



ANNUAL REPORT

2017-2018



Department of Biotechnology
Ministry of Science & Technology
Government of India

"Attaining new heights in biotechnology research, shaping biotechnology into a premier precision tool of the future for creation of wealth and ensuring social justice-specially for the welfare of the poor"

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Annual Report 2017-18**

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2017-18



सत्यमेव जयते

Department of Biotechnology

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01

OVERVIEW

Department of Biotechnology (DBT) under the Ministry of Science and Technology, set up in 1986, has infused fresh momentum to the developments in modern biology and biotechnology. The Department, in the past 30 years, has witnessed discerned maturation from a nascent sector to a sunrise industry, making outstanding achievements in the growth and application of biotechnology in the areas of agriculture, healthcare, animal aquatic sciences, and sustainability of bio-resources & environment and also towards fostering innovations and entrepreneurship ecosystem in the country. Today, India is among the major 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.

Regional Centre for Biotechnology (RCB) Act, 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. The Act has come into effect from 1st March, 2017. RCB Statutes, Ordinances & Regulations were notified in Gazette of India and were laid in both the Houses of Parliament during the winter session of 2017.

National Guidelines for Stem Cell Research, 2017

In association with Indian Council of Medical Research the department has formulated The “National Guidelines for Stem Cell Research, 2017” which was released by the Hon’ble Minister for Health & Family Welfare on 11th October, 2017. The Guidelines lay down standards for stem cell research

and ensure that research with human stem cells is conducted in a responsible and ethically sensitive manner in the country.

Regulations and guidelines on biosafety of recombinant DNA research & biocontainment, 2017

Continuing the reform initiatives for Biosafety regulation, the Department has revised the Recombinant DNA Safety Guidelines, 1990. The new guidelines entitled, “Regulations and guidelines on biosafety of recombinant DNA research & biocontainment, 2017” were released on 5th December, 2017 at Geneva, Switzerland.

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. DBT’s Model Course Curriculum was released on 11th May 2017 at Vigyan Bhawan, New Delhi.

HUMAN RESOURCE DEVELOPMENT

The Department is implementing an Integrated Human Resource Development Programme in Biotechnology comprising of post graduate teaching programme; short term training courses for upgradation of skills of mid-career scientists and UG & PG faculty engaged in teaching and R&D; industrial training of students; fellowship for doctoral and post-doctoral research in frontier areas of life sciences and biotechnology; career advancement and re-orientation for women scientists; scholarships, awards, and also assistance to researchers for organizing conference/ seminar/ symposium. Under HRD scheme, Department is generating critical mass of trained and skilled manpower required for overall development of Biotechnology in the country. The Department has also developed model course

curricula through a consultative process for postgraduate programme in biotechnology. Department has also initiated special steps to start skill development programme in partnership with Indian institutions for entry level students and graduate programme in Big Data Research jointly by 5 partner Indian institutions with Heidelberg University, Germany.

The Ramalingaswami Re-entry Fellowship was conceived with the objective to improve India's human resource capacity in front line areas of life sciences and biotechnology research. The aim of the fellowship is to bring back Indian scientists working in overseas laboratories so that they can pursue their research interests in Indian institutes. During the year, 50 scientists working in overseas research institutes across the globe were selected for this fellowship. So far a total of 396 scientists have been selected in 10 batches.

To popularize biotechnology activities in India, the Department also provides financial assistance towards organizing conferences/seminars/symposium/workshops/training programmes and travel support to the students and researchers.

RESEARCH & DEVELOPMENT

Support for Basic research is essential for fostering the expansion of knowledge towards understanding developmental and disease biology, agricultural and farm based productivity, process & product development and innovation and allied areas. During the period thirty new projects were implemented. The Department has also supported centres of excellence that provide long-term support to outstanding scientists with specific goal to enhance the innovative ability of the institutions and investigators in specific areas of biotechnology.

In Agriculture Biotechnology & allied areas, the focus is on knowledge generation, technology and product development for productivity gains; enhanced

nutrition and ensuring quality; resistance to drought, salinity and high temperature; resistance to pests and diseases; input use efficiency; climate resilience and biosafety. The thrust has also been on biotechnological interventions in forestry, horticulture and plantation crops; germplasm characterization and improvement of crops using molecular biology tools. The nature and types of programs supported include product oriented basic research, translational R&D projects, national networks, centers of excellence, international collaboration, public-private partnership etc

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

In the area of Animal Biotechnology, studies were carried out to develop transgenic animals, molecular characterization of indigenous breeds, identification of urinary proteins biomarkers, various aspects of animal nutrition and utilization of animal byproducts.

In Aquaculture and Marine Biotechnology, the programmes are being implemented for enhancing aquaculture production, productivity increase and development of useful products & processes from marine resources. The broad areas emphasized are fish genomics and transcriptomics, fish and shellfish disease, immune-stimulants and antimicrobial peptides. Projects on development of bioactive molecules, biomaterials, bio-surfactants, cell lines and diagnostics were also pursued through adoption of molecular tools and techniques.

Focus area of the National Bio-resource Development programme includes inventorization and characterization on bio-resources, prospecting of bio-resources for novel genes and genes products, biomolecules and compounds, improvement of economically important bio-resources, and capacity building. Department took initiative towards development of network project

on exploration, discovery and utilization of biological resources for sustainable development in North East India. Efforts are also being made to develop programme on bio-resource documentation and utilization of Western Himalayan region of India.

The Department is also promoting R&D for biofuel technology development recognizing the need for alternate energy for transportation. Many leads have been taken forward for potential translational value in the form of Biofuel products or technologies. During the year 2017, various novel technologies were identified and supported which are able to address the current challenges associated with solid and liquid waste management. The Department is also participating in the Swachh Bharat Mission by supporting research projects on generation of energy from waste.

