know How of CIMAP has started commercialization of their product Relaxomap-a pain reliever oil. Biotech Park is now home for 11 incubatee companies and 4 companies graduated out from the Park this year.

In the area of Human Resource Development, the Park continues to impart training to graduates and postgraduates students in diverse areas of Biotechnology with a view to develop entrepreneurial skills. More than 400 students received short-term & long-term training in different areas of biotechnology round the year. About 6000 students from 50 renowned schools visited Biotech Park and got benefited. The activities of the Park have also got recognition during 'Kisan melas' and 'gosthis'.

Three certificate courses (of six month duration each) namely, Biotechnology Finishing School, Basics in Bioinformatics and Advance course in

Bioinformatics got recognition from Babasaheb Bhimrao Ambedkar University, Lucknow. Biotech Park provided useful analytical services to many users. The Park also received the approval for carrying out tests or analysis on Ayurvedic, Siddha and Unani drugs or raw material used in their manufacturing.

Biotech Park is serving as a Training Centre for Uttar Pradesh Skill Development Mission (UPSDM). During this year, the Park has trained more than 130 trainees under this scheme in the areas of Agriculture and Flavor, Fragrance & Perfume. Six trainees of Biotech Park, who had undergone training in the area of Flavor, Fragrance and Perfume were sent by the UP Government for higher training to Grasse, France. With future vision, the Park aims to expand and modernize its facilities to translate agro technologies for sustainable agriculture, medical and healthcare technologies for improved nutrition, quality life and technologies for clean water and environment.

Three DBT-sponsored national workshops namely *In-silco* Strategies for Diseases Pathway Analysis and Biomarker Discovery (March 29-31, 2016), Recent Trends in Bioinformatics and Computational Biology: An Introduction (September 7-9, 2016) and Emerging Trends in Bioinformatics: Big Data Analysis and Drug Discovery (December 21-23, 2016) were organized during the year, in which a total of 71 persons participated. Biotech Park organized a training program on 'Herbal Cosmetics' during June 7-8, 2016 for the budding entrepreneurs, which was attended by 20 participants.

The National Academy of Sciences (India) [NASI] sponsored workshop 'Bio-Entrepreneurship and Bio-Enterprise Creation' was jointly organized by Biotech Park and BCIL, New Delhi during September 16-17, 2016. Around 200 students from MP, Bihar, Chattisgarh, Delhi and various cities of Uttar Pradesh participated in the workshop. Biotech Park conducted a Winter School of NASI for the students

of intermediate colleges of UP, MP, Uttarakhand, Bihar and Jharkhand at Biotech Park on 26th December 2016. More than 200 students participated at the programme and visited various Biotech Companies located in the Park.

Dr. Harsh Vardhan, Hon'ble Union Minister of Science and Technology and Earth Sciences visited Biotech Park on July 11, 2016 and interacted with the students, scientists and entrepreneurs of the park.



Visit of Dr. Harsh Vardhan, Hon'ble Union Minister of Science and Technology to Biotech Park, Lucknow on July 11, 2017

ii) KRIBS BioNest (Previously KINFRA Biotech Park), Kochi

The Biotech Incubation Facility has been established by DBT in KRIBS BioNest, Kochi. The Facility has started functioning on the basis of providing a shell space for the laboratory for start-up companies with the sophisticated infrastructure. The laboratories are being reconfigured for having

plug and play space in addition to the laboratory shells. Experienced scientific personnel do the management of BioNest with administrative support from personnel at BioNest and RGCB. The incubator facility is functioning on the model of revenue generation based on rental receipts and equipment usage charges.

iii) **Biotechnology Incubation Centre, Hyderabad**

This Incubation Centre has been established by CSIR-IICT and Govt. of AP with support from DBT and is owned by the Society for Biotechnology Incubation Centre (SBTIC). SBTIC has selected Alexandria for operating and managing the facility. This Incubation Centre is being run by Alexandria Innovation Centre, Hyderabad after extensive remodelling into a State-of-the-Art Research Facility for Start Up /Early Stage Companies.

World class facilities have been created for use by entrepreneurs on use and pay basis. There are 12 plug and play modular labs of 350 sq. Ft each which is given out to companies. Business centre approach is being used in this Park and 9 companies are operating, 74 scientists are working there at present. The Park has office spaces supported by wide range of shared scientific equipment, amenities and support services which are accessible by the client tenants without making any substantial upfront investment. The Park has provided support for current good manufacturing practices (cGMP) compliance for Pilot plant facilities, required for quality manufacturing and for minimizing contamination. State-of-the-art cGMP Pilot Plant facilities are being set up with the following specifications:

- Cell Culture Fermentation System (30 L)
- Microbial Fermentation System (20 L)
- Microbial Fermentation System (200 L)

iv) **TIDCO Centre for Life Sciences (TICEL) Biotech Park, Chennai**

The Park was established by Tamil Nadu Industrial Development Corporation Ltd. (TIDCO), an undertaking of the TN State Government with support from DBT. The park is fully funded by TIDCO and savings are being invested for new buildings while the equipment for the BTCIF is being supported by DBT. The core equipment and instrumentation facility are being established includes BTCIF include microbiology, molecular biology, fermentation, downstream processing, purification, analytical support, animal cell culture facilities and utilities. This Park has created infrastructure for Biotech R&D on 5 acres of land in Chennai at a capital outlay of Rs.62.5 Cr. It has now achieved 100% occupancy with National and International clients. The tenancy area has 74 modules of 1525 sq.ft. each, available for clients to develop their own customized R&D labs of BSL2 standards, upgradeable to BSL3, in accordance with GLP standards. Clients can install their facilities appropriate to perform their independent research.

v) **The Golden Jubilee Biotech Park for Women, Chennai**

The park was established by Govt. of Tamilnadu at Siruseri, Kanchipuram District with support from DBT and is fully functional since 2001. The park was registered as a Society under the Tamil Nadu Society's Registration Act 1975. It is a joint project of the Government of Tamil Nadu and DBT. The Park has a Lab facility for providing Quality testing and Training programs for providing hands-on experience and to generate revenue streams for the Park. It is an entrepreneurial facility for Women Scientists aided with managerial skills and capable of making small-scale investment, to independently take up the functioning of the lab. At present the park is fully occupied. 80% Comprises of 1st generation entrepreneurs. All entrepreneurs are

women. In all there are 150 workers which includes 50-60% of women both skilled/unskilled. The total annual turnover is Rs. 5 Cr. The production units that have been set up are for herbal cosmetics, bio-pesticides, bio-Fertilizers, spice fortified with herbs, and essential oil, ready to eat snacks etc.

vi) Guwahati Biotech Park Technology Incubation Centre

The project for the setting up of Guwahati Biotech Park Technology Incubation Centre submitted by the Govt. of Assam has been sanctioned by the DBT. An interim facility for the Incubation Centre has been built in an existing building of IIT Guwahati. This facility now has 8 Modular Laboratories, Specialized & Support Facilities ready to be used. A common instrumentation facility is being equipped with sophisticated instruments. The progress of the development of the Park is regularly monitored by GBPIC Management Committee and Technical

Advisory Committee. This incubator is now trying to attract companies and incubates to develop commercial products based on the rich natural products of the region. Govt. of Assam has recently allotted a land measuring 17 acres to Guwahati Biotech Park in proximity to IIT Guwahati for setting up of GBPIC.

vii) Biotechnology Park, Bangalore

Biotech Incubator Facility in Biotechnology Park, Bangalore sanctioned set up with combined efforts of KBITS and DBT. Common Instrumentation facility, Mammalian and Plant tissue culture, Dark room/ Cold room/Utilities, Animal house/Chemical store, Cafeteria/Meeting rooms/Conference rooms etc. established. Services including Plug and Play modular laboratories, Common equipments facilities, High End Equipments and Facilities, Mentorship, Funding, Networking, Branding, Legal, Finance/Accounting are being made available to incubates and start-up companies.



09 INTERNATIONAL COLLABORATION

Global scientific collaborations are the cornerstone of scientific growth and enrichment. It is a platform to understand, appreciate and work towards bridging cultural and social divide. The basic endeavor of international partnership is to work towards global challenges and finding solutions. International collaboration of the Department of Biotechnology have not just focused on joint research and development programmes, it has also strived to bring excellence to India. The department through collaborations, aims to bring global competitiveness and better the research standards in India.

Belgium : Department has signed a Memorandum of Understanding with The Research Foundation-(FWO) of Belgium in the field of Biotechnology. MoU will encourage research institutions in India and Flanders to develop scientific cooperation.

Canada: Department and IC-IMPACTS (the India-Canada Centre for Innovative Multidisciplinary Partnerships to Accelerate Community Transformation and Sustainability) under the Joint Call for Collaborative Research Innovation Projects in the area of “Portable Diagnostics and Analyzers” for developing miniature, portable, and cartridge based diagnostics and analyzers using bodily fluids such as blood, saliva or urine have agreed to fund five collaborative projects. A Biosensor device was developed for monitoring of water quality for human health.

Researchers from Lovely Professional University, Phagwara; McGill University, Canada and University

of Guelph, Canada have fabricated prototype for biochar production and removed wastewater contaminants.

Denmark: Department in collaboration with Innovation Fund Denmark (IFD) has funded the second translational phase of the project entitled “MUSTER- Musculoskeletal stem cells targeting”. Partnering institutions in the second phase of the project are Centre for Cellular and Molecular Biology, Hyderabad; Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram; Indian Institute of Technology, Kanpur; Christian Medical College, Vellore; University of Southern Denmark and University of Aarhus, Denmark. Researchers have found higher expression of genes responsible in cardio-metabolic diseases and endocrine disorders based on whole genome analysis of cord blood samples from 150 mothers suffering from diabetes.

Finland: Department in collaboration with its innovation partner TEKES, Finland has approved a project entitled “Traffic and air quality in India: Technologies and attitudes” for funding. Partnering institutions in the project are The Energy Resources Institute, New Delhi and Finnish Meteorological Institute (FMI), Finland. In another project, metabolically-engineered *Lactococcus lactis* as well as by the natural producer, *Streptococcus zooepidemicus* was developed. Technology for scale-up of the HA production and purification process has been transferred to Romvijay Biotech Pvt. Ltd. (Puducherry).

Germany : Department in partnership with BMBF, Germany partnered in a Sixth joint call for year 2015-16 with an aim of developing eco-friendly technologies for disposal of urban and rural bio-waste. The priority areas identified were (i) Biotechnology for reuse of biodegradable urban solid waste (ii) Biotechnology for reuse of biogenic raw materials in agriculture. Under the call four projects were recommended for funding.

Under this collaboration, a new imaging technology to visualize fragile X mental retardation protein was developed for detection of mental retardation linked protein in live primary neurons of animal brain. This new diagnostic assay can be used for complex patient samples. Further, a gene panel (testing several genes in one single test) for the low bone mineral density diseases like osteogenesis imperfecta has been identified for genetic diagnosis for about 50 Indian families with osteogenesis imperfecta. Using the panel researchers are providing prenatal diagnosis and genetic counseling to prevent the recurrence of osteogenesis imperfecta.

Spain: Department in collaboration with CDTI, Spain has funded three projects in the areas of diagnostics, plant based fungicide and innovative packaging technologies. Projects involve partnership of industry and academia.

Sweden: Department and the Swedish Governmental Agency for Innovation Systems (VINNOVA) would launch a joint call for proposals during 2016-2017 to promote Indo-Swedish research and innovation aimed at development of Medical diagnostics: Medical devices: Antimicrobial resistance, eHealth for One Health and Innovative food. Researchers have developed a stick and other assistive tools for elderly under the ongoing project “Seamless Affordable Assistive Technologies for Health – SAATH” in the project supported under collaboration.



Figure 1. Assistive stick developed under the project SAATH

The Netherlands: Department and STW/NWO, The Netherlands in their joint initiative “Water for Health” are funding a proposal “Local Treatment of Urban Sewage Streams for Healthy Reuse (LOTUS)” which aims to clean Barapullah drain “Swatch Barapullah”. Project brings a strategic collaboration of Indian institutes (IIT-Delhi, TERI and NEERI) and highly experienced Dutch researchers. Project envisages, finding cost-effective solutions using local resources and adapting state-of-the-art Dutch technology to Indian conditions. The project aims to demonstrate a novel holistic (waste-) water management approach, to produce reusable pathogen free clean water and recovering nutrients and energy. DDA will provide experimental testing sites along the Barapullah drain where testing labs and the demonstration pilot plant will be established. Project is unique with involvement of the end-users (municipality, DDA, DJB, NGO’s) and companies (Shell, Hydrorock, Nijhuis, Berson, etc.). There is also commitment from industry, especially from the Netherlands both in cash and in kind.

United Kingdom: The India UK TECH Summit 2016, India’s largest knowledge and technology conference and exhibition, was held in New Delhi from 7 to 9 November 2016. The India-UK Tech Summit was jointly inaugurated by the Prime Minister of India Shri Narendra Modi and the Prime Minister of United Kingdom, Rt. Theresa May, on 7th November, 2016, at Hotel Taj Palace in New Delhi.

In the Joint Statement issued by the two governments, Prime Ministers of the United Kingdom and India “commended ongoing

collaboration in biotechnology” while announcing the following joint initiatives between DBT & Research Council, UK. (i) Joint Strategic Group on Anti-Microbial Resistance (AMR) with joint investment of up to £13 million, (ii) A £16 million Joint research programme for innovative biotechnologies for cleaning and processing industrial waste, (iii) £12.6 million for the second phase of joint research in women’s and children’s health in low-income settings.



Figure 2. Hon’ble Prime Minister of India Shri Narendra Modi, Hon’ble Prime Minister UK Rt. Theresa May and Hon’ble Minister for S&T and ES Dr. Harsh Vardhan during inauguration of Tech Summit 2017 at New Delhi on 08th November, 2016.

Department has also signed a MoU with Science and Technology Facilities Council (STFC), U.K. and DIAMOND, U.K. in order to provide access to the state of the art, inaccessible and expensive facilities to the Indian researchers. A Workshop on Global Research Programme in Women and Child Health was organized on October 17th -18th, 2016. In the area of Agriculture, Department in collaboration with DBT-BBSRC-Newton-Fund has funded four “Virtual Joint Centres with India in Agricultural Nitrogen”. Optimized use of Nitrogen will contribute in enhancing the income of farmers by reducing cost inputs of fertilizers. The Virtual Joint Centre on Agricultural Nitrogen will address agronomic nitrogen use efficiency, biological nitrogen use efficiency and biological nitrogen fixation.

Under the farmed Animal and Disease Health (FADH) programme in partnership with U.K., technology was developed for *Brucella* detection

using gold nano particles and standardized a paper based LAMP assay for multiplexed detection of *Brucella*, *Leptospira* and IBR virus in biological fluid/secretion. A method for molecular detection of tick born haemoprotozoans was also developed. Serodiagnostic assays (ELISA) for detection of *Brucella* based on the rough lipopolysaccharide (rLPS) and novel glycoconjugates has also been developed.

Reverse-transcription-loop-mediated-isothermal-amplification (RT-LAMP) assays to detect eastern or western topotype of BTV were developed, the sensitivity of the assay was comparable to real-time RT-PCR with ability to detect BTV RNA within 60-90 minutes.

Under the Crop Genomics and Technologies (CGAT) programme, researchers have identified non-synonymous substitution in active glycosyl transferase domain of gene involved in starch synthesis viz. soluble starch synthase (SSS) in three amphipolids viz. PBW114-Ae. tauschii pau 14102, PBW114-Ae. tauschii pau 14170 and PBW114-Ae. tauschii pau 3761. Identified genes substitutions are believed to confer tolerance to heat stress.

In another project, different genotypes of wheat resistant to heat and drought stresses giving optimal yield were also identified



Figure 3. IR thermal imaging for canopy temperature, crop greenness with green seeker and chlorophyll fluorescence measurements.

Multilateral Cooperation

European Union: Department has agreed to partner in EU Research and Innovation Horizon 2020. Several priority areas will be supported: agriculture (including food), biotechnologies, bio-energy, health, water resources, new materials and nanotechnology. Indian researchers, enterprises (MSMEs), research institutions and universities will be able to team up with their European partners to participate in projects under H2020 and make best use of Europe's excellent opportunities in research and innovation. Through participation in H2020, beneficiaries can gain great benefits from access to excellent knowledge, access to research data and access and connection to world-leading scientific networks and research teams.

Department is partnering in "Joint programming initiative on Antimicrobial Resistance (JPIAMR)" in collaboration with European Union. The goal of JPIAMR is to combat the global crises of antimicrobial resistance by aligning international research resources and by providing a platform for collaboration. JPIAMR currently has 22 member states. Department along with Department of Science & Technology in collaboration with geographical ERA-NET "INNO-INDIGO" has partnered in joint S&T call in the area of "Bio-based energy". In collaboration with Infect-ERA NET department has partnered in the fourth joint transnational call of proposals in human infectious diseases for the year 2016-17.

Researchers from Indian Institute of Technology, Kharagpur; University of Bremen, Germany and University of Tartu, Estonia have developed and optimized a two-stage continuously processing MFC with submerged MBR to treat waste water with final effluent with considerably reduced chemical oxygen demand (COD), total kjeldahl nitrogen (TKN) and completely devoid of suspended solids. The combined system is not only offering a better alternative to the existing wastewater treatment

technologies but it can also recover sufficient amount of bioenergy. Further, a compact reverse osmosis (RO) and Nano filtration (NF) water purification system has been designed.

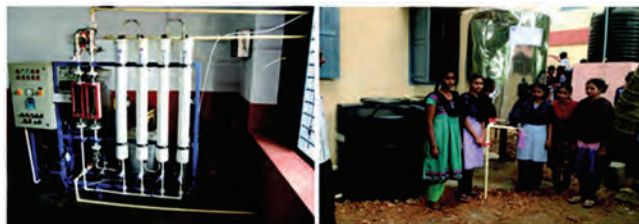


Figure 4. Photograph of NF plant of 1200 L/h capacity installed in ZPH School, Mogallu Village, Bhimavaram Taluk, West Godavari District under the project POMACEA.

Other collaborations

Nobel Media AB of Nobel Foundation: Department signed a Memorandum of Understanding (MoU) with the Nobel Media AB of the Nobel foundation to bring the Nobel Prize Series to India from 2017 to 2022 to India. The first Nobel Prize Series India 2017 was trilateral partnership between Department of Biotechnology, State Government of Gujarat and Nobel Media. The first edition of Nobel Prize series was inaugurated by Hon'ble Prime Minister of India Shri Narendra Modi on January 9, 2017 at the Science City in Ahmedabad as a prelude to Vibrant Gujarat 2017. Theme of the edition was "Science Impacts Lives".



Figure 5. Inauguration of Nobel prize exhibition by Hon'ble Prime Minister of India Shri Narendra Modi, Hon'ble Minister of S&T and ES Dr. Harsh Vardhan, Hon'ble Chief Minister of Gujarat Shri Vijay Bhai Rupani, Deputy Chairman Nobel foundation Mr. Goran Hansson, (Nine Nobel Laureates) Dr. Venkatraman Ramakrishnan, Dr. Richard J. Roberts, Dr. Harold E. Varmus, Dr. Randy W. Schekman, Dr. David J. Gross, Dr. Ada E. Yonath, Dr. Serge Haroche, Dr. William E. Moerner, and Dr. Hartmut Michel.

Nobel Prize Series is a unique programme combining conference, lectures, roundtables, and exhibitions. By bringing together Nobel Laureates, other experts, researchers and students, the programme aims to stimulate innovation and creative thinking. Further, 500 students selected through an Ideathon from across the country participated in the meeting. On January 10, 2017, Nobel Dialogue on “Science Impact Lives” with two themes ‘Basic or applied research? How to best foster a truly innovative environment’ and ‘Local research, global impact-how can biomedical and health research in India deliver greatest benefit in addressing global health challenges’ was organized with the very sage and vocal participation of the visiting Nobel Laureates. The high light of the Nobel Prize series India 2017 is the ongoing Science Exhibition at Science City, Ahmedabad. This is a unique exhibition with exhibits brought from the Nobel Museum Sweden and showcases the achievement of Alfred Nobel, his will and the achievements of Nobel Laureates of now their ideas have impacted/changed human life.

Human Resource Development through Global linkages:

Women leadership development workshop: Department of Biotechnology, India and Cambridge University, U. K under Newton-Bhabha Fund organized a leadership development workshop on Female Leaders in Crop and Agricultural Sciences at Clare College, Cambridge University, UK, on 04th-10th September, 2016. The workshop was meant for mid-career women who are engaged in teaching and research, with an aim to help them building their capacity as mentor and better research manager. 25 women agriculture scientists were selected from various ICAR, DBT, CSIR institutes, IIT and state Agricultural Universities to participate in this program. Under, Newton Bhabha Ph.D. placement Programme: Department in partnership with Department of Science & Technology and British Council, UK has announced the call for the

Newton Bhabha PhD placement programme for the year 2016-17. Under the programme Thirty Five (35) students in the area of Life Sciences were recommended for funding. Under the Khorana Programme for Scholars: Department of Biotechnology (DBT), University of Wisconsin (UW) Madison and the Indo-US Science and Technology Forum (IUSSTF) has selected 35 students of biotechnology and biomedical sciences under the programme for the year **2017-2018**. Students will receive research experience in the state of art facilities.

DBT – Wellcome Trust (India alliance): DBT-WT IA is an initiative to support fellowships in the area of biomedical research. Under the joint co funded partnership of £160 million, 223 Fellows 119 from outside of India have been awarded fellowships in basic, clinical and public health. Fellowship is an attempt toward brain gain and enhancing the research ecosystem of the country. Selected fellows under the programme are placed in 66 institutions across the country.

DBT- EMBO: India became an associate member of EMBO; this provides an opportunity for both Indian and foreign scientists to apply for grants to work in India or Europe. This was established with financial contribution from the Department. Dr. Minhajuddin Sirajuddin of InStem the only applicant from India received the EMBO Young Investigation award for the year 2016.

Biotechnology Entrepreneurship Student Teams (BEST)-India programme: Department in association with Association of Biotechnology Led Enterprises, ABLE – India executes and manages BEST-India (Biotechnology Entrepreneurship Student Teams) programme which is aimed at encouraging young graduate and post-graduate/ Ph.D. students in developing biotechnology entrepreneurship by exposing them to issues involved in commercialization of bio-science. In seven years of the programme, 55 universities, research institutes and colleges across India

participated in the training and induction and 557 young minds trained. Programme has contributed immensely to the startup ecosystem of the country, 14 startup companies have been established by the teams who have won the BEST awards. This programme has helped seed ideas of innovation to startups.

Indo-Australia Biotechnology Fund (IABF): The overall objective of the Indo-Australian Biotechnology Fund is to develop and support collaborative research activities which draw upon strengths in India and Australia. The fund supports Indian and Australian scientists to collaborate in cutting edge areas of science and technology. So far 54 projects and 10 workshops have been supported in the areas of Healthcare, Agriculture and Bioenergy.

Under this programme, a unique set of endothelial Progenitors in patients' blood with Alcoholic Cirrhosis (ALC) and mouse model of alcoholic steatosis was identified. The Indian Investigators at Indian Institute of Science, Bangalore with the objective of confirming that VLPs and DNA encoding the non-structural (NS) proteins NS3/4B/5B proteins from four Hepatitis C virus (HCV) genotypes, viz. gt 1a, 1b, 3a and 4, elicit robust immune responses in mice, individually and collectively, have combined the DNA and the VLP based vaccine for gt3a and have successfully achieved higher humoral as well as cell mediated immune response in mice compared to the DNA and VLP based vaccine individually. The Australian partners have successfully optimized the technology of large scale production of the quadrivalent VLP based vaccine.

Indo-Brazil: Under Indo-Brazil cooperation, the six projects were recommended against the second Joint call for Proposals (2016-19). A project research concluded that serine proteases from *Bothrops jararaca* induce the angiogenesis and metalloproteinase and L-aminoacid oxidases inhibit the angiogenesis. In another project, a antimicrobial

substance called Penisin has been isolated, which effectively inhibits the growth of Gram-negative bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA) and did not exhibit hemolysis activity. In another project, it has been deduced that recycling and reuse of ionic liquid is a economically viable pretreatment method for recovery of lignin.

Indo-France: Under joint agreement between DBT, India and CNRS, France for establishing International Associated Laboratories (LIA) in the area of 'Systems Immunology and Genetics of Infectious Diseases (SIGID)', whose objectives are to promote and enhance the scientific interactions/ collaborations through pooling of resources; to foster the enhanced scientific and technical manpower exchange for training and knowledge up gradation and to carry out the scientific program in this area. The Indian participating institutions are Institute of Life Sciences (ILS), Bhubaneswar - a coordinating Institute; National Institute of Immunology (NII), New Delhi; National Centre for Cell Science (NCCS), Pune and Tata Institute of Fundamental Research (TIFR), Mumbai. Under this project, a discrete cytokine patterns was reported in sub-phenotypes of severe Malaria. It was also revealed that IP-10 associated to Heme had a major contribution in the pathophysiology of Human Cerebral Malaria, which can be used as a biomarker. Further, development of clinical sepsis (a hyper inflammation state) could be prevented by pre-existing chronic filarial infections. A Ph.D. student spent six months in a French collaborating laboratory to study the B-Cell subpopulation involved in the autoantibody response produced during severe Malaria.

Indo-Russia: Under Indo-Russia cooperation a second joint call for proposals (2017-19) have been invited under the four priority areas of 'Genomic & Proteomics Instrumentation'; Nano-Devices; 'Bioenergy - Photosynthesis based only' and Bio-reagents. In total 20 proposals are received.

BRICS: As a party to BRICS cooperation, the 4th

Meeting of BRICS S&T Ministers was held at Jaipur on 8th October 2016. This was preceded by BRICS STI Senior Officials and BRICS STI Funding Working Group Meetings on 6-7th October 2016. The outcomes of these meetings have found adequate coverage in the Goa Declaration of 8th BRICS Summit on 16th October 2016. During these rounds of meeting, a broad action plan and their ways of implementation has been devised. Simultaneously, Department will be the focal point for BRICS activities in the area of Biotechnology as per Moscow Declaration.

Indo-SA Collaborative Research Program on HIV/AIDS and Tuberculosis: In an effort to build clinical capacity in the area of HIV, AIDS and TB and to build a sustainable environment for translational research which promotes discovery of new technologies and products for prevention and management, the Program Division launched a grant call in collaboration with DST, MoS&T, Govt. of India, and Dept. of Science & Technology, Govt. of South Africa to initiate a collaborative research program on HIV/AIDS and TB.

Indo-Swiss Collaboration in Biotechnology: The Indo-Swiss Collaboration in Biotechnology (ISCB) is a **bilateral research and product development programme**, jointly funded and steered by the Indian and Swiss Government (Department of Biotechnology in New Delhi and Swiss Agency for Development & Cooperation in Bern and Embassy of Switzerland in New Delhi). The **overall goal** of ISCB is to contribute towards food security in the Indian context through innovative life sciences and biotechnology approaches, supporting sustainable and climate resilient agriculture. Innovative biotechnological products and processes with relevance to small and marginal farmers' needs & demands are developed and validated. Their dissemination and adoption is promoted through public and private partners. In Phase IV (2013-2017) research networks are funded to work on pest resistance, yield improvement and climate

resistance of cassava, finger millet and pigeon pea integrating the socio-economics with the biotechnology components. Under this collaboration, Cassava Network was formed which was aimed at developing new varieties of cassava with CMV resistance. Wild and transgenic cassava lines having resistance against AFCMV imported from ETH, Zurich were multiplied at CTCRI, Thiruvananthapuram and tested for resistance against SLCMV through whitefly transmission and all of them are found to be susceptible (Fig.6). A Biofertilization and Bioirrigation for sustainable mixed cropping of Pigeon pea and Finger Millet (BIOFI) aimed at assessing the response of AMF to fertilization and inoculation with bio-inoculants and plant growth promoting rhizobacteria (PGPR) in finger millet–pigeon pea inter-cropping system. Six pigeon pea lines with higher water use efficiency have been identified. Socio-economic study has been carried out on ex-ante assessment of the adoption potential of BIOFI technology. Under the Ragi network, potential contrasts and trait donor genotypes for drought adaptation, yield potential and nutrient bioavailability have been identified and Ragi cultivation technologies have been mapped and the traits preferred by producers were also identified. Under, Pigeon pea network, QTLs and DNA markers for plant height, maturity time branching and other yield contributing traits in pigeon pea have been developed. Hairpin gene constructs to target the shortlisted target genes for the control of *M. vitrata* have been developed. A Panel of 1200 germplasm accessions have been characterized with traits like high yielding, deficit moisture stress and flooding tolerance with molecular diversity. In the socio-economic component, district-wise time series secondary data are collected on pigeon pea production and yield gaps in different agro-ecological regions. Information on farmers' and market perception of production constraints and varietal traits preferences have been collected through pilot survey and focus group discussion. A Technology Assessment Unit was formed to facilitate the

transfer of technology to industry for product development in ISCB projects along the value chain. TAU is also involved in management of IP, licensing, monitoring, and regulatory compliance of ISCB networks. The Cry and ASAL technologies transferred to public and private institutes earlier were reviewed to ensure systemic technology management.

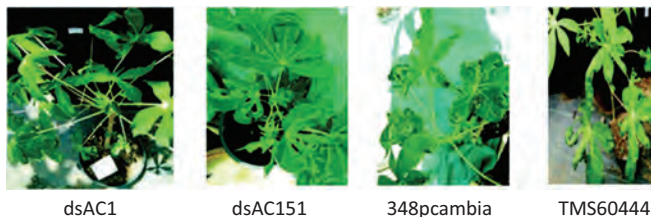


Fig.6 ACMV transgenic lines transmitted with SLCMV through whitefly transmission

Indo-Vietnam: The department had signed a Programme of Cooperation (POC) with Ministry of Science and Technology (MoST), Socialist Republic of Vietnam in March, 2012 for a duration of five years. Discussion on the collaboration are underway.

Indo-Tunisia: Under the joint programme of cooperation, Project has been supported to study the protective effect of a new vaccine composition against Tuberculosis, with major focus on the development of a novel method of vaccination, against tuberculosis (TB), based on enhancement of BCG-mediated apoptosis through FOXO3 activation.



10

AUTONOMOUS INSTITUTIONS AND BIOTECH SCIENCE CLUSTERS

NATIONAL INSTITUTE OF IMMUNOLOGY (NII), NEW DELHI

The programmes of the National Institute of Immunology are focused to study frontier areas of modern biology pertaining to disease processes with special emphasis on the functional aspects of the immune system. The research areas at the Institute are grouped in four broad areas, namely, infection and immunity, molecular design, gene regulation and reproduction and development. Within the ambit of these areas, advanced research in modern biology is being carried out using novel tools and advances to generate knowledge. During the reporting period the Institute continued expansion of scientific programmes in a multi investigator driven mode to ask challenging questions in biology for improvement of healthcare. The scientific findings have so far been published as 92 research papers. More publications of discovery science in reputed high-end journals are expected.

Research focus and outcome: The focus of research activity has been on viral diseases (JEV, HIV, Influenza); bacterial disease pathogens (*Mycobacterium tuberculosis*, *Pneumococcus*, *Salmonella Typhi*, *Helicobacter Pylori*); parasitic diseases (*Leishmania*, Malaria); chronic disease biology (*Diabetes Mellitus*, Multiple Sclerosis, Amyloid Diseases); Cancer Biology, Neurobiology, Developmental Biology and Genetics, Stem Cell Biology, Reproductive Biology, Ageing, Basic Immunology, Structural Biology and Drug Design, Genetics, and Gene Regulation. Emphasis is given

to carry out fundamental research in these above areas with possibility of translational activities. The key outcome is briefed as follows:

Significant Basic Research Outcome: Some of the basic research outcomes published during the current year in high-impact journals are as follows: 1) Bone marrow stem cell therapy partially ameliorates pathological consequences in livers of mice expressing mutant human $\alpha 1$ -antitrypsin; 2) MicroRNA expression profiling of *Leishmania donovani*-infected host cells uncovered the regulatory role of MIR30A-3p in host autophagy; 3) Non-canonical NF κ B mutations reinforces pro-survival TNF response in multiple myeloma through an autoregulatory RelB:p50 NF κ B pathway; 4) Oxidative homeostasis regulates the response to reductive endoplasmic reticulum stress through translation control; 5) Another research finding showed that a novel cancer testis antigen target A-kinase anchor protein (AKAP4) for the early diagnosis and immunotherapy of colon cancer; 6) Late-phase synthesis of I κ B α insulates the TLR4-activated anonical NF- κ B pathway from noncanonical NF- κ B signaling in macrophages; 7) Another finding showed that a chromatin modifier integrates insulin/IGF-1 signalling and dietary restriction to regulate longevity; 8) *Leishmania donovani*-induced increase in macrophage Bcl-2 aids in parasite survival; 9) One of the research activities showed the presence of auto-reactive, MHC class-I restricted, calcium sensing receptor (CaSR) specific CD8(+) T cells in Idiopathic hypoparathyroidism; and 10) Constitutive CD40 Signaling calibrates differentiation outcomes in

responding B cells via multiple molecular pathways.

Translational Research Activity: These are the following translational outcome from the research carried out in the reporting year:

A new liver stage antigen containing DNA-j domain was identified as a candidate vaccine in Malaria. It provides four log scale (10,000 times) reduction in parasite load when challenged with 50 fold excess (compared to natural dose) of sporozoites.

ABC transporter component SP0845 protein of *Streptococcus pneumoniae* protected mice from intraperitoneal challenge with heterologous pneumococcal serotype. Based on its surface accessibility role in virulence and ability to elicit protective immunity was examined. SP0845 may be a potential candidate for a protein-based pneumococcal vaccine.

Heat shock protein 70-2 (HSP70-2) was identified as a novel therapeutic target for colorectal cancer.

Alum was reformulated in powder form to improve its thermostability. It was observed that dry powder alum adsorbed vaccines maintained its immunogenicity when subject to extreme temperature variation. These results open up new possibilities for making dry powder, room temperature-stable vaccines containing alum as the adjuvant.

It was identified that Glmu, PknA, PknB, PstP and enzymes involved in histidine biosynthesis as potential targets for developing drugs / inhibitors for tuberculosis.

Intellectual Property / Technology Transfer / Agreements: An international patent 'A recombinant vaccine against *Clostridium perfringens* infection and Epsilon (Ý) toxin intoxication' has been granted in USA (*US patent no 9408900*) and Australia (*Australian application No. 2011275507*). A technology "Process for obtaining bioactive protein from inclusion bodies" has been transferred to EPR Centre for Cancer

Research and Bioinformatics Private Limited Shamirpet Mandal, Telangana. Institute also provided consultancy services to Oscar Medicare Pvt. Ltd., New Delhi. A license agreement signed between National Institute of Immunology and EPR Centre for Cancer Research and Bioinformatics Pvt Ltd., Hyderabad for transfer of the technology. MoU has been signed between NII and HLL Lifecare Limited, Noida to co-operate in the creation and development of an invention relating to "Herbal Microbicide Formulation for Preventing HIV".

Research Collaborations: Other major scientific collaborations of interdisciplinary nature initiated in the reporting periods which are expected to encourage innovative and groundbreaking strategies in investigating increasingly novel, complex and convoluted areas for research in cancer and tuberculosis which have societal benefits are:

The institute is one of the participating Institutes in Systems Immunology and Genetics of Infectious Diseases (SIGID) consortium at Institute Pasteur de Lille, France which aims to integrate dedicated multidisciplinary teams in India and France to study the Immunology and Genetics of infectious diseases with a particular focus on Malaria, Filariasis and Leishmaniasis and is expected to lead to potential breakthrough in the design of more effective therapies and development of new generation of vaccines. The Institute signed certificate of Memorandum of understanding with Department of Pharmaceutical Sciences, Dr. Hari Singh Gour Central University, Sagar (M.P.) which pertains to promote the research, education and training in the area of pharmaceutical process and development.

New Initiatives: The Institute in the recent past formed a 'Placement Cell' to facilitate its Ph.D scholars to identify their career niche and make them self reliant individuals. So far, three students have got the job in industry through the efforts put by placement cell. During the reporting period, the

Institute conducted a Career Development workshop to prime the Ph.D. students to enhance their career, sharpen their skills required to get placement after Ph.D and expose them to the expectations of recruiters.

Academics: The Institute enrolled 22 students during the year for Ph.D degree with academic affiliation of Jawaharlal Nehru University and 38 postgraduate students were provided training. Around 40 students from Department of Botany, Bharathiar University, Coimbatore, visited NII on September 27, 2016, 40 students from Bhaskaracharya College of Applied Sciences (University of Delhi), visited NII on October 20, 2016 and 50 students from Tamil Nadu Agricultural University visited NII on December 8, 2016. 'Science Setu' which was conceptualized in 2014-15 to enable connectivity between Institute scientists and undergraduate students of 14 colleges of Delhi University and one deemed university of Faridabad, bloomed during the reporting period. NII has provided opportunities to several students for short-term training through various sponsored programmes such as 7 students under Science Setu program and 8 students from Indian Academy of Sciences, Bangalore and 11 students were enrolled as project trainees for six month.

Other notable achievements: Encouraged by the successful results of the immunotherapy route to cancer treatment, The Cancer Institute, Chennai has launched the second phase of the clinical trials in collaboration with NII. The Dendritic cell based Human clinical trials being conducted at Cancer Institute, are employing therapeutic grade SPAG9, recombinant protein which was discovered under Cancer Research Program at NII with DBT support. SPAG9 is a cancer antigen that could help reset the immune system and prepares it with information to target cancer cells

NATIONAL CENTRE FOR CELL SCIENCE (NCCS), PUNE

The National Centre for Cell Science (NCCS) was established with a mandate of three main functions:

National Cell Repository
Research & Development
Human Resource Development.

Major initiatives: In keeping with the vision of NCCS to expand into newer and emerging research areas, new initiatives were undertaken. During the period NCCS has taken steps towards three new initiatives, as described below:

Human Induced Pluripotent Stem Cell Core Banking Facility at NCCS: NCCS has received recommendation for funding by the Technology Board of the DST for the establishment of a "Human Induced Pluripotent Stem Cells" (hiPSCs) at NCCS. Establishment of hiPSC bank for drug screening, disease modeling and studying human disease biology is under consideration. The aim is to develop this as a facility which would initially serve as a depository for human stem cell-lines generated by Indian researchers, and subsequently also as a repository for cell-lines collected from international repositories, making them available to Indian researchers.

The Indian Human Microbiome Project: There is growing evidence that shows an association between dysbiosis of gut microbiota and diseases like diabetes, atherosclerosis, obesity, several intestinal and even psychological disorders. Therefore, several efforts for the characterization of the human microbiome are being made globally, such as the Human Microbiome Project (HMP), Metagenomics of Human Intestinal Track (METAHIT) etc. Since such an organized exercise is lacking in India, NCCS has proposed to lead a multi-institutional initiative to map the human microbiome across the country and study its correlation with genetic and environmental factors.

Edu-Bridge: 'Edu-Bridge' an ongoing programme where the faculty members of NCCS teach the fundamental concepts of science through lectures & hands-on activities to students of the DBT Star College, Jankidevi Bajaj College of Science (JBCS) at Wardha, was initiated.

Salient Achievements: During 2015-16, the national cell repository at NCCS supplied five thousand one hundred cell lines to four hundred research institutions across India. Thirty four research scholars joined the institute for the Ph.D. programme and twenty five research scholars registered as Ph.D. students. The institute had 113 research scholars registered for a Ph.D., as on 31st March, 2016. Thirty four students submitted their theses and six students were awarded the Ph.D. degree during the said year. 34 project trainees & 21 summer trainees also received training at NCCS under the mentorship of our faculty.

Significant Research Findings: NCCS has been at the forefront of cancer research in the country for several years. Dr. Sharmila Bapat's team, one of the research groups studying the biology of cancer at NCCS, has recently been successful in developing a novel method to address the issue of diverse cell composition of tumours. Tumors are known to harbor cellular, molecular and functional intra-tumoral heterogeneity, which confounds our understanding of the perturbation(s) of basic biological processes in the context of cancer. This issue was addressed by Dr. Bapat and her group by using a flow cytometry-based approach. Since these are universal principles, this approach is applicable across different cancer / cell types. Further integration of this real-time definition of cellular heterogeneity with molecular profiling can lead to the assignment of cell-specific functional context(s) within tumors, as against derivation of biological functions based on averaged tumor data. Thus, gene expression studies across sorted cell fractions led to the establishment of a unique association of the surface marker CD53 with regenerative potential in CSCs as well as progenitors within the tumor

regenerative hierarchy. Another interesting finding of their research was the association of cytoskeletal remodeling and epithelial to mesenchymal transition (EMT) with aneuploid fractions under conditions of stress, which emphasizes the contribution of genetic heterogeneity and Darwinian principles of selection during tumor metastases. Tumor deconstruction was also demonstrated to be a convenient tool to overcome limitations of the currently used simplistic drug screening strategies in which consideration of cell line-based cytotoxicity and/or in vivo tumor regression as end-points of drug efficacy fail to address residual regenerative potential following therapeutic regimes.

The scientists at NCCS have also been studying communicable diseases, such as those caused by viruses. Dr. Debashis Mitra and his group has been working on different aspects of the HIV virus, related to host-virus interactions, immune response and drug discovery. The primary objective of their research is to understand the virus and its interactions with the host cell better, which could lead to improved antiviral strategies. This group has recently elucidated the role of the HSP70-binding protein, HspBP1, a co-chaperone molecule of HSP70, in HIV-1 pathogenesis. Their findings revealed that HspBP1 inhibits HIV-1 gene expression and viral replication by interacting with NF- κ B enhancer sequences in the LTR promoter. They also determined that HspBP1 competes with p65 of the NF- κ B heterodimer for recruitment on the κ B enhancer site. The identification of this novel role of HspBP1 as a host intrinsic inhibitor of HIV-1, which negatively regulates HIV-1 gene-expression and replication, could be a promising lead towards identifying new anti-HIV therapeutic strategies.

Dr. Arvind Sahu and his group study other factors that play a role in protection from viral infections, such as host factors, especially the complement cascade of the immune system. Their data demonstrate that the presence of an intact complement is essential for clearing the pandemic

influenza virus infection, wherein locally-synthesized complement plays a major role. Osteoimmunology is another area of research at NCCS. Dr. Mohan Wani and his research group study the role of interleukin-3 (IL-3) in the pathophysiology of bone and cartilage remodelling. Their recent findings revealed for the first time that IL-3 plays a chondroprotective role in osteoarthritis (OA).

Information on any Policy Initiatives during the year: The new Intellectual Property (IP) policy drafted by NCCS was approved by the Governing Body of NCCS.

Bilateral/multilateral agreements with other agencies: NCCS has initiated steps towards developing more extensive academic and research collaborations with organizations within and outside India, and forging partnerships with the industry through MoUs with neighbouring institutions like IISER-Pune, the S. P. Pune University, a university overseas and some private companies

Patents / Technologies

Identification, quantification, monitoring and analysis of Intra-tumor heterogeneity

PCT and Indian Applications filed. Co-inventor : Naik R., NCCS, Pune.

Development and applications of a cytotoxic monoclonal antibody that targets stem and progenitor cells in tumors. Indian Application filed. Co-inventor : Naik R., NCCS, Pune.

Protein based product from fenugreek seeds that regulates dyslipidemia and obesity, and a process for the preparation thereof. European Patent issue No. EP2323676- dated: 15-07-2015(Germany and France) Co-inventors: Pandey, V. and Vijayakumar, M.V., NCCS, Pune.

Method of enrichment of GSCs and ECs from glioma and co-culturing interchangeably in 2D & 3D Country: INDIA. Patent No: 4044/MUM2015. Date: 27.10.2015.

Co-inventor: Aman Sharma, NCCS, Pune.

Identification and multi-parametric analysis of GSC-EC interacting subpopulations in glioblastoma Country: INDIA. Patent No: 4045/MUM2015. Date: 27.10.2015.

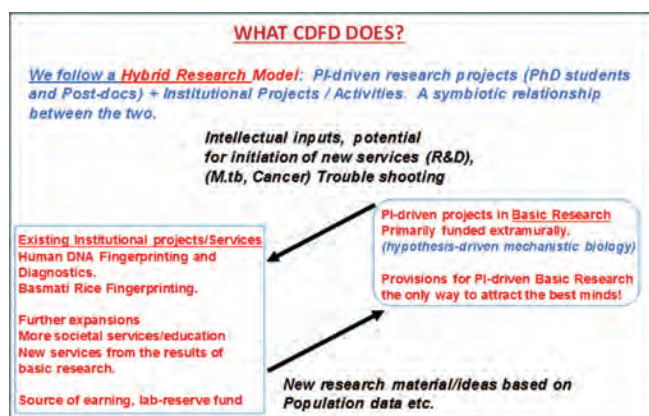
Co-inventor: Aman Sharma, NCCS, Pune.



Visit by Dr. Harsh Vardhan, Hon'ble Union Minister for Science & Technology & Earth Sciences.

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS (CDFD), HYDERABAD

The Centre for DNA Fingerprinting and Diagnostics (CDFD) established in 1996, is the first (and perhaps the only) institute in the country that constitutes a 'hybrid model' including services and research with both components complementing and enriching each other.



The institute's activities can be broadly categorized as below:

Services: Human DNA Fingerprinting: CDFD, being the premier organization in the country for referrals of complex and sensitive cases from various law enforcing agencies analysed 460 samples from 130 cases in 2016. Apart from doing routine cases, CDFD is instrumental in drafting the DNA profiling bill. This division is also involved in developing DNA fingerprinting panels specific for Indian population.

Diagnostic Services: The Diagnostics division at CDFD offers comprehensive diagnosis of genetic diseases (cytogenetic, biochemical and molecular). The center also offers prenatal diagnosis for detection of chromosomal abnormalities, single gene disorders and inborn errors of metabolism. About 6000 samples were tested for various genetic diseases. CDFD aided the establishment of Medical Genetics department at NIMS in order to provide quality care to patients with genetic disorders to train students and for conducting research in the field of Medical Genetics.

Basmati Rice purity testing: Based on the DNA markers developed in CDFD, the institute offers Basmati Rice purity testing to the rice exporters through the APEDA. About 150 samples were tested during 2016. The institute has now expanded this activity into a full-fledged department called Plant DNA fingerprinting services that will be offering new purity testing of different rice varieties and other commercially important crops.

Research activities: Microbiology: The center of excellence in microbial physiology comprised of four research groups made significant progress in various aspects of *E.coli* biology leading to understanding the transcription, replication, amino acid transport and physiology of magic spot, ppGpp. In addition to these, researchers studied molecular basis of pathogenesis of *Candida* and *Xanthomonas*.

Cell Biology: Researchers unraveled various aspects of cell signaling pathways, cell cycle regulation and ubiquitination.

Disease Biology: Progress was made to understand various aspects of biology of malaria, tuberculosis and cancer in humans.

Genetics: Fundamental mechanism of various biological processes in *Neurospora Crassa*, *Drosophila* and Silk Worm were elucidated.

Computational Biology group focused on understanding the fundamental and general principles of human proteins and their variants both (a) at molecular level and (b) at systems level.

The aforementioned research from different PIs were well recognized by international community that lead to 65 peer reviewed research publications (annexure I), earned International research fellowships like Wellcome trust and HFSP grants, INSA fellowship and numerous national research grants from the agencies like, DBT, DST, CSIR and ICMR. A patent has been filed on novel therapeutic in 2016.

Human resource development: CDFD is engaged in number of educational activities related to biological research and training in human resources development. The scientific and technical faculty of CDFD imparts education to students in more than 30 different subjects every year. Over the past five years, CDFD admitted on an average 17 students per year, under its Research Scholars Program, and are registered with either Manipal University, Manipal or University of Hyderabad, Hyderabad for

their Ph.D. degree. CDFD also has a vibrant Summer Training Program in collaboration with the Science Academies of India (Indian National Science Academy, Indian Academy of Sciences and the National Academy of Sciences), and trains about 20 to 25 students every year under this Program. Three different fellowship programs have been initiated under this agreement: (i) DNB in Medical Genetics (in association with the National Board of Examinations, (ii) Society for Indian Academy of Medical Genetics (SIAMG) accredited program in Cytogenetics and molecular genetics, and (iii) SIAMG accredited Short term Clinical fellowship program in Clinical genetics. CDFD has also entered into an MOU with 29 schools and junior colleges in and around Hyderabad under the BRIDGE Program to educate and make students aware of new excitements in various fields of science.

NATIONAL BRAIN RESEACH CENTRE (NBRC), MANESAR

The National Brain Research Centre (NBRC) continues to work arduously towards reducing the burden of brain disorders in the country. The research carried out by NBRC has been greatly valued worldwide. NBRC's research contribution in understanding healthy and diseased brain has placed India at par with international laboratories engaged in brain research. At NBRC, molecular biologists, physicists, computational neurobiologists and clinicians work together towards reducing the burden of brain diseases in Indian population in future. The institutional focus is three folds - 1) Pursue research to understand brain function in health and disease, 2) To generate trained human resources with the capability to carry out interdisciplinary research in neuroscience (NBRC is a deemed university) and, 3) Promote neuroscience in India through networking among institutions across the country.

Major Initiatives: In an attempt to make the

neuroscience research performed at NBRC applicable for human population, NBRC is extending its reach to the people in India in various ways. Some important ones are mentioned below.

A screening tool for children with learning disorders or dyslexia that was initially developed in four Indian languages will be expanded to some other languages, including Gujarati in near future. Further, we are also establishing demonstration outfits for the screening - assessment - amelioration packages recently developed by NBRC in Hindi, Marathi, Kannada and English for its use across states. Additionally, it is proposed to study the use of nutraceuticals for reducing the oxidative stress in the brain of Alzheimer's disease (AD) patients, based on our findings in the metabolic mapping of AD patients.

NBRC has a major initiative in the area of identifying novel therapeutics for brain inflammation, infection and degenerative damage. This is based on earlier success of identifying novel therapeutic candidates for Japanese Encephalitis. The clinical trials with Minocycline are planned to be extended and an attempt will be made to explore the possibility of Minocycline as a standard therapeutic for Acute Encephalitis Syndrome. Based on earlier work done at NBRC, there is also better understanding on identification of cell death mechanism during brain insults. It is important to understand whether it is direct cell death or the effect of bystander damage due to cytokines. This requires identification of possible biomarkers in order to treat brain injury in a rational manner. High throughput analysis, development of mathematical models for understanding big data is also an important component of this initiative.

Among the new initiatives is the development of a model for peripheral nerve injuries, with the possibility of screening drugs for improving their outcome. This is based on a project on model organisms (*C. elegans*) recently initiated at NBRC. In another component of study on inflammation, a

Unit of Excellence has been awarded to NBRC to study how metabolic changes can be induced by inflammation and promote the development of higher grades of cancer in glia, the supporting cells of the brain. Further, an induced pluripotent stem (IPS) cell model has been developed and well characterised neurons are being generated from the same, we plan to develop human iPSCs from patients of neuropsychiatric disorders in near future. Once established, these models will help in understanding various aspects of healthy and diseased human brain.

Salient achievements

Understanding basic biology of neuroinflammation: Accomplishments of NBRC scientists in the area of neuroinflammation have been quite striking. Research findings of NBRC not only provided a new and general therapeutic target of the whole spectrum of neuroinflammatory diseases that include infection of the CNS, but also other neurodegenerative disorders that affect millions of people worldwide. Scientists at NBRC have delineated cellular and molecular intricacies of several brain disorders ranging from Learning and memory, Alzheimer's disease, Huntington's disease, Brain and Spinal Cord injury, virus induced neurodegeneration to glioblastoma multiforme, a highly aggressive form of brain cancer.