The aim of the Environmental Biotechnology programme is to support research and development programme in the areas relevant to waste management and environmental improvement. During the period, focus was on development of microbial technologies for environmental improvement, development of treatment process of industrial effluent, bioremediation of xenobiotic compounds. Scanning of the microbial diversity of various environments and deciphering their genetic information was also carried out with the aim of isolating microorganisms that could be used in the in bioremediation processes.

The Maternal and child health programme emphasizes 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.

Major efforts have also been made to pursue research on non-communicable diseases like chronic kidney disorders, diabetes, cancer, neurological and metabolic disorders.

The overall emphasis of the programs supported under Infectious Disease Biology is to develop preventive, therapeutic and diagnostic tools for major infectious diseases such as Malaria, Tuberculosis, HIV, Dengue, Chikungunya, Cholera, Leishmaniasis, Japanese Encephalitis, Filariasis etc.

The Department has taken major initiatives towards better management of genetic disorders prevalent in our country in terms of facilitation of diagnosis and treatment facility. Considering the highest prevalence of genetic disorders, many consortia based R&D projects on Hemophilia, Hearing loss, Thalassaemia, Cardiomyopathies, Maturity onset diabetes of the young (MODY) and many individual projects on other monogenic disorders have been initiated with the predefined deliverables.

Department of Biotechnology (DBT) has made concerted efforts in strengthening vaccine research and development since its inception in 1986-87 through various endeavours. Currently major efforts are being implemented through the Vaccine Grand Challenge Programme (VGCP) and Indo-US Vaccine Action Programme (VAP). VGCP aims 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 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. The oversight to the program is provided by the VAP Joint Working Group (JWG) comprised of eminent scientists and policymakers from both the countries. The programme is under implementation since 1987. VAP-supported research projects have directly addressed critical health problems relevant to both countries.

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.

Stem cells and regenerative medicine is one of the thrust areas under the medical biotechnology programme of the Department. The mandate is to promote basic, early and late translational research and formulation of regulatory framework for stem cell research in India.

With the aim to develop innovative, indigenous and affordable medical technologies & devices and to train researchers, innovators and entrepreneurs, the Department has also implemented Bio-design and Bioengineering programme. Bioengineering is a highly interdisciplinary area of research involving cross-disciplinary knowledge from engineering and other quantitative sciences for unravelling the complexities of biological systems and provide cost-effective solutions for improved quality of life. With a priority to study emerging diseases, to manipulate/engineer genomes, develop transgenic systems and develop genome-based diagnostics the Department significantly contributes towards Genome Engineering and Editing technologies.

Nano biotechnology provides a new frontier for scientific and technological advances to exploit

biomolecules and materials at nanoscale to address challenges related to health, agriculture, energy and environment. The Department has been engaged in promoting interdisciplinary research, fostering innovation and promoting translational research in various cutting edge areas of Nano Biotechnology.

The Department emphasizes addressal of micronutrient deficiencies, severe acute malnutrition, food fortification, probiotics for human health and well-being, food safety, molecular detection of GM traits in foods, development of low cost foods/supplements and utilization of agricultural residues for value added products and capacity building in Food Science and Nutrition Biology through a defined Public Health, Food and Nutrition programme.

The Department is supporting projects to promote use of biotechnological processes and tools for the benefit of the society comprising rural population, SC/STs and women with an aim 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. Large number of target population including youth have benefited through the implementation of these projects.

To ensure safety from the use of Genetically Engineered (GE) Organisms and products thereof in Healthcare and agriculture sectors, the Department administers Review Committee on Genetic Manipulation (RCGM) as defined under rules, 1989 of Environment (Protection) Act, 1986.

The Department has established Biotechnology Patent Facilitating Cell (BPFC) to provide administrative and financial support to biologists and biotechnologists in filing of national and international patent applications. The cell also plays a major role in creating awareness and understanding related to Intellectual Property Rights (IPR) among students, scientists and teaching professionals.

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.

National Institute of Immunology (NII), New Delhi is a premier research institute in the area of immunology and modern biology. The programs at NII undertake research of high caliber in basic and applied immunology to devise strategies for manipulation of the immune system in order to provide protection as well as intervention against diseases. The research activities at the Institute are grouped in four broad areas, namely, infection and immunity, molecular design, gene regulation and reproduction and development.

National Centre for Cell Science (NCCS), Pune has been successfully enhancing and improving the quality of research and training programs to educate the younger generation. The institute also offers services that facilitate cell biology-based research across the nation and outreach. The research focuses on understanding the operation of the cellular molecular machinery and continues to help gain valuable insights into health and disease.

Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad is a model autonomous institute with service and research components. The primary objective of the institute is to provide services in the form of specialized diagnostics and DNA fingerprinting, and to carry out fundamental research activities, where both areas complement and enrich each other.

National Institute of Plant Genome Research (NIPGR), New Delhi has been effective at generating new knowledge that has potential for genetic enhancement of crops for social benefits and in providing higher education as service to academia and society. Through its infrastructural

base and knowledge-based resources, NIPGR is poised to contribute towards frontier areas of plant biology and agricultural biotechnology.

National Brain Research Centre (NBRC), Manesar has been able to combine basic with translational research to obtain novel insights into the functioning of the brain, as well the application of this knowledge for human welfare. The application of discovery research to the clinic and community is evident from its impact in the areas of management of Acute Encephalitis Syndrome/Viral encephalitis and the screening and the remediation of learning disabilities. In Neuroscience education, the multidisciplinary programme of NBRC continues to attract those students from diverse backgrounds who are keen to gain an in depth understanding of the integrated functioning of the brain.