Early detection of Alzheimer's disease: Another application of neuroscience in clinical research was our finding on the levels of glutathione (a molecule that lowers oxidative stress), which was reduced in people with Alzheimer's disease (AD). Research aimed at identification of early diagnostic marker for AD using magnetic resonance spectroscopy (MRS), found that healthy aged person turn into mild cognitive impairment (MCI) when their glutathione level depleted significantly in the left hippocampus area. This is an important discovery as measuring glutathione level in various brain regions can help us to identify people that may turn from normal healthy individual to MCI. It has been

found that left hippocampus is alkaline when people turn into AD patient. This research opens up the avenue of possible therapeutic development for the prevention of AD. A signal processing package called *Kalpana* has been developed which is very efficient to process any type of MRS data. This package can make a colour coded pH map on the MRI image. As MRS data processing is highly complicated, this package is useful for clinicians to process the data in an automated mode for a more accurate but less cumbersome assessment. Software packages for functional MRI study called BOLDsync, best suited to deliver the stimulus in a short time and efficient manner has been developed.

Creating vibrant brain researchers in India: NBRC, being a Deemed University, has now institutionalised its multidisciplinary character as a Neuroscience teaching institution by widening its admission criteria to include students with diverse background, like physics, chemistry, computer sciences, mathematics and engineering sciences. In addition to regular course work, which includes molecular and cellular neurosciences, systems neuroscience and computational neuroscience, it has commenced teaching a clinical neuroscience module to sensitise basic neuroscience researchers to clinical implications of their research. NBRC also coordinated Brain Awareness Programme in various schools and colleges across the country. This unique programme raises the awareness of the most mysterious organ in the body, the human brain and also ways of protecting its function.

INSTITUTE OF LIFE SCIENCES (ILS), BHUBANESWAR

The three major areas of research in ILS center on infectious diseases biology, various aspects of gene function as well as regulation and translational research through technology development. In this year 18 Ph.D. degrees are awarded to the student and 22 new students have enrolled for Ph.D. programme.

Infectious Disease Biology: In the area of infectious diseases the major initiatives were taken for i) deciphering the mechanism by which physiologically relevant T helper cells convert to a pathologically aberrant cell ii) studying the important component of cancer microenvironment with innumerable cross talks and signalling networks iii) characterization of the molecular mechanisms underlying the immune response perturbations using high-throughput immuno-genomics approach iv) analysis the cellular immune response of macrophages during experimental Chikungunya virus (CHIKV) infection and characterize the interaction between the nsP1 and nsP2 proteins of CHIKV which can be target for antiviral drugs vi) understand the mechanism of bacterial cell division and its coordination with other cellular processes and to discover, design and synthesize small molecules that can inhibit functions of major bacterial cytoskeletal protein FtsZ.

The achievements are i) Established role of MAPK's, ROS, Ca²⁺ signalling in T helper presence and sensitization to death in Auto Immunity ii) Genetically different Haitian *ctxB* and hybrid strains of *V. cholerae* from Silvassa are undergoing global dissemination iii) LPA converts monocytes into macrophages via Akt/mTor pathway and PPARgamma is master regulator of LPA derived macrophages (Figure 1) iv) the immune perturbed DCs have the capability to develop regulatory T cells, anti-viral responses and anti-inflammatory effects in different disease models in mice v) identified that 170 to 288 aa region of nsP1 interacts with the 1-95 aa residues of nsP2 of CHIKV and 17-AAG, a potential HSP90 inhibitor, was found to regulate CHIKV infection, apoptosis and pro-inflammatory cytokine/chemokine productions of host macrophages significantly vi) identification of FDA approved drug doxorubicin that inhibits bacterial growth by interfering with cell division process.

Gene function and regulation: The initiatives were taken to i) identify the complex miRNA-gene

regulatory networks present in the CML lin(-) cells which may help to delineate the disease further ii) study the role of epigenetics in breast cancer progression and to understand the basic mechanisms responsible for growing tamoxifen resistance in breast cancer patients iii) reconstruction of genome scale metabolic model and functional analysis of novel pathways involved in Bio-Geochemical cycle, synthesis of metabolites & drug resistance in bacteria.

The major achievements in this group are i) deciphering the shortest thiosulfate dependent electron transport chain in *Thiomonas bhubaneswarensis* strain S10 (DSM 18181^T) using genomic and functional analysis and identification of novel SXT/R391 integrating conjugative elements in the genome of *Marinomonas fungiae* JCM 18476^T ii) identification of a miRNA-mRNA network in the CD34+ cells isolated from the bone marrow of naive CML cases and the development of a combinatorial therapy, ex-vivo, of Imatinib, the drug of choice of CML and JAK inhibitor I which significantly brings down the proliferation of CML lineage negative cells iii) exploring significant role of orphan nuclear receptors such as ERRα in breast cancer progression and identification of its important downstream transcriptional targets.

Translational Research: The initiatives were to i) load the anti-cancer drug Doxorubicin on the Carbon Quantum Dots and their delivery efficiency to the target cells via *in vitro* treatment of oral squamous cell carcinomas (OSCC) cells was explored ii) start evaluating the anti-cancer activities of the developed nanomedicines in different animal model iii) to discover the differentially expressed protein involved during disease pathogenesis using advanced Proteomics approach iv) characterize the interaction of viral proteins such as Influenza Virus Matrix-1 protein and Dengue Virus Capsid protein with host chromatin elements v) to identify the disease associated genes/variations and to understand their functional significance in otosclerosis disease process.

The major observations are i) human prostate tissues do get infected with different bacteria and bacterial components promote prostate cancer progression ii) Pirfenidone and NAC combination therapy has better effect in suppressing tumor-associated desmoplasia than individual drugs iii) the Good's buffer can be used as the precursor for the synthesis of heteroatom doped Carbon Quantum Dots with an enhanced photoluminescence and anti-cancer property iv) development of different drug loaded nanocarriers for their anticancer effect in different cancer model (in vitro/in vivo) and for different neurodegenerative diseases by crossing the blood brain barrier v) crystal structure of the N-terminal domain of AtClpC1 and AtClpD proteins have been solved to atomic resolution (Figure) vi) a higher prevalence of observed for otosclerosis disease (0.44%) with male predominance in this/ Indian population and the identification of disease associated variants viz. OPG (c.9C>G; c.30+15C>T), TGFB1 (c.-509C>T; -832G>A), RANKL (-643C>T) and RELN (rs3914132) and alteration in OPG/RANKL system and its regulator TGFB1 expression ratios in disease tissue strongly suggest the role of these genes in the disease process.

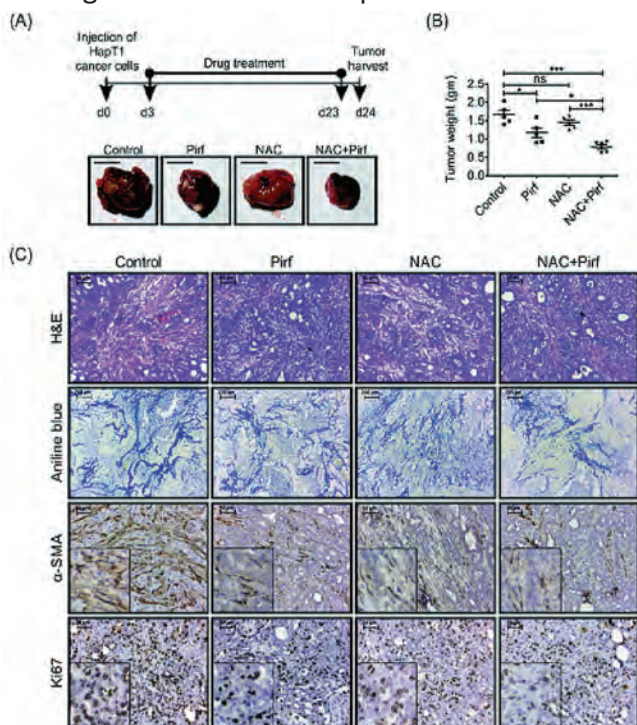


Figure : Effects of pirfenidone and/or N-acetylcysteine (NAC) on the HapT1 orthotopic tumor. Data obtained from animal experiments using HapT1 orthotopic tumor model shows better outcome with a combination therapy of pirfenidone (Pirf) and N-acetylcysteine (NAC).

Patent: Sahoo SK, Dilnawaz F, Singh A and Patro Rajkumar: "An improved magnetic nanoparticle separation device". Indian Patent application No 201631024913 dated 20/07/2016

Patent Granted : A Method For Preparing A Water Dispersible Glyceryl Monooleate(gmo) Magnetic Nanoparticle (Mnp) Formulation And Use Of The Same. Inventors: Sahoo Sk, Fahima D, Abhalaxmi S; Status: (USA, Divisional Patent, Div: Patent Grant Number: 9,271,934); PCT Application Number: PCT/IN09/000639; Indian Patent Application Number: 779/KOL/2009

REGIONAL CENTRE FOR BIOTECHNOLOGY (RCB), FARIDABAD

The Regional Centre for Biotechnology (RCB) has the mandate to provide a platform for biotechnology education, training and research at the interface of multiple disciplines. The vision of the Centre is to produce human resource tailored to drive innovation in biotechnology, particularly in areas of new opportunities and also to fill talent gap in deficient areas. The Centre has been conducting multidisciplinary research in the various areas of biotech sciences geared towards improving the human health. A doctoral program in the broad area of biotech sciences is ongoing that provides training and education opportunities to young scientists. Besides, the Centre has been regularly conducting short-term courses and workshops in the frontier areas of Life Sciences benefitting young and mid-career researchers.

Major initiatives: A multi-institutional pregnancy cohort has been initiated in which RCB is an important partner along with THSTI, NIBMG, Gurgaon General Hospital, Safdarjung Hospital, and Maulana Azad Medical College. Goal of this

program is to understand the biology of PTB with the explicit intent of identifying biomarkers of high predictive value.

Salient Achievements: Several important milestones were reached this year that would define the future of the Centre. The RCB was conferred the status of an institution of national importance through an act of parliament. This enables the Centre to grant degrees in education and research in biotechnology and related fields. To achieve its objectives, the Centre functions in close collaboration with other national, regional and international organizations that include the UNESCO.

The Centre has continued to pursue the various innovative research programs to create knowledge in the broad areas of biotech science. Under the research program on nanomaterials for biomedical applications, lipid-peptide conjugates forming hydrogels encapsulating different anticancer drugs in different combinations were developed. Study showed the anticancer potential of these drug-encapsulated hydrogels in the murine model systems. Studies on platelet activation during dengue virus (DENV) infection show that high copy numbers of virus genome in platelets directly correlated with platelet activation during the early infection. The DENV-mediated platelet activation was directly correlated with platelet lysis and clearance.

Inflammatory bowel disease (IBD) involves chronic inflammation of all or a part of the digestive tract leading to severe diarrhea, pain, fatigue and weight loss. Using the cell culture and the mouse model, an important role for SUMOylation in inflammation during IBD and the colorectal cancer has been found, and these observations have been validated using patient samples.

The academic activities at the RCB have continued with full vigor. Thirteen young scientists are currently mentored by the RCB faculty and there are

77 students pursuing doctoral research, of which 14 joined RCB during this academic session. In addition to this, a number of post-doctoral fellows and research fellows/assistants engaged through extramural grants are adding to the scientific strength of the Centre.

The Centre organized an international workshop on computational crystallography in partnership with the Collaborative Computational Project No. 4 (CCP4) executive of the United Kingdom. More than 60 scientists and researchers attended the workshop across the country and more than 15 national and international speakers mentored in their field of specialization. RCB also hosted the Young Investigators Meeting (YIM-2016), a workshop for Post-Doctoral fellows invited from international universities across the globe. The workshop serves as a platform for sharing the research experiences at the level of post-PhD fellows and their opportunities to work on inter-institutional basis. In addition, RCB co-organized the Ramalingasami Fellowship Conclave-2016 attended by more than 150 scientists and research fellows working in the pioneering areas of biotechnology. The conclave was mentored by 25 eminent scientists.

NATIONAL INSTITUTE OF BIOMEDICAL GENOMICS (NIBMG), KALYANI

NIBMG was established in 2009. Within a brief period since its inception, the National Institute has made a global academic mark by making significant research findings as evidenced by high-quality publications in the areas of cancer genomics, genomics of infectious disease and population genetics. Faculty members of the Institute have successfully obtained extramural research funding and have developed national and international collaborations. The Institute has also played a major role in national genomics capacity building by organizing workshops and hands-on training, independently and in collaboration with

international institutions such as the European Bioinformatics Institute. The Institute has also developed a vibrant public outreach programme, through open houses, public lectures and digital media. To accelerate genomics in health and disease, the Institute has established a Biomedical Genomics Centre on the premises of the largest tertiary-care hospital in Kolkata, and has opened access to its high-end platforms to national institutions in which such infrastructure is wanting. Students and faculty members of the Institute have received national and international awards and recognitions.

Major Initiatives: To accelerate basic and translational research and capacity-building in biomedical genomics by empowering clinicians to carry out independent research and training, a Biomedical Genomics Centre has been established in the precincts of the largest tertiary care and teaching hospital in Kolkata – the SSKM Hospital and Institute of Post-Graduate Medical Education & Research. The Mission of BMGC is to create platforms for research within medical schools and hospitals, to facilitate such research by providing access of clinicians to genomics infrastructure and to promote co-operation between basic and clinical science researchers in relevant areas and in capacity-building.

A number of clinically-driven projects have been undertaken in BMGC, notably on non-alcoholic fatty liver disease, diabetic foot ulcers, etc. The study on “Skin Microbiome” was undertaken to characterize the healthy skin microbiome across different skin types in Indian population and to investigate whether the inter-individual and temporal variations can be significantly explained by variation in sebum and hydration levels in the facial skin. The findings from this study have been published in “*Scientific Reports*” and may have implications in understanding differences in prevalence of various skin conditions, such as acne, psoriasis, dermatitis etc.

The International Cancer Genome Consortium (ICGC) has been organized to launch and coordinate a large number of research projects that have the common aim of elucidating comprehensively the genomic changes present in many forms of cancers that contribute to the burden of disease in people throughout the world. NIBMG played a key role in ensuring that India becomes a founding member of the ICGC. The goal of ICGC is to obtain a comprehensive description of genomic, transcriptomic and epigenomic changes in 50 different tumour types and/or subtypes which are of clinical and societal importance across the globe. The project has progressed well revealing that (a) alterations in tumor suppressor genes drive oral cancer, (b) oral cancer comprises subtypes, with significantly different periods of disease-free survival, discernable by alterations in driver genes, and (c) a major actionable pathway that is altered in oral cancer is the arachidonic acid metabolism pathway; LOX and COX inhibitors of this pathway are available to potentially help therapeutic interventions and germline and somatic alterations in small number genes drive cells from primary tumour to metastasize to the near lymph node. Studies on cervical cancer genomics and epigenomics have revealed several interacting DNA variations and epigenetic alterations in the host and viral genomes that enhance cancer risk, imparting molecular diversity to such cancers, further illustrating the cross-talk between coding HPV16 E7 mRNA and non-coding RNAs (miRNAs and long non-coding RNAs) and the relevance of non-coding DNA variations in disease causation. The findings have been published in *Genome Announcement*, *Cellular Oncology*, and *Tumor Biology*. Studies on breast cancer genomics using whole-exome sequencing on carefully collected tissues from patients, revealed that progesterone in conjunction with surgery leads to inhibition of survival of tumor cells by probably acting as a deterrent for the tumors to cope up to cellular stress. RNA-seq data from a time series experiment on such cancers has been used to develop methods for the detection of

cognizable trends of gene expression and this has been published in the *Journal of Genetics*. Studies on host factors that regulate tuberculosis infection and granuloma have revealed that pathways regulating host cellular homeostasis may be more relevant than pro-inflammatory cytokines, for governing mycobacterial growth at least in the early stage of infection. The results have been published in *Tuberculosis*. Important baseline findings of the “Kalyani Cohort Study” include high prevalence of diabetes, dyslipidimias and hypothyroidism. A recent report of this study has been accepted for publication in *Global Health, Epidemiology and Genomics*. As part of the studies on “Population Genomics” attempts have been made to understand long-term human evolution, genomic diversity and structures of extant human populations and nature and extent of selection pressures on the human genome. A key finding of this study that attracted global attention was that an extinct hominid shared a common ancestor with the Neanderthal and the Denisovan, but had a different history. This has been published in *Nature Genetics*. Systematic analysis of genome-wide data, derived from ethnically representative 18 mainland and 2 island (Andaman and Nicobar Islands) populations has provided the key conclusions that (a) four – not two, as was inferred by other researchers earlier – major ancestral lineages have contributed to extant populations of mainland India, (b) the populations of Andaman archipelago have a distinct ancestry, and (c) widespread admixture among populations in India was rapidly replaced by endogamy about 70 generations ago, coinciding with the historical period of formulation and adoption of sociocultural norms restricting intermarriage in large social strata. These findings have been published in the *Proceedings of the National Academy of Sciences, USA*. Using cell and animal models of Huntington’s disease mechanism (s) gene deregulation were investigated. The findings from this study have been published in *Experimental Cell Research*.

Salient Achievements: Teaching and Training: Two students have acquired PhD degree and one student is awaiting the award of PhD degree. Besides, as part of short term training, a total of 15 trainees were recruited at NIBMG and BMGC of which, 4 were from the Academy Summer Research Fellowship Program and the rest from various Universities across the country.

Establishment of Genetics Service Unit at BMGC: A Genetics Service Unit has also been established in BMGC. With funding from the Government of West Bengal, arrangements have been made to provide diagnostic genetics service free-of-cost to patients attending government hospitals in West Bengal.

Establishment and sustenance of CoTeRI: Grounded on the belief that a publicly-funded national institution must facilitate the spread of its primary objective, NIBMG has formed a Core Technologies Research Initiative (CoTeRI) to *Accelerate Genomics for Health*. NIBMG, through CoTeRI, has made its high-end, high-throughput technology platforms available for academic pursuits of scientists of all publicly-funded institutions in India. Reagents must be provided by users for execution of their work; NIBMG provides all other infrastructural help, including technical manpower help. Through these activities, NIBMG has been able to facilitate high-end training of personnel in various laboratories, particularly in the laboratories of the NE region.

Establishment of SyMeC: A platform – both intellectual and logistical – has been created for generating required biological and medical evidence to accelerate systems medicine. Co-ordinated and spearheaded by NIBMG, the Systems Medicine Cluster (SyMeC) comprises six institutions in Kalyani (NIBMG and IISER) and Kolkata (Bose Institute, IICB, ISI and Tata Medical Centre) who will share resources and work towards a common goal of precipitating systems-level biological evidence to aid the understanding, diagnosis and treatment of diseases, focusing on cancer initially.

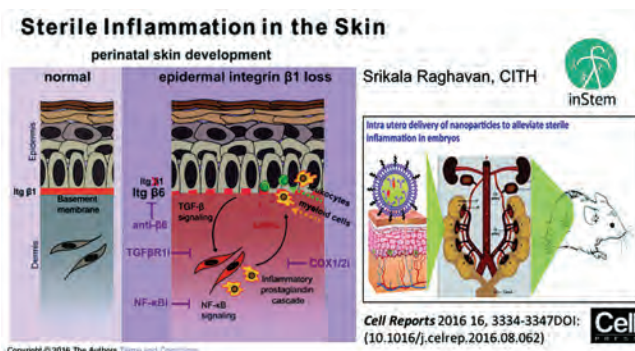
THE INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE MEDICINE (inStem), BENGALURU

The Centre for Inflammation and Tissue Homeostasis (CITH), focuses on stem cell niches and extracellular matrix organization in mammalian skin. The group while studying early development in a mouse model of inflammation, noted that even in the absence of injury, changes in the microenvironment of the dermis (layer of skin, beneath the surface), leads to inflammatory signaling in resident phagocytic populations. This recruits pro-inflammatory cells, resulting in matrix disruption, loss in organization of the epithelial basement membrane and neonatal lethality. Independent verification of these results, came from a collaboration with the research group at the Technologies for the Advancement of Science (TAS), wherein *in utero* drug administration to the developing embryos, resulted in reduced damage to tissue following blockade of the inflammatory response.

Inducible pluripotent stem cells (iPSCs) generated by reprogramming adult cells, which can be further differentiated into various cell types are an important tool to investigate disease biology. A *bigger* challenge is modelling complex diseases and tissues using iPSCs. Several research groups at inStem employ iPSCs to model disease or reparative processes in combination with animal model systems. The team at the Centre for Brain Development and Repair (CBDR) at inStem, which in partnership with colleagues at the University of Edinburgh, UK, are attempting to model human Autism Spectrum Disorders (ASD) “in a dish”. Electrophysiological characterization of cortical neurons, neural stem cells and astrocytes all derived from iPSC lines from Fragile X Syndrome patients with documented clinical diagnosis and iPSC lines from control unaffected donors have been initiated. The team has also established new rodent models of ASD/IDs for circuit and behavioral analysis.

Scientists from the TAS team in collaboration with colleagues in University of Iowa, USA, has lead a study to purify crystals from the mid-gut of the pacific beetle cockroach (*Diplopterapunctata*) embryos. Their analysis showed that these crystals are three times as nutritious by weight compared to buffalo milk. The team’s analysis of the crystal structure revealed the protein:carbohydrate:lipid complex that underpins this property. This study attracted widespread attention, worldwide. This group also identified a protein from the fish *Sanders vitrius* that shows interesting fluorescent properties. By engineering mutations in the protein, naturally found in this fish, they have gone on to show that modified protein, engineered in the laboratory, can be used for tissue and cell imaging.

Patents filed/granted : Blue fluorescent protein and methods of use thereof. US Patent number: US9383366B2. Granted 07/05/2016.



Centre for Stem Cell Research (CSCR, a unit of inStem, Bengaluru)

Christian Medical College Campus, Bagayam, Vellore: The Centre for Stem Cell Research (www.cscr.in) continues to focus on translational research in cell and gene therapy towards regenerative medicine to bring stem cell science and other novel therapies to management of patients with unmet needs. The concept of teams working on specific themes through multidisciplinary collaborations is being further strengthened to help this goal. There are three major themes for translational research at present:

Gene therapy: The major components of this program involve (a) The AAV vector based gene therapy for haemophiliaB in collaboration with University of Florida (UF) and Emory University (EmU), USA. This collaboration has progressed with the signing of a research agreement with UF for the production of the vector for a clinical and preclinical work being contributed by all three collaborators towards developing a novel AAV3 vector. This concept has been presented to the regulatory agencies in India for their approval. A major thrust is also on developing a program for gene therapy for the major haemoglobin disorders. (b) Given the continuing success of lentiviral vector approach in multiple clinical trials this being pursued further while adding on efforts for genome editing based approach by disrupting the BCL11A gene to increase HbF production – all at the preclinical level at this time. (c) Lipid base gene delivery approaches are also being explored.

Therapeutic genome editing for the correction of hemoglobinopathies: A potential target for the reactivation of fetal haemoglobin has been identified. CRISPR/Cas9 based ribonucleoprotein system has been developed for genome editing of the identified target.

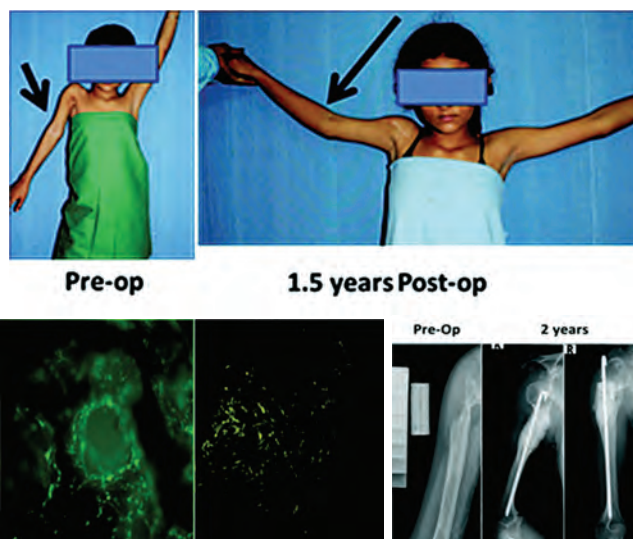
Pre-clinical studies for gene therapy of Wiskott - Aldrich syndrome: Genome editing tools and homologous recombination based GFP reporter construct and WASP transgene constructs were developed. Model cell lines to test the functional activity of the WASP transgene are also being developed.

Therapeutic genome editing for hematological disorders: The current focus of this lab is to develop a novel genome editing approach for the treatment of sickle cell disease, thalassemia and hemophilia-A. For this purpose, targeted genome engineering platform based on CRISPR/CAS9 system is being used to reactivate gamma globin by editing the potent gamma globin repressor in hematopoietic stem cells. This lab has generated guide RNAs

targeting the potential gamma globin repressor and cloned in to the viral vector and have confirmed the successful disruption of target locus in human embryonic kidney cell lines by T7 surveyor assay. In parallel, ribonucleoprotein based system (RNP) is being used to cleave the target locus in hematopoietic stem cells. Further, CRISPR Cas9 system is being used for the targeted expression of Factor VIII in specific progeny of hematopoietic stem cells.

A project for improving safety profile and efficiency of cationic transfections with a novel α -lipooic acid based anti-oxidant lipid is also ongoing under the gene therapy program.

Musculoskeletal Regeneration Program: The focus of this program is on articular and physical cartilage replacement, bone and muscle regeneration in different clinical conditions. Successful implantation of autologous MSC loaded scaffolds has been done in ten children with large segmental bone defects showing radiological union at 2-3 months in all patients. This is one of the first such studies in the world. Furthermore, first 5 patients have completed 1 year of follow up.



a) Photographs showing pre-op range of abduction (left, arrow), b) The radiographs show preoperative nonunion of humerus and postoperative united humerus with incorporation

of the graft at 2 years. c) Live dead assay showing over 98% viable cells (green) on the tissue engineered construct (left), Profuse endogenous phosphatase staining on cell-scaffold construct on day 28. Yellow staining shows the secretion of endogenous phosphatase present in the cytoplasm and showing good osteogenic differentiation of the mesenchymal stem cells.

Applications of iPSC technology: Within this theme, there are two areas of translational research. The first is with regard to developing disease models using the iPSC. Apart from using them to study specific interests in disease mechanisms in Fanconianemia, Diamond Blackfan Syndrome and Congenital Dyserythropoietic Anemia, this platform is also being utilized for genome editing purposes towards gene correction studies in thalassemia and sickle cell disease to establish genome editing platform to complement the work being done for gene therapy.

Apart from the major thematic research programs, there are also several areas of project based translational research that scientists at CSCR are pursuing as follows:

Somatic cell reprogramming: Novel multifaceted approach to widen the therapeutic window of spinal cord injury in SCID mice model using hPD-MSC and/ or PTEN modulation in axons by inducible shRNA:

Tissue Engineering: Evaluating the pathophysiology and Molecular Pathways Regulating Pericyte Phenotype in Type 2 Diabetes: The Gestational Diabetes Mellitus Placental Model.

**NATIONAL AGRI-FOOD
BIOTECHNOLOGY INSTITUTE (NABI),
MOHALI**

National Agri-Food Biotechnology Institute (NABI) was established with the objectives of promoting and coordinating research of high calibre in basic and translational aspects at the interface of Agriculture, Food and Nutrition. Presently the

institute is working in the five core areas that includes, (I) Improving cereals for nutrition and processing quality; (II) Improving fruits for post-harvest quality and nutrition; (III) Basic biology for crop improvement; (IV) Functional foods for better health (V) Computational biology approaches for marker and gene discovery.

Major initiatives: High throughput screening for varying amylose and resistant starch content was performed. Colored wheat rich in anthocyanin content were further transferred to the other high yielding cultivars (PBW550, PBW621 and HD2967). Wheat straw and oat bran polysaccharides combinations were used to develop edible coatings to prevent the post-harvest losses. In the area of Food and Nutrition Biotechnology, potential role of the nutritional benefits of finger millet and kodo millets and their dietary constituents, mainly arabinoxylan (AX), for protecting from high fat diet induced metabolic alterations were studied.. In the area of computational biology, major initiatives were taken to identify novel miRNA from wheat and their possible targets.

Salient achievements: A set of 101 M4 EMS-treated mutant lines developed in an Indian bread wheat (*Triticum aestivum*) variety, 'C 306'

Multiple (10 lines) new coloured wheat lines (blue, purple and black grains) with enhanced anthocyanin content (40-140 ppm) compared to white wheat (5-15 ppm) with antioxidant and health promoting properties have been developed in the background of high yielding cultivars PBW550, PBW621 and HD2967 (Figures1). The color in these lines is due to high anthocyanin content. These lines also showed high micronutrients like iron and zinc.

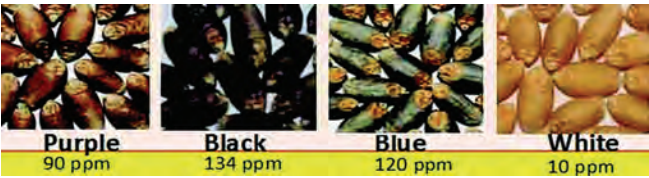


Figure 1: Representative pictures of different coloured wheat with enhanced content of anthocyanins (in ppm).

A novel biodegradable and edible coating with the mixture of wheat straw and oat bran polysaccharides (Yield of 17% and 8% respectively) has been developed to enhance shelf life of fruit crops (Apple and Kinnow)

Finger millet and kodo millet whole grain and bran beneficially modulate the host physiology under high fat diet conditions.

Highly bioavailable iron formulation, “alginate-encapsulated ferric galactose micro-emulsion” and serving as alternative strategy to treat iron deficiency has been developed.

Magnetic nanoparticle was functionalized for immobilization of α -amylase for enhanced reusability in bio-catalytic process.

Non-starch polysaccharide component from finger millet has been found to curtail lipopolysaccharide induced inflammation in murine macrophage (RAW 264.7) cells.

Using a novel protein-based gene knockdown technology, an atlas of b-ZIP53 interacting transcription factors involved in seed development and maturation in model plant *Arabidopsis* has been prepared to develop the seedlessness trait.

Patents obtained/applied:

A provisional Indian patent has been filed on the process of preparation of naturally colored speciality biscuits and other bakery products using anthocyanin rich Indian wheat lines as ingredients(s) (2017: Garg M; Application No: 201711001772)

A process has been developed for immobilization of the chimeric enzyme, Smt3-d-psicose 3-epimerase, and production of nearly zero calorie sugar, D-psicose, from agro-industrial residues. This process is IPR protected by filing a patent in India. (Patent File No. 201611044752) (Sudhir Singh, Nitin Singhal, Rajendra S Sangwan).

Process for encapsulating macrobiomolecules in solid lipid nanoparticles. [TEMP/E-1/2724/2016-DEL]

Dated 28.01.2016.(Indu Pal Kaur, Gaurav Sharma, Kanwaljit Chopra, Sanjeev Puri, Mahendra Bishnoi, Parveen Rishi).

Probiotic formulation for targeting colon cancer Status: Approved by NRDC, New Delhi for funding. In process of filling (PAA 2390/AM/SBS/Y). (Indu Pal Kaur, Parneet Kaur Deol, Mahendra Bishnoi, Kanthi Kiran Kondepudi).

Technology transferred: Agreement has been signed between NABI and Bonn group of industries, Punjab for production of colored (high anthocyanin) wheat based bread, biscuits and other bakery products.

Breeding material transferred: Breeding material (4 lines) with improved bread, biscuit and chapatti making quality has been transferred to wheat breeders at Punjab Agricultural University (PAU) for inclusion in the regular wheat improvement program.

Bilateral/multilateral agreements: Agreement has been signed with industry (Bonn Food Industries) in a public-private –partnership mode to develop colored wheat based bakery products like bread and biscuits.

CENTER OF INNOVATIVE AND APPLIED BIOPROCESSING (CIAB), MOHALI

The institute's mandate area covers the following four major R & D programs:

Value Addition to Primary Processing Residues or Wastes for Edible Products

Valorization of Crop Wastes for Specialty Products and Chemicals

Nutritionals, Nutraceuticals, and Upgradation of Value or of Use of Primary Processing Bioproducts

Biosynthetic Technology/Synthetic Biology for Low Volume-High Value Products and

Industrial Enzymes

Major initiatives:

Development of processes for value added products from liquid whey

Development of processes for value added products from distillation residual Geranium biomass

Processing of guar meal to protein rich edible product

Production of value added products from fruit processing industry waste (pomace)

Valorization of rice straw for production of lignocellulosic biomass-derived high value chemicals

Fermentative production of xylitol from corncob and rice straw

Fragrance improvement of citronella essential oil by its enrichment with rose oxide

Bioprocessing of agro-industrial wastes and by-products for the production of nearly zero calorie functional sugar and prebiotic molecules.

Salient achievements

a.) Value Addition to Primary Processing Residues or Wastes for Edible Products

Fiber rich energy drink has been developed from liquid whey and primary processing fruit industrial waste.

Bench-scale process has been developed for the production of bacterial cellulose using liquid whey.

A process has been developed for production of rose scented natural tartaric acid from Geranium biomass/Geranium biomass hydro-distillation residual water.

A process has been developed for producing edible off-flavour free high protein flour from guar meal. Promising lead has been achieved for incorporation in food products.

Process has been developed for production of p-

cymene sulphonic acid based ionic liquids from citrus waste derived (+) limonene.

b.) Valorization of Crop Wastes for Specialty Products and Chemicals

Valorization of rice straw for production of lignocellulosic biomass-derived high value chemicals

Process has been developed for producing furanic chemicals (e.g. levulinic acid) up to 21% weight of rice straw.

Process has been developed for producing nanocellulose from rice straw through thermochemical processing.

c.) Nutritionals, Nutraceuticals, and Upgradation of Value or Use of Primary Processing Bioproducts"

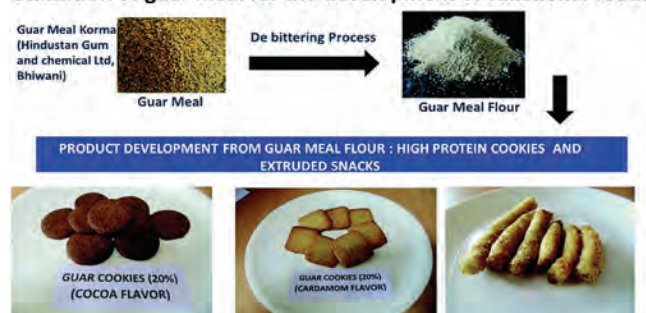
Process has been developed for xylitol production from corncob as well as rice straw.

Process developed for production of value added citronella oil containing ~16% and ~1.5% rose oxide.

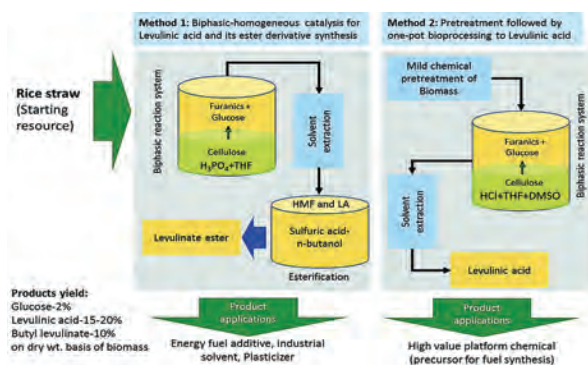
d.) Biosynthetic Technology/Synthetic Biology for Low Volume-High Value Products and Industrial Enzymes"

Process has been developed production of nearly zero calorie alternate and healthful sugar, D-psicose, from fruit and vegetable wastes.

Process has been developed for production of prebiotic oligosaccharides and D-psicose from cane molasses.

Utilization of guar meal for the development of functional foods

Bioprocessing of biomass for specialty chemicals and value added chemicals production



Patents (filed):

A process for magnetic particle immobilization of Smt3-d-psicose 3-epimerase enzyme and post-reaction recovery and recycled use of the immobilized enzyme for production of D-psicose from biomass or bioresource or agro-industrial products or residues, and uses of the same. Patent File No. 201611044752; Inventors: Singh SP, Sangwan RS, Patel SN, Singhal N

Process for producing edible off-flavour free and high protein flour from guar meal Patent File No. 20611024281. Inventors: RS Sangwan, PP Sandhu, K Bains, Gisha.

A process for fragrance improvement of citronella essential oil by its enrichment with rose oxide using hypervalent iodine reagents and uses thereof. PatentFile No. 201611024112, Inventors: BB Mishra, P Dwivedi, U Singh, RS Sangwan

A process for the production of prebiotic oligosaccharides and nearly zero calorie functional sugar from cane molasses, and uses of the same. PatentFile No. 201611016793. Inventors: SP Singh, RS Sangwan, M Sharma, SN Patel, M Krishania, U Singh, K Lata

A process of fragrance improvement of citronella essential oil by its enrichment with rose oxide and a process of production of rose oxide and uses thereof. PatentFile No. 201611009275. Inventors: BB Mishra, U Singh, RS Sangwan

A process for the production of nearly zero calorie sweet sugar from fruit or vegetable plants, plant parts and their extracts and residues, and uses of the same. PatentFile No. 201611003411. Inventors: SP Singh, RS Sangwan, SN Patel, M Sharma, U Singh, V Kumar

A process for the production of natural and scented tartaric acid from geranium biomass/geranium biomass hydro-distillation residual water as a novel biomass. PatentFile No. 1487/DEL/2015. Inventors: RS Sangwan, U Singh

A Process of *Withania somnifera* (Ashwangandha) biomass based production of solanesol and uses thereof. PatentFile No. 3201/DEL/2015. Inventors: R.S Sangwan, U Singh

A green process of non-inflammable volatile biogenic solvents based extraction and isolation of lycopene and other carotenoids from bioresources and other materials and uses thereof. PatentFile No. 3197/DEL/2015. Inventors: RS Sangwan, M Sharma

A process of volatile biogenic solvent(s) aided enhancement of colour and stability of lycopene and other carotenoids in presence or absence of light and uses thereof. PatentFile No. 3228/DEL/2015). Inventors: R.S. Sangwan, M Sharma

NATIONAL INSTITUTE OF ANIMAL BIOTECHNOLOGY (NIAB), HYDERABAD

NIAB is aimed to harness novel and emerging biotechnologies and take up research in the cutting edge areas for improving animal health and productivity. The Institute's focus of research is on Animal Genetics and Genomics, Transgenic Technology, Reproductive Biotechnology, Infectious Diseases, Bioinformatics and Nutrition Enrichment. The institute aims at basic research leading to the development of novel vaccines, diagnostics and improved therapeutic molecules for farm animals.

Research focus of NIAB includes infectious

diseases, reproductive biotechnology, bioinformatics, animal genetics & genomics and nutrition with an aim of improving health and productivity of livestock. Major infectious diseases currently being studied are Brucellosis, Leptospirosis, Staphylococcal mastitis, Newcastle disease, *Peste des petits ruminants* (PPR), Theileriosis, Toxoplasmosis, etc., with the focus on developing new tools for diagnosis and prevention.

Research Highlights

Understanding the virulence mechanisms of the zoonotic pathogen, *Brucella*, to develop efficient vaccines and diagnostic assays for animal and human brucellosis: The aim is to identify and characterise immunodominant antigens of *Brucella*. It was found that TcpB protein attenuates TLR4 signalling by targeted degradation of TLR4 adaptor protein, Tirap by recruiting a host ubiquitin ligase cytoplasmic linker protein 170. Hence, TcpB can be used as a target to tackle brucellosis..

Understanding host immune response and development of subunit vaccine against *Leptospira*: NIAB has identified *Leptospira* surface adhesin (Lsa21) as an activator of strong innate response in *in vitro* conditions. They are in process of screening more proteins for development of subunit vaccines.

Characterization and development of effective tools against Newcastle disease virus (NDV): Work is ongoing to understand the molecular biology of NDV non-structural viral protein- W, which is expressed via co-transcriptional mechanisms and in low quantities only during viral infection. Initial studies have shown that the W protein translocated into nucleus (Fig. 1). Future studies are planned to study the function of W protein with respect to host immune evasion using reverse genetics system and possibly generate W mutant viruses for use as effective recombinant vaccines.

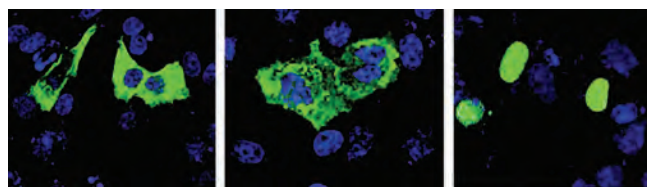


Figure 1. Sub-cellular compartmentalization of P, V and W proteins of NDV: The P gene of NDV is co-transcriptionally edited by stuttering polymerase leading to generation of two nonstructural viral proteins, V and W, by non-templated addition of a single or two 'G' residues. While P (i) and V (ii) are predominantly seen in the cytoplasm, the W protein (iii) was observed to localize in the nucleus.

Understanding the disease pathogenesis of and designing novel diagnostic tools for intracellular livestock pathogens: Functional genomics of disease pathogenesis and resistance in livestock diseases like bovine theileriosis and bovine mastitis are being explored with an aim of designing new diagnostic tools. The study on bovine mastitis due to *Staphylococcus aureus* has shown that genotypically variable strains of *S. aureus* causing bovine mastitis belong to different lineages and are linked to human lineages present in India. In addition NIAB, is extending its services to farmers and veterinarians for timely molecular diagnosis of major haemoprotozoan diseases like Theileriosis, Babesiosis, Anaplasmosis and Trypanosomiasis. Further, a rapid lateral flow based kit for early diagnosis of bovine theileriosis has been developed in collaboration with Genomix Pvt. Ltd. which is currently under validation.

Regulation of reproduction by kisspeptin: The tissue expression profile of kisspeptin and its receptor during pregnancy and role of NPY in kisspeptin mediated LH release in rats was investigated along with the effect of kisspeptin, in comparison with GnRH analogue, on plasma endocrine profile and follicular dynamics in pre-pubertal buffaloes.

Bioinformatics: The genome of *Brevundimonas diminuta*, a model organism for the study of genetics and biochemistry of degrading organophosphorus (OP) compounds that affect animal health and productivity heavily, was sequenced and assembled. With an objective to decipher pathways underlying degradation of OP

compounds, 4.15 Mb genome of bacteria was assembled and annotated with 3966 protein coding, 48 tRNA and 3 rRNA genes. Another bacteria, *Sphingobium fuliginis*, which degrades pollutants affecting animal and human health, has also been decoded using various platforms including Miseq, Hiseq, Ion Torrent and PacBio.

TRANSLATIONAL HEALTH SCIENCE AND TECHNOLOGY INSTITUTE (THSTI), FARIDABAD

Translational Health Science and Technology Institute (THSTI), Faridabad was established with a mission to integrate multidisciplinary scientific teams from the fields of medicine, science, engineering and technology for generating translational knowledge and to make the resulting biomedical innovations accessible to public health. Since its inception about ten years ago, THSTI has grown from an idea to an institution with six centres and an extramural unit, to maximize the value of science generated by others and at THSTI, through innovation and translation.

The **Vaccines and Infectious Diseases Research Centre (VIDRC)** is the first Centre of THSTI. The highlights include: identification of the correlates of severe dengue disease, showing that primary infections can be as severe as secondary infections in children. Other studies examined the attachment, entry and dissemination of Japanese encephalitis virus (JEV) in model systems. Replication and pathogenesis of hepatitis viruses was examined complemented by screening and re-purposing approaches for future therapeutic strategies. The Scientists at VIDRC have also developed CRISPRi based methods to identify potential targets for therapy and the application of systems approaches to the study of mycobacterial survival and pathogenesis. During the year, VIDRC has initiated many new collaborative studies; (a) Study jointly with NBRC, Manesar and AIIMS, Delhi for

understanding the therapeutic role of adult stem cell derived exosome in combating virus induced neurodegenerative disease. (b) Study jointly with RCB for understanding interactions between JEV and host Autophagy Pathway: Implications for Pathogenesis. (c) Development of a novel BAdV isolate as a gene/vaccine delivery vector for use in humans and animals as the ability of BAdV isolate to infect various human cell types and demonstrated absence of BAdV-neutralizing immunity in human sera has been established. (d) Study initiated in collaboration with Delhi University on understanding the role of Rv1955-RV1956 Toxin-antitoxin locus of *Mycobacterium tuberculosis* in pathogen biology funded by DBT.

The **Pediatric Biology Centre (PBC)** was established at THSTI to serve as an interdisciplinary research center where research on childhood health and disease would lead to knowledge-driven interventions and technologies that can be effectively implemented. The inter-institutional program for maternal, neonatal and infant sciences is based at the Gurgaon Civil Hospital, involves state of the art imaging and biological analysis, with a real-time data capture and monitoring system. So far 8350 pregnant women have been screened, of which 1825 women have been enrolled and outcomes have been recorded on 953 cases. The Paediatric Biology Centre continues its exploration of the developmental and functional properties of the neonatal immune system and of the role of zinc in sepsis through clinical collaborations across Delhi and the rest of India. The quality of this work has attracted considerable interest from international funders.

The **Center for Biodesign** was established as a niche center of THSTI with the mission to undertake innovation in medical technologies for affordable health care in India utilizing the bio-design concept and support services that extend from strategic bench work to commercialization.

The **Drug Discovery Research Centre (DDRC)** has

a strong inter-disciplinary team. This team works together on disease interrogation, target identification and early stage development has demonstrated its ability to take on big challenges by focusing on metabolic syndromes, particularly diabetes. With faculty and scientists focused on discovery research, computational proteomics and mass spectrometry, lead discovery and development, mathematical biology and early translation, the DDRC has the potential to inform and support a number of the active and planned clinical programmes at THSTI. Salient achievements of the Centre during the year are: a) Development of a platform technology with novel small molecules as a potent inducers of cellular autophagy having therapeutic application. b) Identification and development of a lead molecule for treatment of HIV-1 infection employing dual action of inducing host cell autophagy as well as inhibition of virus integrase. This is a novel approach of addressing HIV treatment and potentially can overcome the resistance arising from virus integrase mutation. c) Identification of a lead and proof of concept studies in animal model for the treatment of hypertrophic cardiomyopathy. d) Identification of an initial hit for NAFLD

The **Centre for Human Microbial Ecology (CHME)**, is the most recently established THSTI centre at THSTI. This has emerged from studies on malnutrition and the gut microbiota, but has expanded to multiple areas, including multi-drug resistance. The role of the microbiome in the pathogenesis of type 2 diabetes, effect on the immune response and the influence of diet and artificial sweeteners on gut microbial composition are also being explored. Additional work examines the pathogenesis of *Vibrio cholerae*, and preparation to support the Paediatric Biology Centre's pre-term birth cohort through studies in the vaginal microbiota association with specific clinical outcomes. The gut microbiome study of healthy Indians revealed the real microbial community structure in the gut of healthy Indians

living in urban and rural areas. The microbiome works revealed that several factors, including dietary practices, health practices, environment, etc., could influence the diversity and dynamics of microbiome.

Policy Center for Biomedical Research:

The PCBR has been envisaged to bridge the huge gap that exists between health researchers and those who implement and steadily been working on the major interventions of health system like diagnostics (Typhoid, AMR, VL, Pneumonia etc.), Vaccines (Cholera, Pneumonia, Influenza), MCH, Neglected Tropical Diseases (VL, Filaria) etc. The current status, roadmap for elimination of some of the major communicable diseases has been strategically addressed to contribute for elimination plan from the country. The centre rightfully bridges the gap between the researchers, stakeholders (ICMR, MOH, BMGF, NICED, DOVE- JHU, RMRC Bhubaneswar, PGIMER, RGCB, Trivandrum, NIE, WaSH @ UNICEF India, IDEA Asia, WHO GTFCC; Sabin Vaccine Institute, CDC USA; AHREF, GHS, MSD, few State Health Departments, FOGSI etc.), appropriate partners (International Vaccine Access Center (IVAC), Global Health Strategies (GHS), New Delhi, Center for Disease Control- India (CDC India), National Center for Disease Control (NCDC) and Manipal Center for Virus Research (MCVR), Manipal University), and policy makers to fructify for dual goal of meeting local health needs and supply global health technologies in the translation mode by ultimate introduction of the platform technologies to the Public health system.

The **Clinical Development Service Agency (CDSA)** aims to develop an eco-system for training and learning and work with public sector institutions, and small and medium enterprises (SME) to translate innovative technologies into medical products for public good. CDSA advises on regulatory affairs on preclinical and clinical product development and registration in India. CDSA has been involved in clinical monitoring of different

projects related to Severe Acute Malnutrition (SAM), Preterm Birth and Reflexology studies. CDSA has also entered into long-term contract of collaboration with BIRAC, wherein CDSA audits clinical studies and provides specialized clinical study support. CDSA is project managing AIIMS-sponsored study on indigenously developed surfactant for preterm babies with Respiratory Distress Syndrome. CDSA has effectively conducted

various training and clinical research programmes: a) First ever CME program of Andaman and Nicobar Islands. b) Ethics committee programs c) Training on GCP and GCLP at Nepal (Funded by CISMAC & University of Bergen, Norway). d) Bioethics Certificate Course in collaboration with Manipal University e) CDSA-BIRAC – Regulatory Workshops f) Ethics Committee's Registration with CDSCO g) Faculty for GCP, EC Training workshops

Patents Filed (2016-17):

S. No.	Application No.	Date of filing	Title of Patent	Inventors	Applicant(s)	IP status
1	201611021901	27th June, 2016	Isolated single stranded polynucleotides and uses thereof in diagnosis and treatment of Tuberculous Meningitis	Dr. Jaya S. Tyagi, Dr. Tarun Kumar Sharma, Dr. Abhijeet Dhiman, Dr. Chanchal Kumar, Ishara Datta	THSTI AIIMS	Indian Provisional Application
2	201611029904	1st September, 2016	Method of hyperplexing in mass spectrometry to elucidate temporal dynamics of proteome	Dr. Kanury Subba Rao, Dr. Amit Kumar Yadav, Dr. Shilpa Jamwal, Dr. Suruchi Aggarwal, Dr. Ajay Kumar	THSTI	Indian Provisional Application
3	201611031991	20th September, 2016	Mammalian cell lines for enhanced production of Japanese encephalitis virus, the method to produce and uses thereof	Dr. Sudhanshu Vrati, Dr. Manish Sharma, Dr. Manjula Kalia	THSTI	Indian Provisional Application
4	201711001246	12th January, 2017	Novel DNA aptamers against nucleoid-associated protein HupB of Mycobacterium tuberculosis and uses thereof	Dr. Tarun Kumar Sharma, Dr. Jaya Tyagi, Dr. Hanumanthappa Hari Krishna, Priya Kalra	THSTI, AIIMS	Indian Provisional Application

5	US application: 62/334636	11th May, 2016	Engineered recombinant protein antigen of trimeric mimic of HIV-1 envelope glycoprotein spike	Jayanta Bhattacharya, Rajesh Kumar, Vivek Kumar Yadav, Shilpa Patil	THSTI, IAVI	US Provisional Application
6	US application: 62/407,734	13 th October, 2016	Cleaved trimeric HIV Clade B ENV	Supratik Das and Bimal K Chakrabarti	THSTI, IAVI	US Provisional Application
7	US application: 62/407,729	13 th October, 2016	Stabilized Indian Clade C ENV	Shubbir Ahmed, TriptiShrivastava & Bimal k Chakrabarti	THSTI, IAVI	US Provisional Application

Technologies transferred/ commercialized (2016-17):

S. No.	Title of the Technologies	IP covered	Licensee (s)
1	Monoclonal Antibodies specific to Salmonella typhiflagellin, and use thereof	683/DEL/2015	Tritek Innovation Pvt. Ltd.
2	Production of recombinant Cytolethal Distending Toxin B protein and its uses as diagnostic tool thereof	1350/DEL/2015	Tritek Innovation Pvt. Ltd.
3	Mammalian cell lines for enhanced production of Japanese encephalitis virus, the method to produce and uses thereof	201611001550	Aptabharat Innovation Pvt. Ltd.