Institute of Bioresources and Sustainable Development (IBSD), Imphal has continued its efforts to ensure conservation and sustainable utilization of bioresources for the socio-economic development of the north-eastern region.

Institute of Life Sciences (ILS), Bhubaneswar focuses on research in the area of infectious diseases biology, various aspects of gene function and regulation, and translational research through technology development. The institute continued its efforts towards generating quality human resource through its structured Ph.D. programmes.

Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram has major research programs in the areas of Cancer Research, Cardiovascular & Diabetes Biology, Regenerative Biology, Bacterial Viral & Parasite Disease Biology, Plant & Environmental Biology, Neurobiology & Reproduction Biology, Microbiome Biology, Membrane & Cell Physiology and Computational Biology. In addition the institute has major public services arm. The institute also offers training/teaching programs in applied biology and

biotechnology.

Regional Centre for Biotechnology (RCB), Faridabad 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. A multidisciplinary PhD programme has been instituted where 25 students were admitted in the academic year 2017-18. The RCB Act 2016 has also empowered the Centre to conduct an integrated MSc-PhD degree program in Biotechnology, which will commence from the academic session 2018-19.

Translational Health Science and Technology Institute (THSTI), Faridabad 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. 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, University of Chicago etc. The Institute has also developed a vibrant public outreach programme, through open houses, public lectures and digital media.

Institute for Stem Cell Science and Regenerative Medicine (InStem), Bangalore has thrust on interdisciplinary, thematic research with translation emphasis. The institute has also engaged with various international universities/institutes to enhance its technical and scientific capabilities. The institute has established significant partnerships in the clinical settings, which have led to large centre grants with well-defined mandates in the area of translational neuroscience as well as in chemical biology.

National Institute of Biomedical Genomics (NIBMG), Kalyani 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. 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 and University of Chicago.

National Agri-Food Biotechnology Centre (NABI), Mohali has been engaged in development of designer crops with high nutrition, increased shelf life and processing quality. Nanotechnology based approaches are also being explored to address the malnutrition by constituting nano-formulations and detecting food borne pathogens. Multiple computational tools and programs are being developed to assist the researchers in identifying new candidate genes and gene functions for particular traits.

National Institute of Animal Biotechnology (NIAB), Hyderabad is harnessing novel and emerging biotechnologies and taking up research in the cutting edge areas for improving animal health and productivity. The Institute has also been engaged in human resource development across the value chain. Further, the Institute is reaching the local schools and colleges to connect NIAB scientists with national educational needs of schools and colleges.

Center of Innovative and Applied Bioprocessing (CIAB), Mohali is working on development of processes and products from secondary agriculture produce. Institute is also developing bioprocesses and innovative technologies to meet the translational need of industries. Institute is significantly contributing towards human resource generation by imparting training to students in the areas of bioprocessing and secondary agriculture.

International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi

continued its efforts encouraging innovative research in life sciences for the benefit of developing countries. Keeping focus in the three theme areas viz., Molecular Medicine, Plant Biology and Integrative Biology, the centre continues to be very active in research and maintains a high annual publication output, which covers a wide spectrum of scientific investigations. The Centre has taken several initiatives in promoting emerging and interdisciplinary areas, in developing active and close collaboration with research institutions worldwide and in enabling enhanced interactions with the industry through knowledge sharing, translational research and technology transfer.

Biotech Science Clusters: Apart from institutional set up, Biotech Science Clusters are also supported by the Department for multiscale basic and applied research in Biological Sciences.

Systems Medicine Cluster (SyMec), Kalyani has six participating institutions; National Institute of Biomedical Genomics (NIBMG) [Core Institution], Bose Institute (BI), CSIR-Indian Institute of Chemical Biology (IICB), Indian Institute of Science Education & Research (IISER), Indian Statistical Institute (ISI) and Tata Medical Centre (TMC) to investigate and understand the dynamic systems of the human body as part of an integrated whole, and identify perturbations that cause disease, in order to implement Systems Medicine using cancer as an exemplar. The efforts will provide improved tools for prediction, prevention and treatment of diseases using a Systems Biology approach; create a platform for multi-disciplinary training to build a cadre of scientific, clinical and technical personnel required to drive and to sustain Systems Medicine.

Bangalore Life Sciences Cluster, Bengaluru has partnering institutions such as 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). The cluster has been 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, Faridabad has been established at Faridabad by the Department with an overall objective 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.

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

DBT has established a North Eastern Region-Biotechnology Programme Management Cell (NER-BPMC) for conceptualization, implementation and monitoring of biotechnology programmes in NER which is helping to evolve and implement various new programmes in the area of biotechnology for the benefit of NER states. So far more than 480 twinning projects have been implemented as collaborative projects between North East institutions and the rest of India Institutions.

BIOTECH FACILITIES

The Department has made a considerable progress in establishing and creating the research related infrastructural facilities in several universities/institutions. The major facilities created are next generation DNA sequencing, Proteomics, Platform for agriculture and veterinary science, Animal Resource Facility at NCR Biocluster and facilities for educational, teaching and training purpose at various institutions. In addition, extension of the availability

of synchrotron beamline facility at Grenoble was carried out for the science community. A national facility for Gene Function in Health and Disease was established and operationalized at Indian Institute of Science Education and Research (IISER), Pune. The project involves training of personnel in University of Alabama, Alabama, USA. Furthermore, the existing repositories and depositories have been strengthened.

INTERNATIONAL COOPERATION

The Department is successfully running international collaborative programs with more than 20 countries and international philanthropic organizations in different areas of biotechnology. Continuing the collaboration with Noble Media AB, Sweden the Department organized Second Nobel Prize Series, India 2018 in partnership with Government of Goa on February 1-2, 2018 under the theme of "Education and the value of teachers". The concluding session of the Nobel Prize Series was held on February 5, 2018 at the Rashtrapati Bhawan which was graced by the Hon'ble President of India.

INNOVATION AND ENTREPRENEURSHIP

Department has also been engaged in fostering in innovation and entrepreneurship for overall growth of the sector. Department has set up biotech parks and incubators in different states across the country. 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 supporting 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. 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.

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 internal infrastructure of the Department has been renovated and modernized during the current year. The Department has gone for e-office premium version through NICS implemented in various programme division have been given training on office application through NIC.

02

**Human Resource
Development
Programme**

The Department is implementing an Integrated Human Resource Development Programme in Biotechnology comprising of post graduate teaching programme; short term training courses for upgradation of skills of mid-career scientists and UG & PG faculty engaged in teaching and R&D; industrial training of students; fellowship for doctoral and post-doctoral research in frontier areas of life sciences and biotechnology; career advancement and re-orientation for women scientists; scholarships, awards, and also assistance to researchers for organizing conference/ seminar/ symposium. Under HRD scheme, Department is generating critical mass of trained and skilled manpower required for overall development of Biotechnology in the country. The Department has also implemented skill development programmes like biotech finishing school phase-II jointly with Karnataka state government and India-bioscience-young investigators and students workshops. The Department has also developed model course curricula through a consultative process for postgraduate programme in biotechnology. Department has also initiated special steps to start skill development programme in partnership with Indian institutions for entry level students and graduate programme in Big Data Research jointly by 5 partner Indian institutions with Heidelberg University, Germany.

TEACHING PROGRAMMES

Postgraduate Teaching Programmes (M.Sc. / M.Tech. / M.V.Sc.): The post graduate teaching programmes were initiated by DBT in 1985-86 in six universities in close collaboration with University Grants Commission. These programmes were implemented on the basis of core faculty strength, expertise, infrastructural facilities, R&D grants received by proposed university on competitive funding basis, nearby institutions engaged in biotechnology R&D. 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 65 universities. Grants were provided for establishment of equipment facilities essentially required for class room teaching, recurring grants for consumables, studentship, books & journals, travel, visiting faculty, contingency, thesis grant for in-house dissertation, equipment maintenance etc. In-house dissertation has been made mandatory and Department is providing thesis grant of Rs. 50,000/- per student to ensure intensive practical training. A few research articles and reviews in journals of national and international repute and patents have come out from dissertation of M.Sc./M.Tech. students. 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. Selected candidates are offered studentships. DBT supported teaching programmes are periodically reviewed by advisory committees and by DBT-HRD task force. 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. The curriculum revision exercise is undertaken periodically to incorporate the latest developments in biotechnology. During the year, Department completed the exercise for framing model course curriculum for 13 postgraduate degree courses and circulated to all programme coordinators of DBT supported PG teaching programmes for implementation and also uploaded on DBT website

for information and adoption by universities running biotechnology teaching programmes in the country. DBT's Model Course Curriculum was released on 11th May 2017 at Vigyan Bhawan, New Delhi.

Skill Development Programme in Biotechnology: The Department has initiated new skill development programme to provide high quality hands on training in tools and techniques in multidisciplinary areas of biotechnology for entry level students (10+2 and Graduates in Biotechnology) in partnership with State Council of Science & Technology, Universities, R&D laboratories, Colleges. Department announced a call for proposal for inviting proposals from institutions and 159 applications were received for support. Proposals have been evaluated as per approved procedure of the Department.

Biotechnology Finishing School Programme: Department of Biotechnology jointly with Department of IT, BT and S&T Government of Karnataka is supporting Biotech finishing school. During the year, Department has implemented Phase-II of the programme. Department has provision to provide fellowship support to 180 candidates per year under this programme. Students are selected through online entrance test at national level and personal interview. Selection process is very stringent and all selected students are paid fellowship. This programme has been renamed as Biotechnology Skill Enhancement Programme (BiSEP) and Karnataka Government has signed MoU with Life Sciences Sector Skill Development Council (LSSSDC), New Delhi for certification of programme.

Star College Scheme: Star College Scheme has been initiated by DBT in 2008 to support colleges and university departments offering undergraduate education to improve science teaching. The programme aims to improve the skills of teachers by organizing faculty training, improved curriculum and emphasis on practical training to students by

providing access to specialized infrastructure and consumables. Star college scheme has two components viz. strengthening of support for undergraduate education and Star college status. Criteria for selection as a "Star College" are very stringent which is clear from the fact that so far only 26 colleges have been accorded Star Status out of 103 colleges supported initially, all selected colleges are supported under strengthening component for a period of 3 years and are mentored and monitored. Based on progress evaluation, colleges can be continued under strengthening component for 2nd tenure, accorded star status or discontinued. So far, 518 colleges have applied and 180 colleges have been supported under strengthening component. The scheme has pan India presence and location of colleges supported under the scheme is shown in Map of India (Fig. 1). Star college scheme has limited presence in M.P, Rajasthan, U.P, Chhattisgarh, Jharkhand.



Figure 1. State-wise colleges supported under Star College Scheme by DBT

Under the scheme, colleges are conducting practicals, which could not be conducted earlier due to lack of resources. Collaborative teachers training workshops jointly supported by DBT and British Council are being organized by IISER, Pune to train teachers in pedagogical tools, who are then expected to conduct regional workshops for training of teachers from the region.

Colleges from UP and Bihar have been supported under the scheme for the first time. This year 55 colleges got support from the scheme, which also led the number of Star Status of colleges to 26 with the grant amounting to Rs. 10.74 Crore. The Department is envisaging further upgradation in financial support structure for colleges, which would enhance the quality of learning and teaching process and also stimulate original thinking through 'hands-on' exposure to experimental work.