NATIONAL INSTITUTE OF PLANT GENOME RESEARCH (NIPGR), NEW DELHI

The National Institute of Plant Genome Research (NIPGR) was established with the objective of conducting and promoting research of high caliber basic and applied plant molecular biology and agricultural biotechnology to generate new knowledge with an aim to translate the same for genetic enhancement of crops for social benefit. The institute in a short span of about eighteen years has contributed to fundamental understanding of basic plant biology and made efforts that have far-reaching implications in the agricultural sector. The Institute through its infrastructural base for

academia-industry interactions and knowledge based resources, is poised to contribute towards frontier areas of Plant Biology. Advanced research is being conducted by the Institute in four major areas viz., computational biology, plant development and architecture, stress biology, and nutritional genomics. NIPGR scientists have been working on major cereals and legumes, besides several vegetables and oilseeds of economic importance. The institute looks forward to exemplify the growth by focusing not only on relevant basic biology research, but also on development of the technologies and products. NIPGR scientists have collaborated with several national and international institutions. Some of the developments at the Institute, for the period under report are as follows:

Given the importance of cereals as food, especially rice, various projects on enhanced stress tolerance, nutrient accumulation, reproductive development and seed viability were implemented. In one of the projects, NIPGR researchers have successfully elucidated the molecular mechanism behind submergence tolerance. The findings showed that MPK3, a MAP kinase, is activated during submergence in a SUB1A-dependent manner. Further, a comparative nuclear proteome analysis of rice against fungal blast was undertaken, which revealed diverse protein signatures involved in immunity. A separate study revealed that the rice PIMT (protein L-isoaspartylmethyltransferase) isoforms are differentially regulated during seed development and germination, and may play a distinct role for seed vigor and longevity. In foxtail millet, efforts have been made to understand the lignocellulose biosynthesis and gene families involved in cellulose, callose and monolignol biosynthesis.

Legumes contribute 27% of the world's primary crop production and thus the institute continues to augment research in legume biology. In chickpea, significant progress has been made in three major research areas: molecular mapping of important agronomic traits, enhancing seed viability and improving stress tolerance. Several genomic and transcriptomic resources have been developed for gene discovery and molecular mapping studies. Through a genome-wide strategy, natural SNP allelic variants have been identified in two potential candidate genes that govern seed weight and pod number, respectively. During the year, major QTLs of chickpea involved in resistance against *Ascochyta* blight disease have also been fine mapped. Further, proteomic analysis of dehydration-responsive secretome of chickpea led to the identification of several differentially regulated proteins, involved in a variety of cellular functions that include metabolism, cell defense and signal transduction.

Furthermore, overexpression of FvOXDC (oxalate decarboxylase) in grasspea and soybean led to the reduction of anti-nutrients with simultaneous increase in fungal tolerance (Figure).

Besides the major crops mentioned above, NIPGR scientists have also been working on several vegetables and oilseeds of economic importance. In vegetable research, major focus has been on three areas: dissecting immunity against fungus and virus, understanding thermotolerance, and delayed fruit ripening. Ongoing efforts revealed genes associated with defense against *Tomato leaf curl New Delhi virus*. Furthermore, proteometabolomics analyses of transgenic tomato expressing oxalate catabolizing enzyme impinge on defense mechanism against fungal pathogenesis. Suppression of two cell wall catabolizing enzymes viz., α -Man and α -Hex resulted in enhanced shelf life and firmness of tomato fruits. Detailed microarray analysis of ripening mutant unraveled key genes involved in maintaining cellular redox state and metabolism, which might improve storage life of tomato. In sweetpotato, overexpression of a seed albumin led to improved nutrient acquisition. Oilseed mustard is another crop of prime focus, wherein efforts are being made to selectively engineer glucosinolates biosynthesis and transport processes in tissue-specific manner to enhance the food and feed value. These altogether signify NIPGR's concerted efforts to improve the agronomic potential of such crops.

The year 2016 was highly productive and researchers were able to publish 102 articles in high impact journals/books. Seven national/international patents were granted/filed during the last academic year. The number of students enrolled in Ph.D. programme and the researchers involved in various projects showed substantial increase. The institute looks forward to exemplify the growth by focusing not only on relevant basic biology research, but also on development of technologies and products.

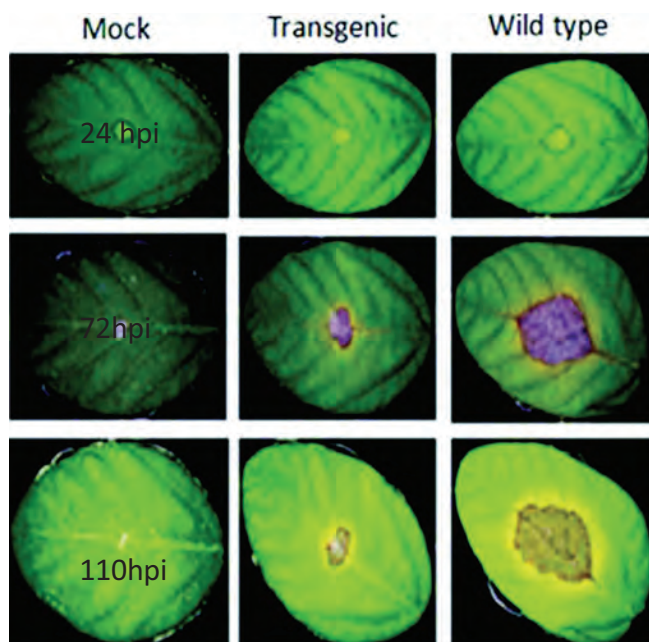


Figure: Transgenic soya bean plants showed an enhanced tolerance to *S. sclerotiorum* infection. Leaves of transgenic and wildtype plants of soya bean were inoculated with equal amount of mycelial suspension. Progression of the disease symptom was observed for 110 h post-inoculation (hpi).

Patent(s)

Chakraborty S, Chakraborty N, Datta A, Asraf N, Basu S, Nag P, and Singh M (2016) Polynucleotides derived from chickpea and uses thereof (APA No. 2010288112).

Chakraborty S, Chakraborty N, Datta A, Asraf N, Basu S, Nag P and Singh M (2015) Polynucleotides derived from chickpea and uses thereof (US Patent No. 9,163,255).

Chakraborty N, Chakraborty S, Datta A, Wardhan V and Jahan K (2015) Polynucleotide encoding CaTLP1 protein and uses thereof (US No.14/399,706).

Datta A, Chakraborty S, Chakraborty N, Ghosh S and Meli VS (2015) Polynucleotide sequence of fruit softening associated A-Mannosidase and its uses for enhancing fruit shelf life [European Patent N. 2315835 (09787597.5)].

Datta A, Chakraborty S, Chakraborty N, Ghosh S and Meli VS (2015) Polynucleotide sequence of fruit softening associated A-Mannosidase and its uses

for enhancing fruit shelf life (US Patent No. 8962918).

Datta A, Chakraborty S, Chakraborty N, Meli VS and Ghosh S (2015) Polynucleotide sequence of fruit softening associated B-D-N-acetylhexosaminidase and its uses for enhancing fruit shelf life (US Patent No. 8987556).

Datta A, Chakraborty S, Chakraborty N, Meli VS and Ghosh S (2015) Polynucleotide sequence of fruit softening associated B-D-N-acetylhexosaminidase and its uses for enhancing fruit shelf life (Japanese Patent No. 5836802).

Technology/Products/Database processed/developed

Developed low glucosinolate *B. juncea* lines having seed glucosinolate as low as 15 $\mu\text{moles g}^{-1}$ DW, through targeted silencing of *BjuMYB28* gene.

Developed *B. juncea* transgenic homozygous lines having significantly high amount of glucoraphanin (43.11 $\mu\text{moles g}^{-1}$ DW), a glucosinolate associated with anti-carcinogenic properties, by suppressing *GSL-ALK* gene family.

LCM-based protocol developed for tissue specific small RNA isolation and expression analysis.

RAJIV GANDHI CENTRE FOR BIOTECHNOLOGY (RGCB), THIRUVANANTHAPURAM

Rajiv Gandhi Centre for Biotechnology (RGCB) continued with significant success innovative research in cellular and molecular mechanisms of human, animal and plant diseases. The program is designed to make the institute a world-class research establishment in molecular and medical aspects of human, animal and plant disease biology integrating theory, modeling, simulation and experiential science encompassing disciplines such as biology, genetics, chemical biology, immunology and many other disciplines.

Mandate 1: Fundamental Research: Understanding the biology that defines basic mechanisms involved in the disease process and its implications for human health

Mandate 2: Translational Science: Trans-disciplinary health science to benefit individual, clinical, and public health decision making to improve health

Mandate 3: Technology Development: Turning research into technology innovation and on to business

Mandate 4: Training and Education: Developing and retaining a sustainable pipeline of biotechnology professionals across a range of related disciplines including fundamental science, technology development, translation, policy and outreach through efforts in education, training, and career development.

The salient achievements are as follows:

The HPV Vaccine Study: RGCB successfully implemented a multi-center clinical trial comparing two doses versus three doses of the human papillomavirus vaccine. Results from the two doses versus three doses of the human papillomavirus vaccine resulted in the recommendation to use 2 doses separated by 6 months or more for routine vaccination of young girls. [The Lancet Oncology. 1 December 2015, [http://dx.doi.org/10.1016/S1470-2045\(15\)00414-3](http://dx.doi.org/10.1016/S1470-2045(15)00414-3)]

The Curcumin Chemoprevention Trial: Oral cancer continues to be one of the most common malignancies in India. Combined clinical and histologic response assessment indicated a significantly better response with curcumin. The treatment did not raise any safety concerns. Treatment of oral leukoplakia with curcumin (3.6 g for six months) thus was well tolerated and demonstrated significant and durable clinical response. [Cancer Prevention Research June 7, 2016; DOI: 10.1158/1940-6207.CAPR-15-0390].

TM1-IR680 peptide for assessment of surgical margin and lymph node metastasis in orthotopic model of oral cancer: Treatment outcome after surgical removal in oral carcinoma is poor due to inadequate methodologies available for making surgical margins. The peptide identified by RGCB was tagged to NIR dyes for the identification of location and size of primary tumor and lymph node metastasis in a patient. The sensitivity of the detection is so high that lymph nodes that harbor dispersed tumor cells before colonization can be detected. [Scientific Reports. 2016 Nov 9;6:36726. doi: 10.1038/srep36726]

Histone chaperones in cellular transition during development: Development and diseased states are frequently associated with a change in phenotype of the cells. Histones chaperones form one of the core components of epigenetic regulation but their role was never addressed during different cellular transitions. For the first time, down-regulation of histone chaperone Aprataxin PNK-like factor (APLF) was reported to enhance both the kinetics and efficiency of the generation of induced pluripotent stem cells (iPSCs) from mouse embryonic fibroblasts. Another interesting facet of development is generation of multi-potent hematopoietic stem cells (HSCs) that arise during development and gradually colonize within liver, spleen, and finally bone marrow. It was also demonstrated that Histone chaperone HIRA interacted with RUNX1, incorporated H3.3 variants within enhancer elements, and regulated downstream targets of RUNX1 implicated in definitive hematopoiesis. This novel HIRA-RUNX1 axis might open up a novel approach in understanding leukemogenesis and could be exploited in deriving enriched engraftable quality of hematopoietic precursor in future. [J Cell Sci, 2016 (in press); J Biol Chem. 2015 May 22; 290(21): 13053-63]. (

Fostering & promoting collaboration and Joint Ventures between Academia, Industry and

Government: A National Facility for Drug Discovery and Developmental Therapeutics [NFDDDT] (Funded by the Department of Science & Technology):

The NFDDDT is a strategic and bold move by the Rajiv Gandhi Centre for Biotechnology (RGCB) to engage the future of drug discovery and therapeutic development. NFDDDT will also enrich existing academic programs at RGCB through education, advancement of cutting edge research, fostering inter-department and inter-institution collaborations particularly with the pharmaceutical and biotechnology industry and facilitate the creation of a global vision in drug discovery. Ultimately, the NFDDDT will help to develop and propagate intellectual property and scholarship, two of RGCB's most valuable assets. NDDFT at RGCB is set apart from other academic institutions and will allow our collaborating basic science and clinical researchers in oncology, infectious diseases, protein chemistry, computational biology and nanotechnology to develop novel therapies into Phase 1, which is the optimal point of entry for strategic commercial partnership.

INSTITUTE OF BIORESOURCES & SUSTAINABLE DEVELOPMENT (IBSD), IMPHAL

IBSD continued its efforts towards bio-resources development and their sustainable use through biotechnological interventions for the socio-economic growth of the North East Region. During the year, IBSD has published more than 28 research publications in peer-review scientific journals.

Scientific Achievements:

In the Plant Resources Programme, the work on germplasm management, characterization and product development of black rice has been undertaken. Currently, 76 species of ginger have been collected and 200 species of orchid have been catalogued. The research on conservation of Seroi

Lily and Dzuko Lily has been initiated.

Extensive R&D activities have been undertaken on some unique medicinal plants of NE for metabolite and genome analysis for identification of bioactive molecules. Studies have been undertaken on *Aconitum*, *Parkia*, *Illicium* and *Berberis*. An extensive cross culture ethno-pharmacological survey was carried out on Manipur Traditional Health Care Practices and Documented Traditional knowledge for 89 traditional practitioners.

In the Microbial Resources Programme, microbial repository has been established exclusively for collection, characterization, identification of economically important microorganisms for agricultural, industrial and therapeutic applications. Presently, 22,000 microorganisms from different agro-climatic habitat collected and deposited in repository. Algal repository having 1719 number of microalgae collected from NE region has been setup. Technology packages is underway after extensive R&D to develop selected fermented food unique to the NE region such as fermented bamboo shoots, fish, soya bean, milk (chhurpi).

In the Animal Resources Programme, work has been initiated on conservation of Sangai deer (Manipur's state animal). A major programme on bioenergy from waste has also been initiated during the year.

During the year, IBSD has initiated a Partnership Programme with leading institutions in the country in research, outreach, demonstration, training etc. in NE states. IBSD took major initiative on Entrepreneurship Development for unemployed youth by conducting training programme on Sustainable utilization of microbial and botanical products for promoting organic farming, fish hatchery & seed production technology and hands-on training program on rearing and post cocoon technology in composite sericulture and special programme on value addition and product development on bamboo. IBSD launched India's first ever Cherry Blossom Festival initiative in the state

of Meghalaya, Manipur and Mizoram, is expected to boost eco-tourism potential of the state and can contribute to state economy in a long run. IBSD also organized India's First Sakura Plantation Ceremony in association with Gifu Cherry Blossom Association, Japan at New Delhi. Further, IBSD signed a MoU with Nakdonggang National Institute of Biological Resources (NNIBR), Ministry of Environment, South Korea for joint research programmes. During the year, IBSD received four important awards, which include Global Sustainability Award 2016, ASEAN Sustainability Leadership Award 2016, 6th eNorth-East Award Summit 2016 and India Sustainability Leadership Award 2015 for the outstanding contribution in the field of Sustainable Development.

BIOTECH SCIENCE CLUSTERS

BIOTECH SCIENCE CLUSTER, KALYANI

The Biotech Science Cluster entitled 'Multi-dimensional Research to Enable Systems Medicine: Acceleration using a Cluster Approach' at Kalyani, West Bengal has been sanctioned for implementation in January 2016. The cluster partnering institutes are, (a) National Institute of Biomedical Genomics (NIMMG), (b) Tata Medical Center (TMC), (c) CSIR – Indian Institute of Chemical Biology (CSIR-IICB), (d) Bose Institute, (e) Indian Statistical Institute (ISI), and Indian Institute of Science Education and Research (IISER, Kolkata). The mandate of the cluster is (i) To investigate and understand the dynamic systems of the human body as part of an integrated whole, incorporating biochemical, physiological, and environmental interactions that sustain life, and identify perturbations that cause disease in order to implement Systems Medicine, (ii) Provide improved tools for prediction, prevention and treatment of diseases using Systems Biology approach, and (iii) Create a platform for multi-disciplinary training to build a cadre of scientific, clinical and technical personnel required to drive and sustain Systems Medicine.

NCR BIOTECH SCIENCE CLUSTER, FARIDABAD

The NCR- Biotech Science Cluster (NCR-BSC) at Faridabad has been established by the Department to promote common infrastructural resources for research, translation, innovation, validation, entrepreneurship and techno-business partnership between institutions within cluster and with other stakeholders in the city. The five autonomous entities i.e. NII, NIPGR, NBRC, THSTI and RCB, are presently part of the cluster and have entered into a joint MoU with DBT. The two major initiatives of the cluster are: (i) Establishment of Advanced Technology Platform Centre (ATPC) and (ii) A Bioincubator.

ATPC that would act as a catalyst for multidisciplinary basic and translational research by providing relevant instrumentation, training and professional services for the stakeholders and others alike on behalf of the Biotech Science Cluster in Faridabad is almost functional. This incubator is being established in partnership with BIRAC, would provide new and emerging companies with a compatible environment to support their start-up phase and increase their likelihood of success. In addition, the incubator will also facilitate prototype to product conversion for devices and implants.

BANGALORE LIFE SCIENCES CLUSTER FOR MULTISCALE BASIC AND APPLIED RESEARCH IN BIOLOGICAL SCIENCES (B-LIFE)

The Bangalore Biocluster was established in January, 2015 with the partnering institutes as Institute for Stem Cell Science and Regenerative Medicine (inStem) Bangalore; National Centre for Biological Sciences (NCBS), Bangalore; Centre for Cellular and Molecular Platforms (C-CAMP), Bangalore; and Institute of Bioinformatics and Applied Biotechnology (IBAB), Bangalore. Under this cluster, large data analysis work is being carried out on problems ranging from plant pathogen interactions to understanding neuronal circuits. A number of

courses in data science are being taught by the faculty of IBAB. In preparation for using the 300 keV electron cryo-microscope, data was collected in Leiden (microscopy facility) and MRC lab Cambridge on samples prepared in the Ramaswamy laboratory in Bangalore and was used to compute maps. The work was done in collaboration with Dr.VinothKumar at MRC, Cambridge, who is joining NCBS as a faculty member and Prof.Sowdhamini at NCBS. The current map of the protein PaaZ is shown below.

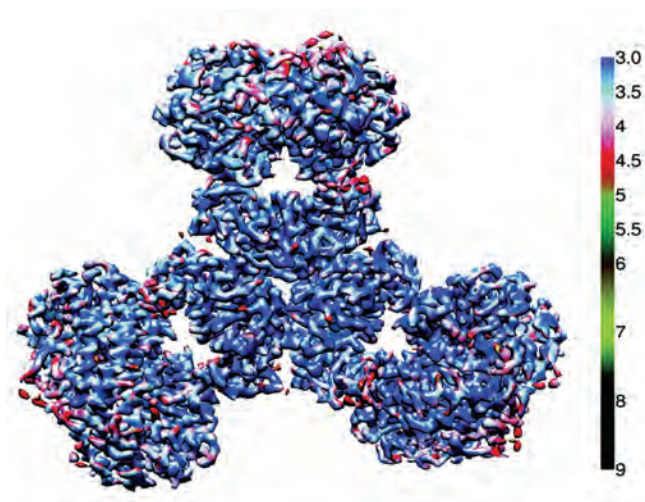


Figure 1: The structure of PaaZ, a bifunctional enzyme involved in phenyl acetic acid degradation. The inner triangle is a trimer of hydratase domain dimers and the outer three blobs are each dimer of aldehyde dehydrogenase. The colour bar on the right shows the resolution of the structure in Å units obtained from the electron cryo-microscopy data collected on a Titan Cryos.



11

PUBLIC SECTOR UNDERTAKING

BHARAT IMMUNOLOGICALS AND BIOLOGICALS CORPORATION LIMITED (BIBCOL)

Bharat Immunologicals and Biologicals Corporation Limited (BIBCOL) is a Central Public Sector Unit (PSU), under the administrative control of the Department of Biotechnology (DBT), Ministry of Science & Technology, Govt. of India. BIBCOL is a leading biotechnology company based in Bulandshahr, Uttar Pradesh. BIBCOL was established in 1989 with the novel theme to achieve polio free India. It started its commercial production of oral polio vaccine in 1996 and since then has supplied billion of doses of oral polio vaccine to Ministry of Health & Family Welfare for its polio eradication program. BIBCOL has played an important role in eliminating polio from our country. The World Health Organization (WHO) has declared our country a polio free nation. Company has very ambitious plans for its long term sustainability and growth.

Major initiatives: BIBCOL started its journey with single product i.e oral polio vaccine but gradually added more products and now produces Diarrhoea Management Kit, Zinc Dispersible Tablet and bivalent oral polio vaccine. BIBCOL has developed a ready -to-use therapeutic food (RUTF) with the name “BIB POSHAN” for the severely malnourished children. BIBCOL is gearing up for its licensing from FSSAI. Under diversification plan of the company for its long term sustainability and growth, one major project has been identified i.e. Plasma Derived Medicines (PDMs). RUTF and plasma

derived medicines as albumin, immunoglobulins and factors have huge market potential.

BIBCOL is producing and supplying huge quantities of oral polio vaccine to Ministry of Health and Family Welfare, GOI. In the year 2016 – 17, BIBCOL has supplied 206.25 million doses of bivalent oral polio vaccine and 221001 zinc dispersible tablets. Thus by producing and supplying the oral polio vaccine to GOI, BIBCOL is contributing significantly in keeping our country free from polio. BIBCOL supplied more than 241 million doses of trivalent and bivalent oral polio vaccine to GOI in the year 2015 – 2016 and 146006 zinc dispersible tablets.

Financial Status:

S. No.	Year	Turnover (Rs. crores)	Profit before tax (Rs. crores)
1	2011-12	47.24	5.96
2	2012-13	172.80	6.87
3	2013-14	202.75	11.0
4	2014-15	146.22	2.01
5	2015-16	128.03	(7.07)
6	2016-17) (Estimated	124.00	8.08

For the severely malnourished children in India where majority of the world’s malnourished children live, BIBCOL developed a formulation with technical inputs from CTI, United States of America. The ready to use therapeutic food (RUTF), named as “BIBPOSHAN” has been produced and stability

studies have been conducted and currently under licensing process. Once the license is obtained, commercial production and supply will start to central and state governments at very low prices so that it can be consumed by severely malnourished children and the lives of thousands of such children can be saved.

The plasma derived medicines which are lifesaving drugs, are available in lesser quantities with very high prices as they are imported. They are out of reach of a common man. To make them available at affordable prices, BIBCOL is planning to manufacture these products in the premises.



Vaccine Vials



INDIAN VACCINES CORPORATION LIMITED (IVCOL):

Indian Vaccines Corporation Limited was incorporated in March 1989 as a Joint Venture Company promoted by Govt. of India (Dept. of Biotechnology-DBT,) Pasteur Merieux Serum & Vaccines (PMSV) France and Indian Petrochemicals Corporation. Ltd. (IPCL- a PSU) with a paid up capital of Rs. 18.78 crores, for manufacturing of vaccines

based on Vero cell Technology to be supplied by PMSV France. The company came into inception after a joint venture was signed on 1st February 1989.

The main objective of the company was to manufacture Injectable Polio Vaccines (IPV) to be incorporated in the mass immunization programme of Govt. of India. However, IPV was not approved by W.H.O as a result the project was put on "HOLD" in February 1992. Thereafter P.M.S.V. got disinterested in the project and expressed its desire to exit from the Venture. PMSV exited from the J.V. in 1998 by selling its shares to DBT. In the year 1999, Govt. of India decided to set up National Brain Research Centre (NBRC) (An Autonomous Body) and 38.78 acres of land was leased out to them on thirty years lease, at a nominal lease rent of Rs.10 lacs per annum. This is the only income of the company at present. The company has no trading or commercial activity at present and is maintaining establishment to look after site and complying with the statutory obligations under the company's act 2013. IVCOL is presently being controlled by a board of Directors, with two Directors representing RIL and two Directors representing GOI (DBT),

Company has been incurring losses for the last two years (Rs.164.37lacs for 2014-15 and 208.22 lacs for 2015-16) and has accumulated losses for Rs.785.38 lacs as on 31.03.2016.

Share holding of IVCOL at present is as under.

Govt. of India (DBT)	66.67%
Reliance Industries Ltd	33.33%

BIOTECHNOLOGY INDUSTRY RESEARCH ASSISTANCE COUNCIL (BIRAC)

Biotechnology Industry Research Assistance Council (BIRAC) is a not-for-profit PSU under the aegis of Department of Biotechnology (DBT) and has the mandate of fostering and nurturing the Biotech Enterprises specially start-ups and SME's

for enhancing their innovation research capacities and promoting affordable product development. BIRAC supports Industry-Academia interaction, serve as a single window for the emerging biotech industry, helps establish connectivity with professional and institutional networks, and provides financial support for quality innovation targeted at affordable solutions and product development.