DBT FELLOWSHIPS PROGRAMMES FOR STUDENTS AND RESEARCH FELLOWS

DBT Junior Research Fellowship (DBT- JRF) Programme: The Department of Biotechnology initiated DBT-JRF programme in 2004 to provide opportunities for pursuing doctoral research in biotechnology for students coming out of DBT supported teaching programmes. Subsequently, the program has been expanded to cover all B.Tech, M.Sc., M.Tech students in biotech from any recognized University/Institute in the country. The program has contributed in building human resource capital and institutional capacity and nurtured excellence in basic and applied research in biotechnology. Students are selected through online Biotechnology Eligibility Test (BET) conducted at 44 centres in country. Students are selected under two Categories viz., Category I: The programme has provision to select top 275 JRF's each year in this Category. Candidates selected are eligible to avail fellowship under DBT-JRF at any university/institute in India once they are registered for PhD and 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 extramural project funds. There is no binding on institutions to select project personnel from category II. During the year, 10,781 applications were received. Merit list of 291 students in category-I and 118 students in Category-II was announced in 2017-18 (Fig.2).

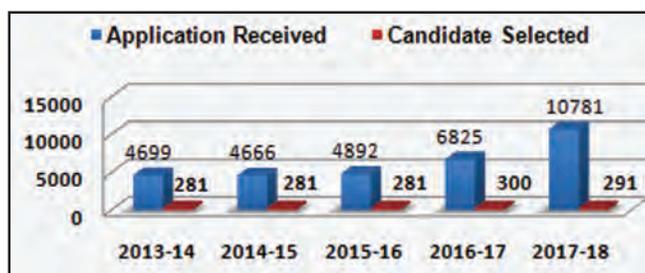


Figure 2. No. of applicants vs. selected under DBT-JRF in last five years

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 trained manpower in modern areas of biology and biotechnology and build a robust postdoctoral base in country. During the year 2017-18, in response to two advertisements, 528 applications were received and 54 candidates were selected for award of fellowship. The stringency in selection process is very evident from number of applicants selected in last five years (Fig. 3).

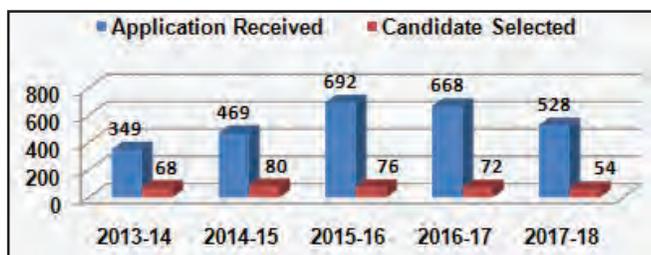


Figure 3. No. of applicants vs. selected under DBT-RA programme in last five years

Ramalingaswami Re-entry Fellowship: The objective of the scheme is to improve India's human resource capacity in front line areas of life sciences and biotechnology research; both in terms of development, translation and diffusion by means of attracting Indian scientists working in overseas laboratories. The aim of the fellowship is to bring back Indian scientists working in overseas laboratories so that they can pursue their research interests in Indian institutes. Fellows can be considered for second term on a fresh appraisal; however, those fellows who are able to seek permanent faculty positions are not considered for another term.

During the year 50 scientists working in overseas research institutes across the globe were selected for this fellowship. So far a total of 396 scientists have been selected in 10 batches. 275 fellows have already been relocated to various Indian Institutes and several of them (181) have been able to secure permanent faculty positions. Scientists selected have been able to publish their findings in peer reviewed journals.

Publications: Total No. (2017-18): 155 || Impact factor < 5: 125 || Impact factor \geq 5: 30 || Spin off Company: 2

Wellcome Trust/ DBT India Alliance: The Wellcome Trust/DBT India Alliance is an equally funded partnership between The Wellcome Trust (UK) and the Department of Biotechnology, Ministry of Science and Technology, Government of India. It aims to improve the biomedical research landscape

in India through mechanisms that support exceptional researchers at Indian institutions, and facilitate the recruitment of highly trained and qualified scientists from overseas. This is done through (1) a Fellowship Programme with three types of fellowships (early, intermediate and senior), (2) a culture of transparency, international quality and timeliness to grants management, and (3) effective engagement to develop the next generation of research (and policy) leadership.

During 2017, 45 Fellowships were awarded to scientists at 31 different institutions in 15 Indian cities. India Alliance Fellows also received prestigious national and international awards and recognitions during 2017, which include SERB Women Excellence Award; Howard Hughes Medical Institute International Research Scholar; EMBO Young Investigator and Shanti Swarup Bhatnagar Award. Fellows published 96 peer-reviewed papers in high-ranking international journals and made further impact through translational and policy-oriented research.

India Alliance organized seven one-and two-day Science Communication workshops that trained more than 400 PhD students and postdoctoral researchers. A two-day Visualizing Science workshop introduced 50 scientists and those in allied fields with visual tools and methods to effectively convey their research. The first Developing Indian Physician Scientists (DIPS) workshop introduced 37 young doctors to research methodology and discussed the relevance of biomedical research and career options. Through its India EMBO Symposia funding scheme, India Alliance (and EMBO) has funded four meetings in India that aim to address discovery and innovation in life sciences through an interdisciplinary approach. Various public engagements with science events were supported. These include - (1) *Actors and Doctors: Staging Public Health matters* that used theater to initiate a two-way learning process between social and scientific enquiry and to make

health research more accessible to the public; (2) *Life of Science: chronicling the lives of women scientists in India*, to highlight the work and challenges faced by women scientists and to showcase them as role models for young girls; (3) *Art + Science programme* designed to advance projects that explore artistic applications of emerging thoughts and technologies with the help of partners from the science academia and industry.