To serve various dimensions of its mandate, BIRAC operates mainly in 3 verticals viz.:

Investment: Providing risk capture across the Product Development value chain

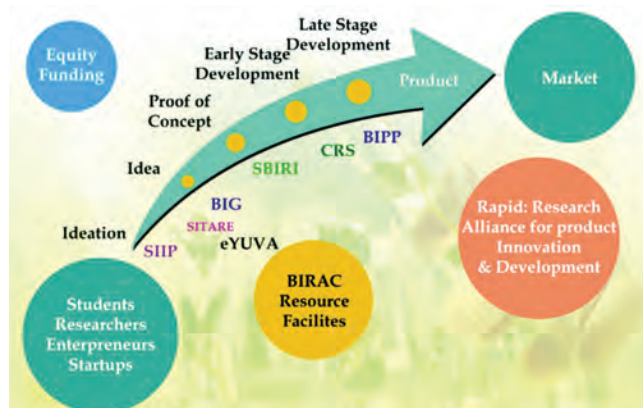
Entrepreneurship Development: Nurturing the ecosystem by providing the enabling environment

Strategic Partnership group: Leveraging and fostering global and national partnerships for meeting its mandate

Investment: BIRAC provides funding support to entrepreneurs, start-ups, SMEs and Biotech Companies for all stages of the product development value chain from discovery to proof of concept to early and late stage development to validation and scale up, right upto pre-commercialization. There are also special product development missions. The second vertical is Entrepreneurship Development which focuses not only on the funding support, but also on making available the right infrastructure, mentoring and other networks for technology transfer and licensing, IP and business mentoring including regulatory guidance. Lastly BIRAC's Strategic Partnership group works closely with all partners – national and international which includes Government departments and Ministries both Central and State, industry organizations, international bilateral agencies, philanthropic organizations and corporate sector, to leverage the strength and expertise and mobilize resources and extend the outreach of its activities.

Empowering, Enabling & Scaling the Indian Biotech Innovation Ecosystem for Affordable Product Development: BIRAC supports affordable product development by empowering and enabling Indian biotech innovation ecosystem. The funding schemes cover all aspects of the innovation pipeline.

Driving Product Development



Investment Schemes of BIRAC:

Biotechnology Ignition Grant (BIG): The focus of BIG is to support entrepreneurs and entrepreneurial individuals who would like to move their innovative ideas to a proof-of-concept stage. A total of 192 BIG projects have been supported- amongst which are 121 start-ups and 49 entrepreneurial individuals. The programme has also facilitated creation of 60 new biotech start-ups and has provided employment to close to 600 high skilled personnel. About 20 products are in the later stages of validation and at least 5-6 products will enter the market in 2017-18. More than 40 BIG grantees have secured follow-on funding from public and private agencies amounting to INR76 crores.

Small Business Innovation Research Initiative (SBIRI): SBIRI scheme was conceptualized to prioritize early stage funding for high risk innovative research. The projects with high societal relevance supported under the scheme have resulted in prominent outcomes in the form of products which have been commercialized. A total of 210 projects

have been supported until now through this scheme.

Biotechnology Industry Partnership Programme (BIPP): BIPP is an advanced technology scheme which supports high risk, high innovation accelerated technology development and operates on a cost sharing basis with the industry and encourages collaborations and partnerships, between industry-academia and industry– industry. Ever since its inception, BIPP has made a tremendous impact and has supported more than 166 projects involving 138 companies and 47 academic institutes.

Contract Research Scheme (CRS): The scheme focuses on enabling validation of academia research that has commercialization potential and to engage the contract research and manufacturing (CRAMS) industry to carry out the validation of a process or a prototype. Since the launch of the scheme in April 2012, 10 calls for proposals have been launched under which 21 projects have been supported.

BIRAC’s Impact so far: Since its inception BIRAC has created an ecosystem which supports affordable product development by empowering and enabling Indian biotech companies. Through its various funding schemes BIRAC is able to create the following impact:



Looking back at 2016-17, BIRAC has supported 322

projects in all areas of biotechnology from innovations that aim to derive value out of silk industries, protect shrimp farming through disease detection, to vaccines, drug delivery systems, medical technologies and agricultural innovations. 67 new projects were supported from April 16 to Jan 17 which has led to the development and commercialisation of 9 new products/technologies and generation of 15 IPs.



Some of the products/technologies developed in 2016-17

Fostering Innovation by Promoting Entrepreneurship Development: In order to foster innovation BIRAC has taken several initiatives to promote entrepreneurship and has achieved considerable success. BIRAC has a strong belief that the “*bio-innovation capital*” of the nation would come from novel ideas which have a commercialization potential and that evolve out from start-ups or academic spin-offs.

BIRAC BioNEST (BIRAC–Bio-incubation: Nurturing Entrepreneurs for Scaling up Technology): The BioNEST programme of BIRAC has helped to create and support 20 bio-incubators across the country with creation of 200000 sq. ft. of incubation space and funding commitment of INR 150 crores. Till date, about 200 start-ups have been supported from BIRAC incubators.

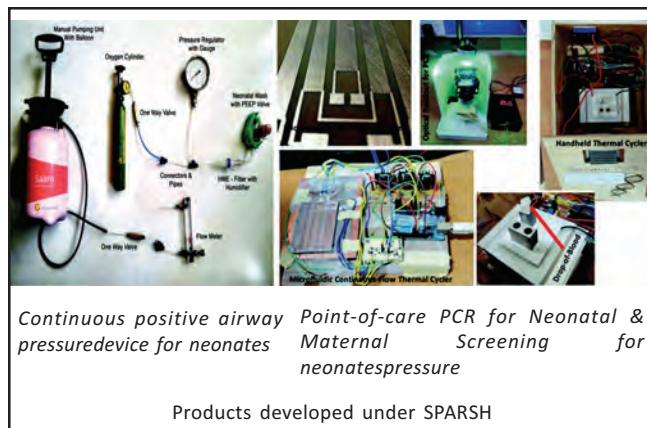
SITARE (Students Innovations for Advancement of Research Explorations): BIRAC has collaborated with Society for Research and Initiatives for Sustainable Technologies and Institutions (SRISTI) to support grass-root level innovations. Two categories of Awards – BIRAC-SRISTI GYTI Awards and BIRAC-SRISTI GYTI Appreciation Awards – have been constituted to support and mentor the young innovators working at universities and schools. The awards are aimed at nurturing the grass-root innovations to make them ready for next level of funding to take the innovation to a PoC stage. In 2016-17, 19 innovators have been awarded the BIRAC-SRISTI GYTI Awards.

e-YUVA (Encouraging Youth for Undertaking Innovative Research through Vibrant Acceleration): BIRAC initiated the University Innovation Cluster (UIC) programme with the aim of promoting innovation research & development in Indian academia. The programme was launched in 2013 and 5 universities were chosen to develop an innovation cluster as well as support innovation research through postdoctoral and post-masters fellows who receive fellowships as well as grant to conduct their R&D. Currently 15 fellows are pursuing

translational R&D under UIC programme.

Social Innovation programme for Products Affordable & Relevant to Societal Health (SPARSH): SPARSH is the social innovation program of BIRAC that highlights the need of Innovative solutions to society’s most pressing social problems. First two calls of SPARSH are aligned with the UN Millennium Development Goal 4 and 5 i.e., reducing Child mortality and Improving Maternal Health. SPARSH third call was on “Waste to Value” and is in line with the Millennium Development Goal (MDG) 7. The focus of SPARSH third call also reflects the mandate of Swatch Bharat mission.

The Social Innovation Immersion Program (SIIP) of SPARSH till date has supported 14 social innovators who are trying to develop solutions for most pressing problems in the field of Maternal and Child Health (MCH).



BIRAC SEED Fund: In 2016, BIRAC launched an equity fund scheme (BIRAC SEED Fund) which will support Incubators by providing them with capital which can be further invested in biotech start-ups as equity thus helping start-ups to grow. BIRAC operationalized the SEED Fund in 2016-17.

Mentorship and Capacity Building:

BIRAC Regional Innovation Centre (BRIC) at IKP Knowledge Park, Hyderabad: BIRAC Regional Innovation Centre (BRIC) at IKP Knowledge Park, Hyderabad has conducted an extensive regional innovation system (RIS) mapping in South India

where more than 70% of biotechnology firms are located which was published and released as a report in Oct 2016 at IKMC Hyderabad. The report aims to understand the current status of the innovation ecosystem in four clusters in southern India and focuses on the academic research capabilities in pharma, bio-pharma, medical technology and healthcare.

BIRAC Regional Entrepreneurship Centre (BREC) at C-CAMP: BIRAC has launched BIRAC Regional Entrepreneurship Centre (BREC) at CCAMP, Bangalore. BREC aims to impart bio-entrepreneurs with the necessary knowledge and skills required for converting innovative ideas into successful ventures. Through its various programmes to be conducted over a period of 3 years BREC targets to train around 200 researchers and 300 entrepreneurs. In addition 150-200 start ups shall be connected with early stage investors.

Ignite Boot Camp: In the year 2016, BIRAC along with its Biotechnology Ignition Grant partners selected 4th batch of five candidates to attend the intensive programme at Cambridge to explore their innovative ideas towards business plans.

Roadshows and IP Management Workshops: BIRAC organized a series of workshops on Grant writing, Bio-Entrepreneurship and IP Management at Goa, Jammu, Chennai, Varanasi and Delhi in 2016 to enhance outreach.

Supporting Ecosystem:

Make in India Facilitation Cell: 'Make in India' initiative was launched on September 25, 2014 by the Government of India with an aim to give Indian economy global recognition. The programme includes major new initiatives designed to facilitate investment, foster innovation, protect intellectual property, and build best-in-class manufacturing infrastructure. DBT has established the Make in India Facilitation Cell in BIRAC. The cell regularly interfaces with DIPP and other Ministries to provide information and update on DBT's and BIRAC's plans

for boosting Make in India as well as the Startup India programme.

In 2016-17, the cell initiated a high level report on the Make in India opportunities and identified several areas for support in high value manufacturing. The report was released by Hon. Minister for S&T and Hon. State Minister for S&T in the 5th Innovator Meet in September 2016.

Startup India Action Plan: BIRAC has an integral role in the Startup India initiative of the Government. Under the purview of Startup India Action Plan, BIRAC endeavours to (i) scale up the number of Startups in the sector by nurturing approximately 300-500 new Startups each year to have around 2,000 Startups by 2020 (ii) Setup 50 Bio-Incubators and 150 technology transfer offices across India (iii) Launch a Biotech Equity Fund – BIRAC AcE Fund which will provide financial assistance to young entrepreneurs and start-ups and (iv) Establish 5 Regional centres of BIRAC in the next 5 years. (2 Regional Centres are operational)

Service Tax Exemption (Budget 2016-17): To promote and support the Biotech ecosystem BIRAC has rolled out major initiative in the form of service tax exemption on services provided by BIRAC approved biotechnology incubators to incubatees from 1.4.2016

Swachh Bharat:

Waste to Energy Mission Program: BIRAC has initiated a mission program for conversion of Municipal Solid Waste (MSW) to energy. Expression of interest document for mixed waste and modalities of funding are being finalized. Stakeholder meetings have been held and priority areas have been identified.

Bio-toilets in Schools in North East India: An initiative to address the problem of sanitation in India and for the development of safe and affordable sanitation was laid down when DBT/ BIRAC partnered with Bill and Melinda Gates

Foundation in announcing the Reinvent the Toilet Challenge-India. BIRAC has already supported 6 projects under the RTTC –India initiative.



Next Generation Toilets

Building Strategic Alliances for Affordable Product Development: BIRAC has always emphasized on building collaborative frameworks for fostering and nurturing the Indian Innovation ecosystem.

National and International Alliances:

Grand Challenges India: DBT-BIRAC GATES Foundation: The Program Management Unit housed at BIRAC (PMU-BIRAC), was created and co-funded in collaboration by DBT and BMGF to jointly administer the Grand Challenges India framework. PMU-BIRAC works closely with strategic partners to identify and support scientific and technological opportunities with clearly articulated governance and implementation principles. The unit is also supported by USAID & Wellcome Trust. The following niche areas were supported: (i) Achieving healthy growth through agriculture & nutrition (AGN) (ii) All Children Thriving (ACT), (iii) Grand Challenges Explorations – India (GCE-India) (iv) Knowledge Integration and Translational Platform (KnIT) and (v) Healthy Birth, Growth and Development Knowledge Integration (HBGDki - India)

DeitY-BIRAC Industry Innovation Program on Medical Electronics (IIPME): IIPME is a collaborative scheme between DeitY (Department of Electronics and Information technology) and

BIRAC. The project goal is to fund a portfolio of Indian Led pilot Projects targeting innovations in the multi-disciplinary areas comprising of electronics, engineering, medical devices, healthcare, software, algorithms and information technology. Projects were funded in areas such as imaging and navigation, technologies for chronic diseases, convergence of medical device and bioinformatics and increasing the outreach through medical electronics.

Indo-French Centre for the Promotion of Advanced Research (CEFIPRA): BIRAC has joined hands with CEFIPRA to support high quality bilateral research, encourage and enable Indo-French collaboration between public, private research groups, industry, clinicians and end-users. Under this initiative, BIRAC has implemented two partnership programs with French continent. One in the area of molecular diagnostics for cardiovascular diseases and the second one in the area of Molecular diagnostics for prediction of Alzheimer's & other dementia, New assisting technologies for mobility of physically challenged (incl. prosthesis and robotics applications) and Biomaterials and cell engineering for health applications.

Wellcome Trust, UK: BIRAC has collaborated with Wellcome Trust, a global charity organization of UK, to scout and support innovations in translational medicine in the domain of diagnostics for infectious diseases..

USAID and IKP Knowledge Park: BIRAC is supporting new diagnostics for TB in collaboration with IKP/ USAID. IKP has entered into an agreement with USAID and secured a grant to support 'Innovations in tuberculosis (TB) control in India' at a 1:1 leverage with funds raised by IKP from other sources.

New Partnerships: During the year 2016 BIRAC continued its efforts for establishing partnerships with like-minded organizations and culminated seven such collaborations:

BIRAC–WISH Foundation: BIRAC collaborated with WISH to scale up the innovations supported by

BIRAC. Through this partnership BIRAC aims to commercialize the innovations supported by its programmes, by leveraging the networks and established SCALE programme of WISH, which aims to scale up the innovations in primary healthcare sector through the route of State Governments.

BIRAC-UK Trade and Investment (UKTI): BIRAC partnered with UKTI to enable BIRAC supported innovators to access the UK and other European markets through the online portal of the UKTI. The partnership intends to enhance the networking opportunities and market access for the BIRAC supported innovators.

BIRAC-Horticulture Innovation Australia (HIA): For promoting sustainable Horticulture, BIRAC and HIA have collaborated for a joint funding programme for supporting innovative technologies and solutions for sustainable and productive horticulture at global level. The funding commitment from BIRAC and Hort Innovation is up to AUD 6 Million for over a period of 3 years.

BIRAC-Nesta: BIRAC and Nesta, a charity organization in UK, have initiated the collaborative measures to populate the innovators' pipeline for competing in the coveted Longitude Prize-a-challenge programme having a prize fund of 10 million pound, to help solve the problem of global antibiotic resistance. BIRAC has committed an amount of £100,000 for the Discovery Awards to support the teams working in the AMR domain and this could eventually lead to their participation in the Longitude Prize.

BIRAC-Tekes: BIRAC has signed a letter of intent with Tekes- Finnish Funding Agency for Innovation, to explore opportunities for improving competitiveness of Indian and Finnish industries through promoting collaboration in different phases of knowledge innovation chain.

BIRAC-TISS: BIRAC and Tata Institute of Social Sciences (TISS) have come together to mentor the social innovators supported by BIRAC, so as to help them evolve in the social entrepreneurship arena.

TiE: BIRAC and TiE-Delhi NCR has partnered to create platforms to showcase startups and connect them with other companies and relevant organisations, and opportunities to explore markets and facilitate a focused interaction with venture funds.

Industry – Academic Interaction

4th Foundation Day of BIRAC: BIRAC celebrated its 4th Foundation day at India Habitat Centre, New Delhi on 20th -21st March 2016. The occasion was celebrated with great enthusiasm by the BIRAC community along with dignitaries representing the Government, academia, industry, start-ups and budding entrepreneurs. The theme of the event was Scaling Bio-Entrepreneurship: Foundation for Sustainable Future.

BIRAC's 5th Innovators Meet was organized on 22-23 September 2016 at New Delhi. The event witnessed the confluence of around 300 Scientists, Entrepreneurs, Industry Experts and Policy-makers. Theme of the meet was "Biotechnology Innovation Ecosystem: Strategizing for the Next Leap". The Hon'ble Union Minister of Science & Technology & Earth Sciences, Dr Harsh Vardhan was the Chief Guest and Hon'ble Minister of State for Science & Technology & Earth Sciences, Shri Y.S. Chowdary was the Guest of Honour for the 5th Innovators Meet. Mr. Yigal Erlich, Founder, TheYozma Group, Israel delivered the keynote address. The inaugural session included the announcement of the prestigious BIRAC Innovator Awards. For the first time Innovation Market Place was created where 23 Innovators showcased their technologies/ prototype to investors and audiences.

2nd BIG Conclave: BIRAC along with its BIG partner C-CAMP organized the 2nd BIG Conclave in June 2016 which was attended by 120 BIG grantees along with experts from industry, venture funding and academia. Over the two days, BIG entrepreneurs presented their journeys, interacted with important stakeholders and explored collaborative opportunities.



12

INTERNATIONAL CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY (ICGEB)

The International Centre for Genetic Engineering and Biotechnology (ICGEB) conducts innovative research in life sciences for the benefit of developing countries. ICGEB has operated as an independent organization with a current network of 64 member states, 86 signatory states and 42 affiliated centers those extensively cooperate on themes of common interests with Directorate in Trieste, Italy, and three components in New Delhi, India, Trieste Italy and Cape Town, South Africa.

The Centre has acquired an excellent reputation in research, both in basic and translational sciences. The research at the New Delhi component can be broadly categorized in three areas viz. integrative biology, molecular medicine and plant biology. Integrative Biology focuses towards structural biology approaches to understand host-pathogen interaction associated with infection and immunity using x-ray diffraction, NMR and bioinformatics techniques and to develop technology for production of biofuels from agricultural wastes and algae. Molecular Medicine projects are pursued in Malaria (basic biology of malaria parasite and drug and vaccine development for Malaria), Dengue & Chikungunya (Development of sub-unit Dengue vaccine and to study pathogenesis of Dengue and Chikungunya), Tuberculosis (the biology of host-pathogen interaction during infection by *Mycobacterium tuberculosis* and biomarkers) and development of diagnostics kits. Plant Biology research addresses abiotic and biotic plant stresses and crop improvement through biotransformation.

Research Initiatives and Significant Achievements:

Integrative Biology: The major focus of the Bioenergy research is on Enzyme research, C5/C6 fermentation and Algal Biofuels. Projects are being implemented towards expression, biochemical characterization and engineering for improved activity of the cellulolytic enzymes from fungi and gut symbionts and engineering microbes for C5 fermentation into ethanol, microbial engineering for butanol and 2, 3 butanediol and alkane production using Indian cyanobacterial isolates. Efforts are made to engineer Microalgae for enhanced lipid production. As an important development, in the field of yeast metabolic engineering and recombinant protein production, a thermo tolerant yeast strains capable of fermenting ethanol has also been isolated.

Research on Omics of algae focuses on understanding biological systems through integrated omics to engineered cell factories. The marine microalgae *Parachlorella kessleri* has been sequenced and annotated. The genome scale metabolic model of prokaryotes has been successfully reconstructed and efforts are being made to analyze metabolism under different conditions to identify best gene target for overproduction of desired product and predict the effect of gene modulations.

The structures of several RNA binding proteins have been determined which leads to successfully address mechanisms of transcriptional regulation.

Under another important study, the NMR based metabolomics of human biofluids such as urine; saliva and plasma are being used as diagnostic tool for HIV and ART Patients. The core research focus on Translational Bioinformatics area is towards development of tool and data bases, artificial intelligence, computer aided drug design, comparative genomics and Proteomics in *P. falciparum*. Understanding the physiological processes of self-non self discrimination has been a major focus of the Structural Immunology Group. This Group has extensively investigated the structural principles of antibody pluripotency and addressed structural proteomics of food allergens.

Molecular Medicine: Along with the efforts on dengue infection, the emphasis is also given to the research on Chikungunya, the other prevalent viral disease in the country. The studies are being carried out to understand viral evolution in India, molecular signatures and basis of CHIKV virulence. Work to understand the clinical aspects and metabolic changes during CHIKV dengue co-infection is also being conducted.

The focus of the research in Malaria field is in three major areas viz; malaria drug development, malaria vaccine development and to understand host – pathogen interaction. As an advanced development in the field of malaria drug development, *Plasmodium* ClpQ protease machinery, specific inhibitors for falcipain-2 enzyme and ODCase enzymes, H₂ formation complex, Falcipain-2 and Mitochondrial and apicoplast proteases have been identified, as novel drug targets. Efforts are also being made towards development of malaria drugs through natural sources such as marine organisms, medicinal plants, fungi and cyanobacteria. A sponge derived antimalarial molecule has been isolated, identified and chemically synthesized. Realizing that in India both *P. falciparum* and *P. vivax* are equally prevalent, the Centre is focusing on development of vaccines for both these malaria parasites that infect humans. Two candidates for *P. falciparum* and

one candidate for *P. vivax* have been taken up for product and clinical development.

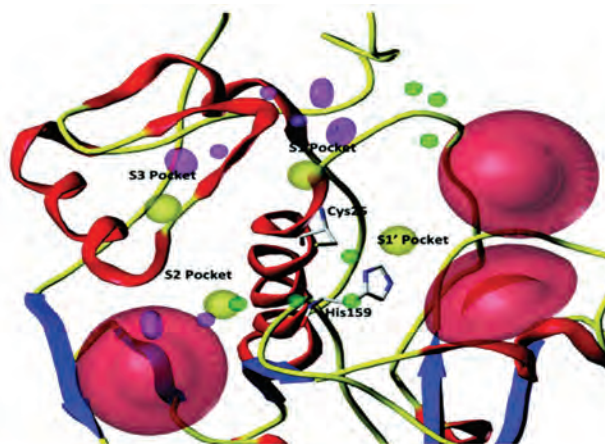


Fig. 1 : Falcipain-2/HDP inhibitor(s) as novel antimalarial

Core focus of Tuberculosis research is to study macrophage response to *Mycobacterium tuberculosis* infection. Studies are also being conducted to understand phagocytosis in macrophages, gene regulatory networks and transcriptome analysis to decipher host responses to Mtb infections. Further, research is being carried out to develop non-invasive diagnostic methods for tuberculosis using urine and breath samples. Gender and location specific volatile profile are also being identified.

Plant Biology: The focus of Plant Biology domain is on stress and crop improvement. The major projects of plant group are generation of transgenic rice plants with double herbicide tolerance. The Group has successfully edited Rice EPSPS and ALS genes with CRISPR/Cas9 to develop double herbicide tolerance. Research on for generation of salinity and drought stress tolerant rice through Glyoxalase Pathway engineering and enhancing the stress tolerance limits by gene pyramiding for sustainable productivity. The first project in this area is currently under field trials with an Indian seed company. Under the gene pyramiding study, it is shown that triple (Gly+GlyII+NHX) transgenic rice plants exhibit better grain yield as compared to double (GlyI+GlyII) or single (NHX1) transgenic lines

and WT plants under salinity stress conditions. The role of miRNA in controlling grain formation and enhancing virus resistance and high temperature tolerance has been elucidated. The stress regulated Novel miRNA has been identified and a database for rice miRNAs in the context of an Indian cultivar has been established.



Figure: Triple (Gly+GlyII+NHX) transgenic rice plants show better GRAIN YIELD as compared to double (GlyI+GlyII) or single (NHX1) transgenic lines and WT plants under salinity stress conditions

Trans-Institutional Partnerships: The futuristic project for ICGEB, New Delhi is to encourage building trans-institutional partnerships. The Centre is planning to establish a consortium involving neighboring Institutes such as NII, JNU to develop novel drug targets for malaria. In addition, collaboration is being developed with a Group at University of Hyderabad who has established a mosquitarium and liver cycle of mouse malaria parasite; *P. berghei* to understand the role of many *Plasmodium* proteins at sexual and extra erythrocytic stages. Efforts are in progress to establish collaborations with Regional Centre for Biotechnology (RCB, Faridabad), Jawaharlal Nehru University (JNU, New Delhi), National Institute of Plant Genome Research (NIPGR, New Delhi), Indian Agriculture Research Institute (IARI, New Delhi) and International Rice Research Institute (IRRI, Philippines) in plant science area.

List of Patents

S. No.	Patent No.	Title	Inventor	Date of filing	Status
1.	361/DEL/2015 PCT/IN2016/050051	Over-expression of a rice-specific miRNA, MiR820 leads to plant and panicle vigour	PMB Neeti Sanan Mishra Neha Sharma	10.02.15	Indian patent PENDING PCT Pending
2.	1714/DEL/2015 PCT/IN2016/050225	A method for obtaining a composition for biomass hydrolysis	SBB Syed Shams Yazdani Ogunmolu Funso Emmanuel	09.06.15	Indian patent PENDING PCT Pending
3.	201611008172	Depeptide leucine-á-â dehydrophenylalanine based hydrogel	MAL V. S. Chauhan Nitin Yadav Thota Chaitanya Kumar	09.03.16	Indian patent PENDING
4.	201611022234	A synergistic composition and process for preparation thereof	IR Sujatha Sunil Jaspreet Jain Vimal Narayanan	29.06.16	Indian patent PENDING



13

PROMOTION OF BIOTECHNOLOGY IN NORTH EASTERN STATES OF INDIA

NER-BPMC: Promoting Biotechnology-based Development in NER

The North East Region (NER), of India is a treasure house of exceptional natural beauty, floral and faunal biodiversity and abundant mineral, water and forest resources. It has been identified as one of the biodiversity hotspots of the world. Rich bio-resources spread across NER's diverse ecosystems and nurtured by indigenous communities, provide ample opportunities for furthering economic development of the region. However, NER has remained arguably the most backward region of the country, prompting the Government of India to make unprecedented commitment to allocate 10% of its total budget for the development of NER. Accordingly, the Department of Biotechnology has earmarked 10% of its total annual budget towards biotechnology-backed development activities in the North Eastern Region of India. Towards this commitment, DBT established the North Eastern Region-Biotechnology Programme Management Cell (NER-BPMC) in 2009-10, functioning through Biotech Consortium India Limited (BCIL), for implementation and monitoring of biotechnology programmes in the NER.