Fig. 4. L-R: (1) Participants with a Mentor at the 2-day Science Communication workshop, New Delhi. (2) Fellows' meeting; Hyderabad

Tata Innovation Fellowship: The department initiated the scheme in 2006 to reward the scientists/researchers engaged in innovation and in the pursuit of path breaking solutions to major challenges, interdisciplinary work and with an emphasis on

translational research in life sciences, agriculture, biomedical science and related areas of biotechnology. The awardees are provided a fellowship in addition to regular salary and annual contingency grant. The duration of the fellowship is initially for three years which can be extended further by two years on a fresh appraisal. A maximum of five fellowships can be provided in a year. Altogether, 52 scientists have been awarded the fellowship since its inception. For current year, advertisement has been published for inviting applications for selection of Tata Innovation Fellows.

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 awardee 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 2017, out of 14 nominations received, two awardees were selected for two awards of Rs. 2.00 lakh each.

National Women Bioscientist Award: The National Women Bioscientist Awards are given every year under two categories. These are (i) National Women Bioscientist 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 Bioscientist 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.

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 @ Rs. 5.00 lakh per year for a period of 03 years. Upto 10 Awards are given every year, subject to the availability of suitable candidates.

DBT Biology Scholarship: DBT 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 one time scholarship is Rs. 20,000/- per student selected for the purpose and a maximum of upto 100 students are selected for this scholarship each

year. The Award also carries a medal and a certificate of merit.

The Innovative Young Biotechnologist Award (IYBA): The Innovative Young Biotechnologist Award (IYBA), initiated in 2005, is a career-oriented award to identify and nurture outstanding young scientist 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 also includes scientists without regular employment. Since its inception more than 120 researchers have been supported by this scheme. Post financial (SFC) approval, the programmes would observe increased grant allocation for young scientists. Efforts are being made to bring all the IYBA awardees on a platform where regular exchanges of ideas, technology and innovations may be done.

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 20-25 participants. During the year, 17 programmes were supported.

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 in biotech industries. 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. During the year, total 2167 applications were received and 900 candidates were selected for industrial training. Around 125 companies are involved in imparting training. Department is providing stipend of Rs. 10,000 p.m. to all selected candidates and bench fee of Rs. 50,000 to trainer companies. This programme is very popular among biotech students as is evident from number of applications received in last five years (Fig.5).

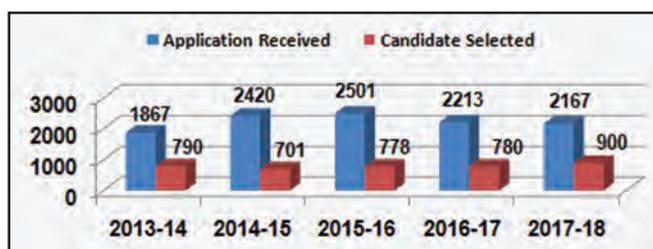


Figure 5. Number of applicants and candidates selected for six months industrial training in last five years.

RESEARCH OPPORTUNITIES FOR WOMEN SCIENTISTS

Biotechnology Career Advancement and Re-orientation (BIOCARE) Programme for the Women Scientists: The programme was initiated in the year 2011. Four calls have been announced so far. 315 women scientists (165 unemployed and 150 employed) have been supported so far. Out of 165 women scientists who were unemployed at the time of getting their respective BioCARE projects, 17 have got permanent employment. More than 100 papers have been published. 2 patents have been filed and 2 are under process for filing.

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 with domicile of North-East or those who have studied for past 3 years in university/institute in North Eastern states under two

programmes viz., DBT-RA and DBT-BITP.

DBT-RA for North East: The Programme is being coordinated by Indian Institute of Science, Bengaluru. During the year, total 64 applications were received and 16 candidates were selected for award of DBT-RA Fellowship.

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 101 applications were received and 69 candidates were selected for training.

INDIA BIOSCIENCE-YOUNG INVESTIGATOR MEETINGS AND STUDENTS WORKSHOPS

Department is supporting meetings and workshops for young investigators (Teachers and Scientists), Post-Doctoral Fellows and PhD students. The objective of this programme is to promote and disseminate information about R&D environment and opportunities in Biotechnology sector in country. The programme features included seminars, posters and panel discussions that focus on a wide variety of topics ranging from choosing the right research problem, publication, personnel management, funding opportunities and mentorship. Senior scientists describe their own scientific journey in meetings and workshops. During the year, Department has supported India Bioscience-Young Investigator meetings and student workshops phase-II programme at NCBS, Bangalore.

SMART INDIA HACKATHON

Ministry of Human Resource Development, New Delhi initiated Smart India Hackathon 2017, a unique

initiative to identify new and disruptive digital technology innovations for solving the challenges faced by Government Department/Ministry. The objective of programme is to institutionalize a model for harnessing the creativity and technical expertise. During the year, Department of Biotechnology identified 17 problems seeking digital solutions and projected for participation in Smart India Hackathon 2017. The 36 hours non-stop digital competition was held on 1st and 2nd April 2017 at C.V. Raman college of Engineering, Bhubaneshwar, which was identified as the Nodal Centre for Ministry of Science and Technology. The software prototype created by student's teams in Hackathon were evaluated by judges drawn from the respective ministry, industry and academic experts and the best solutions were awarded @ Rs. 1 lakh, Rs. 75,000 and Rs. 50,000 for the top three teams respectively. Department has selected two prototypes proven by student teams in digital competition for further support.

showcase the achievements of Indian science and technology organizations and R&D institutions in the field of biotechnology to the general public, students, researchers, business community, etc.

POPULARIZATION & PROMOTION OF BIOTECHNOLOGY

The programme envisages financial assistance towards organizing conference/ seminar/ symposium and 'travel support' to the researchers for presenting their papers in the conferences organized outside the country. It also extends support for organizing popular lectures, and exhibitions held within the country as well as outside the country.

In the year 2017-18, 529 proposals (Conferences-106, Travel-407, Exhibitions-09, Popular lectures-07) with financial support of almost Rs. 5.0 crore have been supported by DBT. Guidelines for applying through this program have also been changed for better management and smooth functioning of work. Further, DBT also participated in prestigious national and international events such as Indian Science Congress, Bio USA 2017, India International Science Festival-2017, etc. The prime objective behind Department's participation in these events is to

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Biotech Facilities, Technology Platforms & Research Resources

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, and linking research to education at every opportunity through creation/reengineering/remodelling/up-gradation of life science departments in central/state universities.

BIOTECH FACILITIES

The outcome of the research activities supported for strengthening the research infrastructure in Universities and Institutions are as follows;

A Bemline-14 Program Coordination Unit (DBT-BM14-PCU) at Regional Centre for Biotechnology, Faridabad has been supported by the Department for providing access to Indian Scientific community to synchrotron X-ray Beam line (BM14) in Grenoble, France. To provide continuous access to the Indian scientific community, a new agreement has been signed between European Synchrotron Radiation Facility, Grenoble, France and Regional centre for Biotechnology (RCB), Faridabad, India. The agreement facilitated the access to six high intensity beam lines and SAXS Facility. During the year, 75 new proposals have been considered for data collection. The total number of crystals shipped is 2782 and the total number of data sets collected was 786 with deposition of 118 structures in PDB database. A total of 62 peer reviewed publications came out of this support.

The Department supported renovation and maintenance of National Repository for Filarial Parasites & Reagents at Mahatma Gandhi Institute of Medical Sciences, Sevagram, MH. A series of synthesized compounds (thiazolidine and thiazine) obtained from other collaborators were screened

(total of 21 compounds) against *Brugia malayi* microfilariae. Out of the 21 compounds screened, only four were found to be pharmacologically effective as displayed by their impact on loss of motility of the parasites in *in vitro*. The present study on testing different filarial molecules as vaccine candidates using rodent model (mastomys) helped in confirming the vaccine potential of BmALT2 (*B. malayi* vespid venom Allergen homolog-like protein) and BmPO.

A Tuberculosis Aerosol Challenge facility has been supported for maintenance at International Centre for Genetic Engineering & Biotechnology (ICGEB), New Delhi. In addition to the DBT supported FACS sorter, ICGEB has also been supported for upgradation of an existing high-content screening platform as a national facility.

The Department launched DBT-BUILDER (Boost to University Interdisciplinary Departments of Life Sciences for Education and Research) scheme for upgradation/reengineering/remodelling/creation of Life Science departments in central and state universities to boost advanced education and promotion of interdisciplinary research and technology development. Till now, 25 universities received support under this programme. The programme is now merged with Research Resources, Service Facilities and Platform as per the recommendations of the Expert Committee constituted for evaluation of schemes/programmes of the Department for continuation beyond 12th Plan. The progress reports of some of the supported universities are ●at Guru Ghasi Das Vishwavidyalaya, Bilaspur, Chhattisgarh, the teaching and research laboratories have been strengthened; ● at Anna University, Chennai, Tamil Nadu, the teaching and research laboratories have been tremendously boosted and the major infrastructure has been established; ● at Patna University, Bihar, Central Instrumentation facility has been established for Department of Biotechnology. In addition, one

research corridor in Dept. of Botany and one state-of-the-art laboratory renovated in Dept. of Biotechnology; ● Support at Jawaharlal Nehru University, New Delhi resulted in the maintenance of 26 cutting edge equipment of Advanced Instrumentation Research Facility (AIRF), and classroom training of quality manpower through workshops/seminars and advanced courses. 17 workshops were conducted for more than 300 graduate & post graduate students, research scholars, post-docs and faculties on state-of-art equipments including Atomic Force Microscope (AFM) with Confocal Raman spectroscopy, Field Emission Scanning Electron Microscope (FESEM) and FESEM based e-beam lithography at AIRF; ● at Kuvempu University, Karnataka, existing plant tissue culture laboratory and mycology laboratories were upgraded with construction of central instrumentation laboratory. Survey and documentation of medicinal plants was carried out in the forest ranges of Kigga range, Kargal range and Hosagunda Sacred Grove range, Kemmangundi forest area and Mookambika Wild Life Sanctuary. Herbarium of 500 species was prepared, documented and maintained. Micropropagation and mass multiplication of endemic medicinal plants like *Mammea suriga*, *Bredelia scandense*, *Ceaesalpinea bunducella*, *Celastrus paniculata*, *Litsea glutinosa*, *Buchananea lanzan* was achieved. Toxicity studies of phytochemicals have also been evaluated for anticancerous property.

A partnership platform for contemporary research, services and skill development in advanced life science technologies has been established in SRM University, Tamilnadu. GLP complied facilities have been established for providing service as well as for skill development. The platform is being utilized by the faculties from SRM and other academic institutions. Till now whole genome sequencing (4), whole exome sequencing (4), whole transcriptome sequencing (10), Cytokine analysis (400) and Chemokine analysis (200) have been carried out. A

PG diploma course with focus on technical skill development in association with biotech industries started in August 2017. Two hands-on training workshops on qPCR and advanced molecular platforms was conducted. The Facility services have been offered to institutions - Karolinska Institutet, Sweden; Mahatma Gandhi Medical College, Pondicherry; Sri Ramachandra Medical College, Chennai and JSS Hospital, Mysore.