A NER-BPMC of DBT is helping to evolve and implement various new programmes in the area of biotechnology for the benefit of NER states. The Twinning R&D programme has made a huge impact in NE states for implementing hard core biotechnology in association with rest of India institutions. So far more than 450 twinning projects have been implemented as collaborative projects

between North East institutions and the rest of India Institutions. To create an environment of training and research in Medical Biotechnology, the department provided support to 11 medical colleges in NER. 126 Biotech Hubs have been established at various institutions, universities & colleges to promote education, training & research in biological sciences including biotechnology. 18 institutions of NER are part of DBT e-Library consortium (DeLCON) which provides access to more than 900 high impact peer reviewed e-journals. Biotech infrastructural facilities have been created at NRC Yak; NRC Mithun and NEIGRIHMS. 15 colleges have been recognized so far as Star Colleges in NER. 170 Scientists from NER were supported through a special scheme of DBT's Overseas Associateship and more than 150 scientists have already availed this fellowships. Through yet another program of similar nature, 11 Scientists were provided National Associateship for advanced training at leading institutions in India. 88 Senior Secondary Schools from NER have been selected for setting up of Biotechnology Labs under "Biotechnology Labs in Senior Secondary schools (BLISS)" Scheme. During this year, 30 Scientists/Faculty have been selected for bringing advancement in the Biotechnology and Life Science related activities in various institutions of research and higher learning in the NER under "DBT-NER Visiting Research Professorship (VRP) Scheme".

A Centre of Excellence in Agriculture Biotechnology named DBT-AAU Centre for Agri Biotech and another on Fisheries & Aquaculture Biotechnology (FAB) has been supported to Assam Agricultural University, Jorhat and College of Fisheries, CAU, Tripura

respectively. A regional level Animal House facility is being established at RMRC, Dibrugarh (Assam), which will be accessible to entire biomedical research community of NER for carrying out critical animal experiments in disease biology, molecular medicine, vaccinology and pharmacology.

The NER of India, owing to its unique geographical location sharing five international borders, bears constant threat of exotic trans-boundary diseases of our valuable livestock. To address this issue a programme on “Advance Animal Disease Diagnostic & Management Consortium (ADMaC)” has been initiated by involving NIVEDI, Bangalore; NRC on Equines, Hissar; NIHSAD, Bhopal and institutions from NER. This programme is aimed at strengthening regional infrastructure and capabilities for developing latest diagnostics and organizing rigorous surveillance for the highly contagious and ravaging diseases so that forecasting model on disease outbreaks in the region can be developed for a formidable defense to guard the territories.

A major collaborative research programme on Chemical Ecology of North Eastern Region has been initiated involving scientists from reputed national institutions (National Centre for Biological Sciences (NCBS), Indian Institute of Science (IISc), University of Agricultural Sciences) and NER institutions.

In the healthcare/ medical biotechnology sector, in order to enhance the quality of patient care and diagnostic services, DBT program on Development of Infrastructure in Medical Colleges in the NER was initiated in the year 2009. The program is now operational in 11 medical colleges/ institutions in four states of the Region, namely Assam, Nagaland, Tripura and Manipur.



Labs of 21 Principal Investigators have been renovated/upgraded for providing quality diagnostic services as well as for carrying out research on various health problems prevalent in the region using modern biotechnology tools and technologies. High end equipment including flow cytometer, Real-Time PCR machine, Hi-speed centrifuges, Deep freezers etc. installed. An impressive six-storey DBT Healthcare Laboratory established at the Naga Health Authority-Kohima (NHAK) is the first of its kind facility in Nagaland, bringing efficient diagnostic services to the door step of patients in the state.

A “Comprehensive Facility for Diagnosis and Management of Genetic Disorders” has been established at the Assam Medical College & Hospital, Dibrugarh (Assam), facilitating studies in Biochemical Genetics, Molecular Genetics & Cytogenetics, as well as providing genetic counseling services to the families at risk. This facility continues to provide timely and accurate diagnosis of genetic diseases due to chromosomal aberrations, single gene mutations, haemoglobinopathies, etc. The facility is fast emerging as a nucleus for the emergence of a centre of excellence for quality education and research in Medical Genetics in NER.

A “Molecular Diagnostic Laboratory” has been established at the Mizoram State Cancer Institute, Aizawl (Mizoram). Recognizing that accurate and

precise diagnosis is the cornerstone of any successful cancer treatment, DBT has established this molecular laboratory which is contributing to not only enhancing the quality of comprehensive cancer care but also to quality research in understanding the factors underlying high incidence of cancer in the State. The initial focus of the research project is on three cancer types commonly encountered in Mizoram: 1. Chronic myeloid leukemia (BCR-ABL translocation); 2. Breast cancer (HER2/neu), and 3. Lung cancer (EGFR).



DBT has provided crucial support for establishing sophisticated infrastructure for improved diagnostic services in pathology, hematology and genetics departments at the North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences (NEIGRIHMS), Shillong (Meghalaya). The support is expected to significantly improve the efficiency of the diagnostic services of the institute, and help generate credible statistics about various diseases as well. These facilities will specifically help in establishing viral etiology of nasopharyngeal carcinoma (EBV), and oral squamous cell carcinoma (HPV); in unraveling pattern of neoplastic renal diseases and hematolymphoid neoplasma, and in molecular typing of minor blood group antigens in NER.



Under the Agri-Biotechnology section, a Centre of Excellence (COE) named “DBT-AAU Centre for Agriculture Biotechnology in NER” has been established at the Assam Agriculture University, Jorhat (Assam). This Centre focuses on research in the areas of Gene technology, Allele mining, Molecular breeding and Microbial gene prospecting. It is engaged in developing skilled/trained human resource, generating bio-inputs to assist eco-farming in NER, and documentation and genetic cataloguing of bioresources for IP management of IP-related issues. The Centre has successfully generated transgenic chickpeas and blackgram lines using *Bt* genes to confer protection against pod borers; 750 rice germplasm are genotyped using 120 SSR markers; Biofertilizers and biopesticides generated at headquarter and at satellite centres are being distributed to the farmers.



A view of DBT – AAU Centre for Agriculture Biotechnology at AAU, Jorhat

A project in a consortium mode on “NER-Scented rice” was implemented during the year. North Eastern Region of India possess a rich diversity of aromatic rice (AR). The aromatic rice of NER especially Joha and Black rice are of premium value because of their aroma and medicinal characteristics. But these are also poor yielders and susceptible to pest attacks. Hence, biotechnological intervention was required to ameliorate the agronomic characteristics of this aromatic rice.

A multi-centric programme on value addition in jackfruit and commercialization of its processed products aims at identification of superior genotypes of jackfruit and their molecular characterization on the one hand, and validation and commercialization of technologies for value added products from Jackfruit, on the other. This programme has identified more than 40 elite jackfruit genotypes from Karnataka, Assam and Tripura for culinary or table purposes, organized training workshops for farmers for existing jackfruit technologies, and produced value added products like pickle, curry, bhaji, tikki, chips, squash, wine, jam, papad, etc. Marketing and supply chain is being developed through involvement of farmers and entrepreneurs.

The Value Chain Development in Citrus programme aims at using modern technologies for mass production of citrus plants and value-added citrus products. This collaborative DBT programme is being implemented by ICAR-RC, Nagaland; ICAR-RC for NEH Region, Shillong, Meghalaya; NRC for Citrus (ICAR), Nagpur, and IIT, Kharagpur, West Bengal. Under this programme, more than 2000 seedlings of rough lemon have been raised, Khasi mandarin and sweet orange have been successful grafted, and processing of citrus juice has been standardized. A Poly-house for multiplication of citrus rootstocks has also been constructed.



A network research programme on Chemical Ecology of North Eastern Region has been launched, with scientists from institutions in Bangalore (National Centre for Biological Sciences (NCBS), Indian Institute of Science (IISc), University of Agricultural Sciences) and those from NER institutions [IBSD, Imphal, (Manipur), Regional Centre of IBSD, Gangtok (Sikkim), NEHU, Shillong (Meghalaya), Nagaland S&T Council, Kohima (Nagaland), Rajiv Gandhi University, Itanagar, (Arunachal Pradesh)], being the partners in this programme. The programme focuses on identification of the origins and compositions of plant, insect and vertebrate pheromones and semio-chemicals; analysis and (re)

engineering of chemical communication mechanisms; molecular and structural mechanisms; behavioral and neural mechanisms; biochemical, genetic and physiological mechanisms, governing interactions between flora and fauna of NER.

A multi-centric network programme has been implemented for promoting eco-friendly agriculture practices in 14 districts across all 8 NE states, with emphasis upon the application of bio-inputs (biopesticides, biofertilizers) for organic farming of key high value crops (HVCs) of NER, mass multiplication of required bio-inputs and evaluation of their efficacy. The programme has provided training to nearly 1400 farmers in the use of bio inputs in organic farming of 9 target crops (5 spices, 2 fruits and 2 vegetable crops). An area of 156 hectare was developed and certified for organic farming. The programme has shown success of technology in field demonstrations with some target crops such as Tomato, King Chilli, French Bean, Turmeric, Ginger, Pineapple and Mandarin Orange. Results from these field demonstrations have indicated high possibility of substituting chemical fertilizers and synthetic pesticides with safe and effective bio-inputs. A considerable yield increment has been reported during bio inputs under the project.



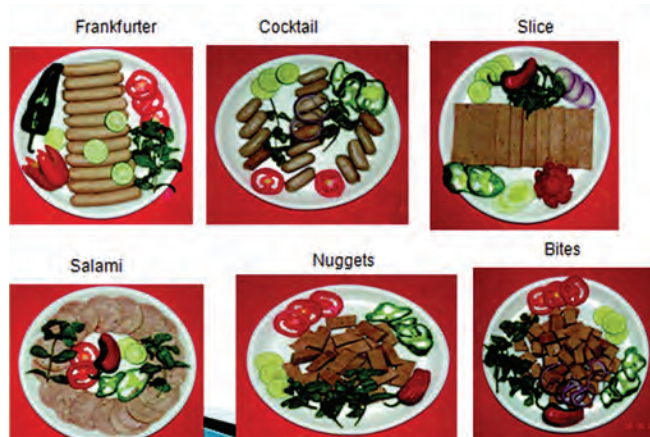
DBT has also supported a multicentric programme on assessment of impact of Jhum cultivation on soil microbiota and on restoration of diverse agro-ecosystem in NER. The specific objectives include estimating the genetic and biochemical diversity of untapped microbial pool, screening for heat and acidity tolerant microbes, bio-prospecting studies for stress tolerant genes and Allele mining, defining roles of hardy native plant spp. resilient to slash & burn practices in Jhum system, developing rapid multiplication technique for eco-restoration during fallow periods, and exploring the possibility of establishing symbiotic relationship between native plant species and potential microbes.

In the area of Animal Biotechnology, DBT has recently launched an ambitious programme on Advanced Diagnostics and Services in Animal Health and Disease for surveillance and control of trans-boundary, exotic and zoonotic pathogens. The programme, renamed as Advanced Animal Disease Diagnosis and Management Consortium (ADMaC), envisages establishing three core laboratories across the NER for carrying out research and training activities in trans-boundary and endemic animal diseases. This programme is aimed at strengthening regional infrastructure and capabilities for developing latest diagnostics and organizing rigorous surveillance for the highly contagious and ravaging diseases so that forecasting model on disease outbreaks in the region can be developed

for a formidable defense to guard the territories against possible onslaught by exotic virulent pathogens.

A DBT-supported programme on Augmenting Clean Pork Production and Value Addition, being implemented at the National Research Centre for Pig, Guwahati, Assam, is designed to develop shelf stable pork products and to refine & standardize the technologies for producing a wide range of value added pork products to provide variety to the pork consumers. Production of pork sausages has already been initiated. With more than 75% non-vegetarian population (with special attraction towards pork and pork products) in the North-Eastern Region, the technologies developed herein could be taken up at commercial scale with possible turnover of about 150-200 tonnes of pork products per annum in the coming years.

Value Added Processed Pork Products



For strengthening the Fisheries and Aquaculture Biotechnology (FAB) related R&D activity in the NER region, DBT has established a FAB-Centre of Excellence (FAB-COE) at College of Fisheries, Central Agricultural University, Lembucherra, Tripura. The objectives are to improve the yield of fish production in NER, to explore the fish biodiversity across all the eight North Eastern States, understand the lineage of species diversity, development of protocols for breeding, seed

production and farming of economically viable species, fish resource management education and capacity building, and R&D on feed development.

In addition, DBT has made intensive efforts in capacity building and human resource development (HRD) for the benefit of entire North Eastern Region of India, as follows:

Sophisticated biotech infrastructural facilities have been created at National Research Centre on Yak at Dirang (Arunachal Pradesh), for strengthening research dynamics for desirable gains in Yak husbandry, and at National Research Centre on Mithun at Jharnapani, Medziphema (Nagaland) for improving research activities on Mithun husbandry, genomics and conservation.

To give a strong fillip to research in experimental medical sciences and in herbal medicine, DBT has initiated establishment of a state-of-the-art, *Regional Animal House Facility* at Regional Medical Research Centre (RMRC), Dibrugarh. It will provide well-equipped and fully-functional lab space to the researchers from entire NER for carrying out critical experiments in disease biology, molecular medicine, immunology/vaccinology, drug development and molecular pharmacology. This facility will facilitate availability of specific-pathogen free (SPF) and genetically defined lab animals. Imparting training to the biomedical research staff in standard procedures in animal experimentation will be yet another important activity of this facility.

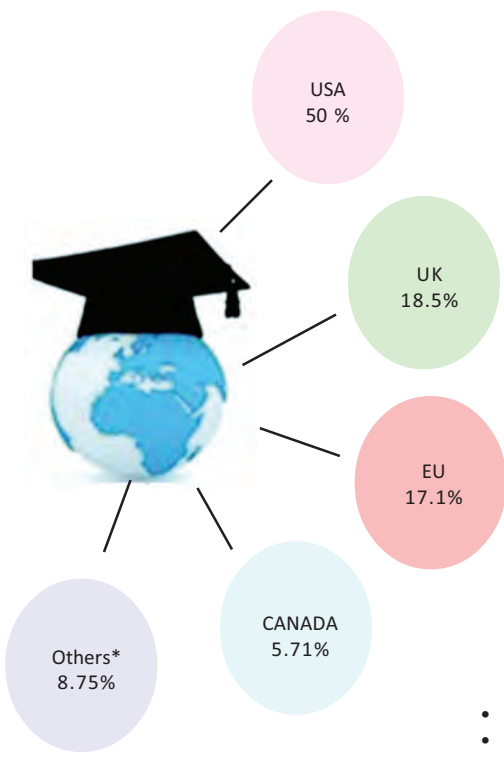
DBT has established a network of 126 Biotech Hubs across NER, providing necessary infrastructure in universities/ colleges/ institutions and the required training in sophisticated technologies so as to support and promote biotechnology education and research. At this juncture, there are 6 State-Level and 120 Institutional Level vibrantly active Biotech Hubs spread across all the eight states of NER. Together these hubs have conducted more than 600 training programmes and supported more than 500

PG and PhD students. More than 250 research papers, published in peer reviewed journals, underline the quality of research being undertaken at some of the Biotech Hubs.



An Overseas Associateship Scheme for NER Scientists continued to support scientists in their

skill enhancement in scientific research/training in Overseas laboratories for short term as well as long term. So far, 170 scientists have been awarded the Associateship. As of now, more than 150 scientists have availed this Associateship. This Overseas Associateship has resulted in more than 50 research papers in peer reviewed journals.



- Boston Children Hospital, Harvard Medical School
- Cornell University
- Washington State University
- University of Texas
- United States Department of Agriculture (USDA)
- University of California
- University of Wisconsin
- The Vaccine Research Institute of San Diego

- University of Glasgow
- University of Strathclyde Science
- The Food and Environment Research Agency
- University of Aberdeen
- University of Wolverhampton

- Uppsala University, Sweden
- Gent University, Belgium
- University of Regensburg, Germany
- Institute of farm Animal Genetics, Germany
- IFAPA Centre, Alameda del Obispo, Spain
- Laboratoire Interactions Plantes Microbes, CNRS-INRA, France

- Lakehead University
- Concordia University
- University of British Columbia

- National Institute of Biomedical Innovation, Japan
- CSIRO, Canberra, Australia
- Yat-sen University Cancer Centre, China
- University of Southern Queensland, Australia
- Invermay Agricultural Centre, New Zealand

DBT has initiated a scheme for establishing “*Biotechnology Labs in Senior Secondary schools (BLISS)*” across all 8 states of NER. In the first round, 88 Senior Secondary Schools from NER have been selected by DBT for support under the BLISS scheme, with financial support of upto Rs. 18.00 lakhs in 3 years. A basic set of laboratory equipment alongwith recurring support is being provided under this scheme.

DBT has also initiated a “*Visiting Research Professorship (VRP)*” Scheme to utilize the expertise of outstanding biotechnology professionals for bringing advancement in the Biotechnology and Life Science related activities in various institutions of research and higher learning in the NER States of India. In the first phase, 14 scientists/faculties have been selected for “VRP in NER” scheme. In the current financial year, 19 VRP/VRF have been selected to work at various institutions/universities in NER.

DBT has established a Centre for empowerment of human resources at NEHU, for conducting trainings/workshops for faculty/research students of the region in niche areas of Biotechnology for undertaking R&D activities. Distinguished faculty with national/international credentials are invited to impart advanced training to the participants.

The centre also organized an Autumn School in Plant Sciences for the benefit of graduate students of the region. An important contribution of the centre has been a greater inquisitiveness in the students of this region to take up science as a career. This is reflected in substantial increase in the number of students from NER qualifying various national examinations like NET, GATE, BINC, etc.



Students of school of Meghalaya being explained the functioning of different equipment



A hands on Training workshop in progress

Twenty nine bioinformatics centers have been established in all the 8 states of the NER and are networked as the North Eastern Bioinformatics Network (NEBINet). These Bioinformatics centres are provided with latest IT equipment to support the research activities of the host institutions in NER. Two new bioinformatics centres were established during the last year, at College of Fisheries, Central Agricultural University, Lembucherra, Tripura and National Research Centre on Mithun (ICAR), Nagaland.

DBT's e-Library Consortia for North Eastern Region (NER-DeLCON) was established in the year 2010 through which access to more than 900 High Impact e-journals were subscribed by DBT. The facility is being offered to 18 selected NER institutions free of cost; it is being extensively used by scientists, faculty and students of these 18 institutions. A separate website www.delcon.gov.in has been created for DeLCON.

Capacity Building Workshops in Grant Writing Skills and Effective Management of Intellectual Property Rights (IPR) in Biotechnology: DBT has organized a series of three-day capacity-building workshops on effective grant writing skills and basics of Intellectual Property Rights (IPR) for the research institutions and universities of the North-East Region. Young faculty and researchers from NER institutions were trained during these workshops through hands on group exercises. The useful

interactions were beneficial to the participants who gained more clarity on the basics of grant writing skills from reviewer's perspective. The participants were also introduced to the basics and best practices for protection of their novel research outcomes through appropriate tools of IPR.

Training of NER researchers at ICAR-NIHSAD, Bhopal: The North Eastern Region of India has a long International border which pose as a challenge to deal with inevitable inflow of transboundary pathogens which, if left uncontrolled, may be potentially lethal, zoonotic or exotic. To address this NER researchers in the pathogen handling and bio-safety issues were trained at ICAR- National Institute of High Security Animal Diseases (ICAR-NIHSAD earlier HSADL), Bhopal.

In collaboration with the Govt of Assam, DBT has established a Biotech Park at Guwahati, Assam, as a meeting point of technological innovation for knowledge-based biotechnology enterprises and to provide sustainable linkages between the industry, research institutions and academia to boost the region's competitiveness. The park actively promotes formal and operational links between centers of knowledge creation such as national R&D laboratories, Universities, Medical Institutions and research organizations in India and abroad, and creates a strong network.

Programme Support on Fundamental Molecular Investigations in Biotechnology at IIT, Guwahati

Work has been initiated to develop nontoxic methods and processes to generate metal nanoclusters for therapeutic and diagnostic applications. The delivery of suicide gene into cells by composite NPs has been demonstrated. Amphiphile-loaded nanocomposites have been generated that can either breach the biofilm eDNA barrier and eliminate underlying cells or hinder the fundamental resistance mechanism of drug-resistant bacteria and predispose the cells to antibiotic-mediated killing. The target biomarker proteins have been



developed for *Plasmodium falciparum* lactate dehydrogenase (PfLDH), Histidine rich protein-II (HRP-II) for malaria and heart type fatty acid binding protein (HFBP3) for acute myocardial infarction. Aptamers for all these biomarkers were developed and characterized. Mathematical models have been created to understand the architecture and controls in the PI3K/Akt/mTOR/S6k pathway. This pathway is hyperactive in various types of cancers. Recombinant receptor-binding domain of Diphtheria toxin (RDT) has been used for cell specific drug delivery. Nanoparticles have been coated with recombinant RDT. Coating of RDT allows receptor-mediated cell specific delivery of these

nanoparticles. Arabidopsis ABA receptor (AtPYL9) have been cloned, prepared stress inducible plant overexpression construct, and generated putative transformed mung bean plants with AtPYL9 gene for further analysis. Besides, transgenic lines have been developed in several plants such as mung bean expressing AtNHX1 for salinity tolerance, cis-genic cowpea expressing VuDREB2A for evaluation for drought tolerance, enhanced seed and leaf oil content in biofuel plant *Jatropha* overexpressing AtDGAT1, drought and salinity tolerant transgenic Indian mustard overexpressing AtLEA4-1, and MYMIV resistant cowpea through RNAi approach.



14 ADMINISTRATION AND FINANCE

Administration

Administration is responsible for providing a good and ambient working atmosphere for the in-house scientists, officers and staff. Logistic supports were provided for organizing various Task Force & Expert Committee meetings. This included support provided for successful organisation of the Global Biotechnology Summit held on 5th - 6th February, 2016 at Vigyan Bhawan, New Delhi. Being a scientific department, a large number of meetings, interactions and quick referral with technical experts, specialists, academicians and scholars from far reaching places and across the world are held for which technical support was provided.

Department housed in Block No.2, CGO Complex, New Delhi does not have its own building or campus and is facing shortage of office space. The additional office space of 11,000 sq.ft allotted to the Department at Block 3 has now been allotted to the officers & staff of the Department with required furniture, office equipment, etc. for efficient and speedy disposal of the official work.

Swachh Bharat Abhiyan

In consonance with the call of Hon'ble Prime Minister, the Department of Biotechnology (DBT) alongwith its 15 Autonomous Bodies and 2 PSUs decided to launch "Swachh Bharat Abhiyan" from its campuses in different parts of India from 2nd October, 2014. Also DBT geared up its employees to launch "Swachh Bharat Mission" from 25th September, 2015 to 31st October, 2015 and 18th December, 2015 to 27th December, 2015 with a

'Cleanliness drive' on the concept of Mahatma Gandhi's vision, "sanitation is more important than Independence". The Cabinet Secretary inspected DBT premises on 27th December, 2015 and appreciated the cleanliness and ambience of the Department offices and Canteen facilities. All DBT employees agreed to dedicate at least 100 hours every year towards 'Swachh Bharat Abhiyan'. It was decided that on the last Friday of every month, all DBT employees would earmark two hours between 3.30 & 5.30 for 'Swachha Abhiyan' at DBT to assist and voluntarily contribute for the maintenance of cleanliness of the office building and surroundings.

e-Office in DBT

The e-Office is one the Mission Mode Project (MMPs) under the Digital India Programme is being implemented in the Department of Biotechnology under the guidelines with DARPG. The Department has decided to go for the e-office Premium version through NICS for which financial assistance has been sought from the DARPG. Demonstration of e-office to the Officers of DBT was organized in July, 2016. Digitization of file is being started. Procurement of hardware and software is being initiated to implement e-office in the Department. Officers of various programme division have been given training on e-office application through NIC. In house training of Senior Officers will be taken up soon. e-Office project will be implemented by 31.03.2017.

Web enabled Project Management Information System: Department has introduced a web portal, **eProMIS**, a Web enabled Project Management

Information System with the active support of NIC. It is developed for the submission, evaluation, management, monitoring and closure proposals. The application is hosted at the NIC server with all security measures with URL <http://www.dbtepromis.nic.in>. This is a single window application which covers the complete life cycle of proposals received online like registration, submission, peer review, assigning sanction numbers, monitoring and closure. This is operational for quite sometimes and regular enhancement is being incorporated using state-of-art ICT tools for ease in operation by the scientific community.

Network enhancement and e-Governance activities: LAN has been extended to the additional space of DBT in 4th and 5th floor of Block-3, CGO Complex with the active support of NIC. All old switches and hubs were replaced with IPV6 compliant switches. To implement time bound recommendation of 7th CPC and there after Cabinet decision on that, significant contribution was made by Cell in fixing new basic pay of Department employees to enable Department to release their salary in new pay structure and arrears in time. Relevant web based scripts for pay slip generation in Hindi and in bilingual format were also modified in accordance with 7th CPC recommendations. State-of-art Video Conferencing facility in the department is very much in use for organizing scientific deliberations with the scientists across the globe and also for routine GOI activities like PRAGATI (Pro-Active Governance And Timely Implementation). Support is being provided by NIC to aware all autonomous institutes of DBT about GOI guidelines on ICT matters and also to scale up their e-governance activities.

Establishment Section

Establishment Section in the Department is entrusted with the following functions:-

- a) Recruitment and promotion to various posts : During the period under report, two posts

of Scientist 'H' decided to be filled up on direct recruitment basis were revived with the approval of Department of Expenditure. The process to fill up these vacancies has already been initiated. One post of Scientist 'H' will fall vacant on account of superannuation of Dr. Rajesh Kapur on 31.01.2017. The process to fill up this vacancy has also been initiated.

- b) Ante-dating the date of promotion : In pursuance of the CAT's Order and ACC's approval, ante-dating of the promotion date was done in respect of two Scientists 'G' in the Department with all consequential benefits.
- c) Recruitment Rules: The proposal for framing revised Recruitment Rules with regard to the Scientific and Technical staff in the Department has been taken up with Department of Personnel & Training and Department of Expenditure.
- d) Modified Assured Career Progression Scheme: The cases for grant of Modified Assured Career Progression Scheme to eligible officials are processed from time to time.
- e) Training : The officers and staff were deputed for various training programmes conducted by the Institute of Secretariat Training & Management (ISTM), National Institute of Financial Management (NIFM), Faridabad and Indian Institute of Public Administration, New Delhi to enhance their skills in relevant fields.
- f) Grant of Advances and Reimbursements: The cases of grant of various advances, medical reimbursement and other allowances were processed as per rules in a time bound manner.
- g) Miscellaneous: In order to fill up the vacant

posts of Junior Technical Assistants, the Staff Selection Commission (SSC) has recently placed an advertisement on its website seeking applications for filling up 08 posts of Junior Technical Assistants in the Department.

The category wise position of posts sanctioned and filled as on 31.12.2016 is as under:-

Category of posts	Posts sanctioned	Posts filled
Group 'A'	74	54
Group 'B'	89	58
Group 'C'	86+1 Plan	52+1 Plan
Total	249+1 Plan	164+1 Plan

Parliament Matters

The meeting of the parliament standing Committee on Science and Technology, Environment & Forest was held on 30-03-2016 in the Parliament House, to consider the demands for Grants (2016-17) of the Department of the Biotechnology

Grievance Redressal

Department has established an effective grievance redressal mechanism to deal with the public as well as staff grievance petitions. The Department regularly updates progress, disposal and pendency of public grievance on the website of the

Department of Administrative Reforms & Public Grievance (DARPG).

Vigilance Unit

A vigilance cell is functioning in the Department to handle vigilance and complaint cases expeditiously. Complaints received from various sources were processed timely. In pursuance of the instructions of the 'Central Vigilance Commission', a Vigilance Awareness Week was observed in the Department with taking Pledge on 31-12-2016. A meeting of the Vigilance Officers of the Autonomous Institutes and Public Sector Undertakings of the Department of Biotechnology was convened on 27-12-2016 by the Chief Vigilance Officer of the Department.

Finance

Department of Biotechnology was allocated an Amount of Rs.1820.00 Crore for the year 2016-17. This was revised to Rs. 1917.23 Crore (Rs.1895.20 Crore under plan and Rs. 22.03 Crore under Non-plan). The Financial Statement showing the details of actual expenditure during 2015-16, B.E. and R.E of 2016-17 in respect of various programmes/ schemes are given in Annexure I.

Status of Audit Observations

In compliance with the instructions of Department of Expenditure, Ministry of Finance vide O.M.No.12(4)/ E.Coord./ 2014 dated 15.04.2014, gist of audit observations made by C&AG for the year 2015-16 is placed at Annexure-II.

Annexure- I

(Rs. In crores)

S. No.	Name of the programme Scheme	2015-16 Actual Expenditure			B.E. 2016-17			RE 2016-17		
		Plan	Non-Plan	Total	Plan	Non-Plan	Total	Plan	Non-Plan	Total
1	2	3	4	5	6	7	8	12	13	14
	REVENUE SECTION	1537.54	16.72	1519.72	1800.00	20.00	1820.00	1895.20	22.03	1917.23
1	Secretariat Economic Services									
1.01	Secretariat	0.00	16.72	16.72	0.00	20.00	20.00	0.00	22.03	22.03
2.01	Biotechnology Industry Research Assistance (BIRAC)	20.00	0.00	20.00	25.00	0.00	25.00	25.00	0.00	25.00
2.02	Support to Autonomous R&D Institutions *	561.60	0.00	561.60	660.00	0.00	660.00	660.00	0.00	660.00
3.00	Assistance to other Scientific Bodies									
3.01	HUMAN RESOURCE DEVELOPMENT	115.42	0.00	115.42	0.00	0.00	0.00	0.00	0.00	0.00
3.02	BIOINFORMATICS	46.54	0.00	25.00	0.00	0.00	0.00	0.00	0.00	0.00
3.03	BIOTECHNOLOGY RESEARCH & DEVELOPMENT	545.85	0.00	545.85	920.00	0.00	920.00	1018.20	0.00	1018.20
3.04	BIOTECHNOLOGY FOR SOCIETAL DEVELOPMENT	10.09	0.00	10.09	0.00	0.00	0.00	0.00	0.00	0.00
3.05	GRAND CHALLENGE PROGRAMMES	29.81	0.00	29.81	0.00	0.00	0.00	0.00	0.00	0.00
3.06	PROGRAMME FOR PROMOTION OF EXCELLENCE & INNOVATION	67.33	0.00	67.33	0.00	0.00	0.00	0.00	0.00	0.00
3.07	BIOTECH FACILITIES	58.29	0.00	58.29	0.00	0.00	0.00	0.00	0.00	0.00
4.01	INDUSTRIAL AND ENTREPRENEURSHIP DEVELOPMENT	69.61	0.00	69.61	195.00	0.00	195.00	192.00	0.00	192.00
5.00	Biotechnology Clusters	13.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
6.00	Provisions for projects/ schemes for the benefit of North Eastern Region and Sikkim	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	TOTAL = Revenue Section	1537.54	16.72	1519.72	1800.00	20.00	1820.00	1895.20	22.03	1917.23

* Institutions includes 15 Autonomous Bodies namely National Institute of Immunology, New Delhi ; National Centre for Cell Science, Pune ; Centre for DNA Finger Printing and Diagnostics, Hyderabad ; National Brain Research Centre, Gurgaon ; National Centre for Plant Genome Research, New Delhi; Institute of Bioresources & Sustainable Development, Imphal; Institute of Life Sciences, Bhubaneswar ; Translational Health Science & Technology Institute, Faridabad ; Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram ; Regional Centre for Education and Training, National Agri-Food Biotechnology Institute & Bioprocessing Unit, Mohali ; Institute for Stem Cell Research & Regenerative Medicine, Bengaluru ; National Institute of Biomedical Genomics, Kalyani ; National Institute of Animal Biotechnology, Hyderabad; and one International Institute namely International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi

Annexure- II

S.No.	Audit Observations for the year 2015-16	Action Taken
	Part-II (A)	
Para 1	Over payment of Transport Allowance.	Information from the Division is being sought
	Part –II (B)	
Para 2	Improper award of Renovation work to the organization not notified by MoUD.	Information from the Division is being sought
Para 3	Irregular Establishment of Clinical Development Services Agency as Autonomous Body.	Reply sent on 3.2.2017
Para 4	Establishment of the Centre for “National Hub for Veterinary Vaccines and Diagnostics (TRPVB- Translational Research Platform for Veterinary Biological.	Information from the Division is being sought
Para 5	Non-achievement of objectives- Failure in Development of vaccine for Bovine Herpesvirus- 1 and a companion diagnostic test.	Information from the Division is being sought
Para 6	Project on “Development of two stage Anaerobic Bacterial Process for Butanol Production from Industrial waster.	Information from the Division is being sought
Para 7	Improper/inefficient management of research project by scientific/technical staff of DBT.	Reply sent on 3.2.2017
Para 8	Improper award of AMC for hiring of cars in violation of GFR.	Information from the Division is being sought
Para 9	Non disposal of unserviceable vehicles.	Information from the Division is being sought
Para 10	Non-utilization of furniture and kitchen equipments costing Rs.98.08 lakh.	Information from the Division is being sought
Para 11	Non-conducting Peer Review of the Autonomous Organization (s) under administrative control of DBT.	Reply sent on 3.2.2017
Para 12	Improper operation of Departmental Canteen (Tiffin Room) of DBT without obtaining FSSAI License under Food Safety and Standards Act 2006.	Information from the Division is being sought
Para 13	Non production of record.	Information from the Division is being sought



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MISSION PROGRAMMES

Biotech-Krishi Innovation Science Application Network (Biotech-KISAN)

A new scheme on Biotech-Krishi Innovation Science Application Network (Biotech-KISAN) has been conceptualized and initiated during the year with an objective to link available science and technology laboratories to the farm by first understanding the problem of the local farmer and provide solutions to those problems. This programme aims to work with small and marginal farmers especially the woman farmer for better agriculture productivity through scientific intervention and evolving best farming practices in the Indian context. The scheme will provide supporting the following components:

The Hub: Establishment of Biotech-KISAN Hub in each of 15 agro-climatic zones of the country under the leadership of a Facilitator. Each Hub will create a network by developing strong linkages with top quality scientific institutions / State Agricultural Universities (SAUs) / Krishi Vigyan Kendras (KVKs) / existing state agriculture extension services / system and other Farmers' organizations in the region as well as linkages with leading international institutions / organizations. Biotech-KISAN Hub will have a tinkering laboratory.

Training programmes: Training programmes for farmers in laboratories of scientific research institutions to expose them to leading science laboratories to develop them as scientific leaders at grass root level and provide solution and support to agriculture problems. Training programmes for

scientists in agricultural farms for better understand the problems of farmers at ground level and address / implement solutions.

International Training: Short-term Training (STT) Programmes is also the component under KISAN Biotech in partnership with International organisations / universities, where farmers will be exposed to best global farm management and practices.

A Call for Proposals has been given against which 87 proposals were received, which were screened by a Programme Steering and Monitoring Committee (PSMC). The programme will ultimately help in establishing Biotech KISAN Hubs in different agro-climatic zones.

Space Mission

The Department of Biotechnology has already taken a major initiative on biodiversity mapping in mainland India in collaboration with the Department of Space. This is part of the initiative on the effective use of Space Technology in the field of Biotechnology. The study 'Biodiversity Characterization at Landscape Level using satellite remote sensing and Geographical information System' was conducted by the DBT in collaboration with the Department of Space. Under this study, a national level assessment of biodiversity richness was undertaken for the first time in India using spatial data on a 1:50,000 scale to identify and to map potential biodiversity-rich areas in the country. So far 84% of the Country's forest cover has been characterized.

Mission Innovation- Accelerating the Clean Energy Revolution

The 'Mission Innovation (MI)' was launched during PM's visit to Paris in November 2015. Besides India and US, 18 other countries are members of this initiative led by US to drive forward clean energy innovation in a global scale. MI members aim to encourage increased engagement from the global research community, industry and investors while also providing opportunities for new collaborations between MI members. Commitment to MI envisions creation of jobs and building more low-cost broadly deployable clean energy options. Collectively MI members encompass over 80% of the world's public funding for energy R&D. Under the initiative, members have pledged to double their collective investments in energy R&D funding of over USD 15 Billion annually to over 30 billion by 2021.

The first Ministerial meeting was held in June 2016 in San Francisco. The meeting identified consolidated MI doubling target and the innovation priorities. Subsequent to the Ministerial meeting discussions were held and recognized that targeted technology advances could accelerate breakthroughs and reduction in cost and launched 7 innovation challenges. These challenges are global calls to action that complement efforts already underway by MI countries.

- Smart Grids Innovation Challenge
- Off Grid Access to Electricity Innovation Challenge
- Carbon Capture Innovation Challenge
- Sustainable Biofuels Innovation Challenge
- Converting Sunlight Innovation Challenge
- Clean Energy Materials Innovation Challenge

- Affordable Heating and Cooling of Buildings Innovation Challenge

DBT has been identified as nodal agency to coordinate national efforts in clean energy for Mission Innovation activities on behalf of Government of India. DST, Ministry of Power, MNRE are other ministries participating in addressing the challenges. India will be partnering in all the challenges. India will be leading the Smart Grids innovation challenge and co-lead the sustainable biofuels innovation challenge and is collaborating in all the challenges identified.

Health Mission: Nutrition

Demonstration Unit for production of Iron Fortified Rice pre-mix: Appropriate technology has been developed on Iron fortified rice premix from broken rice kernels through extrusion process and a Demonstration unit has been set-up in IIT-Kharagpur. This iron fortified rice premix matches with the normal rice kernel in shape and size, and when mixed with normal rice in the ratio of 1:100 to provide 50% of recommended daily allowance (RDA) of Iron to the Children. Consultations are underway with Ministry of Food Processing Industries for dissemination of this indigenous technology.

Make in India

The 'Make in India' initiative was launched on September 25, 2014 by the Government of India with an aim to give Indian economy global recognition. The programme includes major new initiatives designed to facilitate investment, foster innovation, protect intellectual property, and build best-in-class manufacturing infrastructure. The Department of Biotechnology has been foundational partner in the "Make in India" initiatives as it has specific relevance to the biotechnology sector in India, owing to the fact that the country's biotechnology industry is in the growth phase where the opportunities are immense. Considering the importance of Biotechnology sector in the program,

the Department has initiated establishing a Make in India Facilitation Cell at BIRAC with the responsibility of creating an enabling ecosystem in the country to promote manufacturing and research & development capabilities of Indian biotech sector. Major Activities of the programme during the year are as:

The Make in India Facilitation Cell prepared a high level report on the Make in India initiatives and identified several areas for support in high value manufacturing. The report was released by Hon'ble Minister for S&T and Hon'ble Minister of State for S&T in the 5th Innovator Meet in September 2016. The report highlighted the global and Indian biotechnology research and industrial landscape; underlined the challenges faced by the Indian biotech industry; and brought out the fiscal and policy incentives offered by the Government for the biotech industry and startups in India

The Cell ensures wider dissemination of the Government programmes and other information relevant to the establishment and growth of startups. A dedicated website has been developed for the information dissemination and handholding startups <http://birac.nic.in/mii/index.php>

The cell coordinates with DIPP on a regular basis for updates in MII action plan on the online web portal.

The Cell has also brought out a compilation of Products developed by the innovators with the support of BIRAC.

The Cell has contributed to the creation of Innovation Market Place at BIRAC's fifth Innovators Meet. The purpose behind organizing an Innovation Market Place was to showcase the products, indigenously developed by the innovators supported by BIRAC, to relevant Investors and stakeholders

Cell has also provided strategic inputs to NITI Aayog for framing the Atal Innovation Mission and Grand

Challenges.

The cell provides continuous inputs for Startup India Action Plan also.

Along with the above roles, the Cell also respond to the queries related to Make in India, Start up India and others related to Entrepreneurship, Startups & Ease of doing business.

The Detailed Action Plan was formulated under the Make in India initiative for the biotechnology sector. The Action plan is being implemented by the Department and Biotechnology Industry Research Assistance Council (BIRAC), a centrally sponsored Public Sector Undertaking of the Department. The broad activities being undertaken are as follows:

Injection of capital in segments such as Biosimilars, MedTech, BioAgri, BioPharma, Big data analytics, Genomics, Chemical Ecology, Marine Biotechnology

Budgetary allocation with earmarked funds through empowering special purpose vehicles such as BIRAC for Bio-manufacturing and Entrepreneurship development

Setting up of infrastructure for product development

Facilitate research and nurturing of skilled graduates at a university level

Create Bio-clusters to enhance conversion and visibility of indigenous innovative ideas to promote manufacturing in India

Technology transfer to encourage public private partnership for fostering biotech manufacturing in India

Start-up India

Start-up India is a flagship initiative of the Government of India, intended to build a strong ecosystem for nurturing innovation and Start-ups in the country that will drive sustainable economic growth and generate large scale employment opportunities. The Government through this initiative aims to

empower Startups to grow through innovation and design. The startup India initiative was launched on January 16, 2016 by the Hon'ble Prime Minister of India. In order to foster a fruitful culture of innovation and to make India a hub of innovation, design and Start-ups, the Start-up India Action Plan has been formulated and Biotechnology sector has been given due importance considering the opportunities & growth momentum and the sector is highlighted in Action Point no. 17. The main features of the Action Point are as follows:

Roles and Responsibilities

DBT endeavors to scale up the number of Start-ups in the sector by nurturing approximately 300-500 new Startups each year to have around 2,000 Startups by 2020. In order to promote Startups in the sector, DBT shall be implementing the following measures along with BIRAC:

I Bio-incubators, Seed Fund and Equity Funding

5 new Bio-clusters, 50 new Bio-Incubators, 150 technology transfer offices and 20 Bio-Connect offices will be set up in research institutes and universities across India.

Biotech Equity Fund – BIRAC AcE Fund in partnership with National and Global Equity Funds (Bharat Fund, India Aspiration Fund amongst others) will provide financial assistance to young Biotech Startups.

II Encouraging and leveraging global partnerships:

Bengaluru-Boston Biotech Gateway to India has been formed. Letter of Intent has been signed between DBT, GoI and Department of IT, Government of Karnataka for the same. Through this initiative, a range of institutes in Boston (Harvard/ MIT) and Bengaluru will be able to connect to share ideas and mentor the entrepreneurs especially in the areas of Genomics, Computational Biology, Drug Discovery and new vaccines.

Amplification of Bio-entrepreneurship through BIRAC Regional Entrepreneurship Centres (BREC). The BREC aims to impart bio-entrepreneurs with the necessary knowledge and skills required for converting innovative ideas into successful ventures. Department of Biotechnology shall set up 5 Regional centres or Mini-BIRACs in the next 5 years.

The Department of Biotechnology and BIRAC have initiated several activities and also implemented some of the activities mentioned in the Action Plan. The Department has supported 02 Bio-clusters at National Capital Region and Bengaluru, respectively, 20 bio-incubators across the country and also implemented Bengaluru-Boston Biotech Gateways to India Program (B4 program) during the year. The Department is working on the implementation of remaining action points.

Industry-Academia Collaborative Mission For Accelerating Discovery Research To Early Development For Biopharmaceuticals:

During the implementation earlier plans, a special emphasis was given on promoting innovation and excellence in biotechnology & currently there is a special focus on improving healthcare conditions for better quality of life.

Thus, it is essential that research and innovation in discovery, validation and manufacturing of biopharmaceuticals go hand-in-hand for transforming India's health scenario. The Mission Program is therefore critical to nurture indigenous innovation and accelerate commercialization process for inclusive development and competitiveness in India. The Department is evolving a PAN India Mission Programme with the main aim of enabling and nurturing the ecosystem for Innovation Research and Product Development capabilities in Bio-pharmaceuticals to enable the sector to be globally competitive over the next decade and transform the health of Indian population. Through these efforts it is proposed that

India would work towards achieving its target of \$100 billion Biotech Industry by 2025 and also capturing 5% of the Global Biopharmaceutical market share. The Mission will be designed in a manner in which it addresses the key components of the Vision outlined in the National Missions - Make in India and Start up India and also aims to take forward the commitments made by DBT in the National Biotechnology Development Strategy.

The mission will focus on:

Development of product leads that are at advanced stages of the product development lifecycle and relevant to the public health need by focusing on managed partnerships.

Establishment and strengthening of shared infrastructure facilities and product discovery/ validation and manufacturing.

Development of human capital by providing specific trainings to address the critical skills gap among nascent biotech companies across the product development value chain, including in business plan development, and market penetration.

Creation and enhancement technology transfer capabilities in public and private sector.

Harnessing the Blue Economy:

Under the Blue Economy, the Department is giving emphasis on Ocean research and marine biotechnology. A proposal on the establishment of Institute of Ocean Biology: Neel has been formulated in joint collaboration with MoES which is under consideration for approval. The efforts would help in deep sea research and sustainable ocean resource development.

Abbreviations

AAU	:	Anand Agricultural University
ADF	:	<i>Acid Detergent Fiber</i>
AICAR	:	5-Amino imidazole-4- carboxamide ribonucleotide
Akt	:	Protein kinase B (PKB)
AML	:	Acute Myeloid Leukemia
AP-1	:	Activator protein 1
APC	:	Adenomatous polyposis coli
AT1	:	Angiotensin II Type1
AX	:	arabinoxylan
AXIN	:	Axis inhibition protein
BAC	:	Bacterial artificial chromosome
BiFC	:	Bimolecular fluorescence complementation
BLAST	:	Basic Local Alignment Sequence Tool
BLM	:	Bloom Syndrome Gene
BSL	:	Bio Safety Level
CABYR	:	Calcium Binding tyrosine phosphorylation regulated
CDFD	:	Centre for DNA Fingerprinting and Diagnostics
cDNA	:	Complementary Deoxyribonucleic acid
CDS	:	Coding Sequences
CIFA	:	Central Institute of Freshwater Aquaculture
CIFE	:	Central Institute of Fisheries Education
CME	:	Continuing Medical Education
CO 1	:	cytochrome c oxidase I
COE	:	Centre of excellence
COL18A1	:	Collagen Type XVIII Alpha 1 Chain
CSC	:	Cancer stem cell
c-Src	:	Proto-oncogene c-Src
CTNNB	:	Catenin beta
Cyp19A1	:	cytochrome P450, family 19, subfamily A, polypeptide 1

DCFR	:	Directorate of Coldwater Fisheries Research
DCFR	:	Directorate of Coldwater Fisheries Research
DGKZ	:	Diacylglycerol kinase zeta
DNA	:	Deoxyribo Nucleic Acid
DSBs	:	Double-Strand Breaks
DVL	:	Dishevelled
EAE	:	Experimental Autoimmune Encephalomyelitis
EGF	:	Epidermal Growth Factor
EGFP	:	<i>Enhanced Green Fluorescent Protein</i>
ELISA	:	Enzyme Link Immuno Sorbent Assay
EMT	:	Epithelial Mesenchymal Transition
ERK	:	Extracellular Signal-Regulated Kinase
ET calves	:	Embryo Transfer
FANCI	:	Fanconi anemia complementation group
FCR	:	Feed conversion ratio
FLIM	:	Fluorescence Life Time Imaging
FSH	:	Follicle-stimulating hormone
FZD	:	Frizzled Class Receptor
GDP	:	Guanosine di phosphate
GH	:	Growth hormone
GO	:	Gene Ontology
GPI	:	Glycophosphatidylinositol
hCG	:	Human chorionic gonadotropin
HFD	:	high fat diet
HIV	:	Human Immunodeficiency Virus
Hsp	:	Heat Shock Protein
HSP90B1	:	Heat Shock Protein 90 Beta Family Member 1
HspBP1	:	HSP70-binding protein
IASRI	:	Indian Agricultural Statistics Research Institute
IBDV	:	Infectious Bursal Disease virus
ICAR	:	Indian Council of Agriculture Research
ICGEB	:	International Centre for Genetic Engineering and Biotechnology
IFI16	:	Interferon Gamma Inducible Protein 16
IGF-1	:	Insulin-like growth factor 1
IGF1R	:	Insulin-like growth factor 1 receptor
IISc	:	Indian Institute of Science
IISER	:	Indian Institutes of Science Education & Research
IIT	:	Indian Institute of Technology

IL-3	:	Interleukin-3
IMTech	:	Institute of Microbial Technology
iPS	:	Induced pluripotent stem cells
ISG15	:	Interferon-stimulated gene 15
IVDMD	:	In vitro dry matter digestibility
JNK	:	c-Jun N-terminal kinases
JNU	:	Jawaharlal Nehru University
KVK	:	Krishi Vigyan Kendra
LAMP	:	Loop mediated isothermal amplification
LFA	:	Lateral Flow Assay
LH	:	Luteinizing hormone
L-NAME	:	N(G)-Nitro-L-arginine-methyl ester
LoIs	:	Letter of Intent
LPS	:	Lipopolysaccharide
MADF-BESS	:	Boundary element associated factor
MAPK	:	Mitogen-activated protein kinases
miRNA	:	micro RNA
mRNA	:	Messenger RNA
mRNA	:	Mitochondrial RNA
MTDH	:	Metadherin
NBFGR	:	National Bureau of Fish Genetic Resources
NBRI	:	National Botanical Research Institute
NBS	:	New Born Screening
NCBI	:	National Center for Biotechnology Information
NDF	:	<i>Neutral Detergent Fiber</i>
NDV	:	New Castle Disease Virus
NF-kB	:	Nuclear factor kappa-light-chain-enhancer of activated B cells
NII	:	National Institute of Immunology
NIT	:	National Institute of Technology
NOX4	:	Nicotinamide adenine dinucleotide phosphate oxidase
OA	:	Osteoarthritis
OAS1	:	Oligoadenylate Synthetase 1
ORF	:	Open reading frame
OSCC	:	Oral cancer cell carcinoma
PA	:	phytic acid
PCR	:	Polymerase Chain Reaction
PGF _{2α}	:	Prostaglandin F2-alpha
PGFM	:	Prostaglandin F2-alpha metabolite

PGM2	:	Phosphoglucomutase 2
PKP3	:	Plakophilin 3
Ppm	:	parts per million
PPR	:	Peste des Petits Ruminants
PVPFRA	:	Protection of Plant Varieties and Farmers' Rights Authority
R & D	:	Research and development
RAF	:	Rapidly Accelerated Fibrosarcoma
RECK	:	Reversion inducing cysteine rich protein
RNA	:	Ribo Nucleic Acid
RNAi	:	RNA interference
RT-PCR	:	Reverse Transcription- Polymerase Chain Reaction
RT-PCR	:	Real time Polymerase Chain Reaction
SC/ST	:	Scheduled Cast/ Scheduled Tribe
SCID	:	Severe Immunodeficiency
SCTIMS	:	Sree Chitra Tirunal Institute for Medical Sciences and Technology
SKIMS	:	Sher-I-Kashmir Istitute of Medical Sciences
SNP	:	Single nucleotide polymorphism
SNV	:	Single <i>nucleotide</i> variation
SOD	:	<i>Superoxide Dismutase</i>
TAF4b	:	TATA-Box Binding Protein Associated Factor 4b
TB	:	Tuberculosis
TGFBR3	:	Transforming growth factor beta receptor III
TIM-3	:	T cell immunoglobulin and mucin domain-containing-3
Tip	:	TCV-interacting protein
TLR	:	Toll Like Receptor
TMX4	:	Thioredoxin Related Transmembrane Protein 4
TRL4	:	Toll-like receptor 4
tRNA	:	Transfer Ribonucleic Acid
TSNAX	:	Translin Associated Factor X
UP	:	Uttar Pradesh
UV	:	Ultraviolet
VEGF	:	Vascular endothelial growth factor
WHO	:	World Health Organization
WNT	:	Wingless-type MMTV integration site family member
WSSV	:	White Spot Syndrome Virus
Zn	:	Zinc



Department of Biotechnology
Ministry of Science & Technology
Government of India