A national facility for Gene Function in Health and Disease was established and operationalized at Indian Institute of Science Education and Research (IISER), Pune. The project involves training of personnel in University of Alabama, Alabama, USA. The building has been made operational along with desired equipments (Figure 1). Import of transgenic Mice from Jackson Laboratory, USA; University of Heidelberg, Germany and The Scripps Research Institute, USA has been done and well established colonies are being used for experimental purpose. Immune-compromised and other oncology models have been received and the expansion of these strains is in process. Multiple *Drosophila* and zebra fish strains are also being maintained in the facility.



Figure 1. National Facility for Laboratory Model Organisms at IISER, Pune for generation of transgenic knockout animals and providing services.

The Department supported a partnership project with Indian Institute of Science (IISc), Bangalore for advanced research in Biological Sciences and Bioengineering. This support has further

supplemented 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. Under the said project number of facilities like Bio-imaging, 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, Bioimaging Facility were established. The facility caters to 14 departments. The facility organized six teaching and training programmes and resulted in 20 peer reviewed articles from this facility. The facility also provides open access to non-IISc academic and corporate users.

A Biosafety Level-3 (BSL-3) facility consisting of three labs for *in-vitro* work and one small infection-cum-necropsy room for animal experiments has also been supported by the Department. Currently, more than 40 students from different laboratories of IISc are using this facility. The facility provides services in the area of animal experiments, training, health checkup, teaching and holding open day session at IISc to spread awareness about infectious diseases among youth from various schools and colleges of Bangalore. It has resulted in publication of 4 scientific articles in high quality journals.

CENTRE FOR CELLULAR AND MOLECULAR PLATFORMS (C-CAMP), BANGALORE

Centre for Cellular and Molecular Platforms (C-CAMP) was instituted in June 2009 with the mandate of enabling cutting-edge research by making available state-of-the-art technologies and providing training on these platforms. 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 (BLiSC) 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.

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.

Technology Platforms & Activities: From inception 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; • Proteomics Facility; • Glycomics and Glycoproteomics Facility; • Metabolomics Facility; • Drosophila Facility; • Microfluidics & Microfabrication Facility; • Next Generation Genomics Facility; • Electron Microscopy Facility.

These 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 research publications. Further, 27 technologies are available for Licensing through C-CAMP. This year, C-CAMP organized 9 hands-on training programmes (till March 2017) across different technology platforms.

Innovation & Entrepreneurship: As a part of the

mandate of promoting innovation and entrepreneurship, following activities have been undertaken by C-CAMP

a) Funding & Mentorship: C-CAMP has partnered with BIRAC, DBT to help with the Biotechnology Ignition Grant (BIG) scheme that funds start-up companies and individual scientific entrepreneurs to establish proof-of-concept, nurture and transform these innovative ideas into viable competitive products and enterprises.

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) Discovery to Innovation Accelerator: C-CAMP builds on its Discovery Innovation Accelerator program which focuses on making early stage discoveries from academic laboratories to make them “industry ready” and to take them closer to the market through a possible license or spin-off.

Achievements:

- Received National Award for Entrepreneurship 2017 (Govt. Category) from Ministry of Skill Development and Entrepreneurship



Figure 2. National Award for Entrepreneurship 2017 from Ministry of Skill Development and Entrepreneurship

- Received Niti Aayog AIM funding for scale-up incubation programme
- Received BREC centre with BIRAC funding
- Funded 20 innovative biotech start-ups/spin-

offs

- Incubated 14 start-ups/spin-offs
- Till date, C-CAMP has supported nearly 90 start-ups/spin-offs through funding, incubation and mentorship.



Figure 3. A collage depicting start-ups/spin-offs supported by C-CAMP

ADVANCED TECHNOLOGY PLATFORMS CENTRE

The Advanced Technology Platforms Centre (ATPC) in the NCR Biotech Science Cluster at Faridabad is managed by the Regional Centre for Biotechnology. The aim of the ATPC is to provide an access to cutting-edge technologies to biotech science researchers in India. The centre will also provide support to start-up biotech companies that will be part of the planned Bio-Incubator within the Bio-Cluster. Based on inputs from a Committee of Experts, the following facilities are envisioned at the ATPC: (i) Mass Spectrometry Facility, (ii) Molecular Interactions & Protein Purification Facility, (iii) FACS facility, (iv) Electron Microscopy Facility, (v) Optical Microscopy Facility, (vi) Genetics & Genomics Facility, (vii) Animal Experiment Platforms, and (ix) Liquid Nitrogen Dispensing Facility. The FACS facility, the protein purification facility, and the Mass Spectrometry facility are currently operational and processing samples from different

facilities are in advanced stages of procurement and will be installed soon at the ATPC. The first round of personnel hiring has occurred and the recruited ATPC staff will accelerate the development and execution of robust workflows for different facilities. The ATPC will be fully functional within a year and greatly accelerate innovation in the Bio-Cluster and other research institutes in India.

CENTRE FOR CHEMICAL BIOLOGY AND THERAPEUTICS

The Centre for Chemical Biology and Therapeutics (CCBT) is an integrated multidisciplinary research initiative that aims to pioneer new approaches to create small-molecule tools that target novel classes of targets, and use them to conduct hypothesis-driven research on experimental systems of biomedical importance. The CCBT's long-term vision is to foster knowledge-driven therapeutic interventions for important human diseases through fundamental new insights into disease biology.

The CCBT is funded by the Department as an inter-institutional collaborative centre between inStem and NCBS. The CCBT's first scientific focus is to explore new approaches for the modulation of intracellular signalling pathways disrupted in disease, by targeting the molecular recognition of key classes of post-transcriptional protein modifications.

Salient achievements:

- Protein domains recognizing pSer/pThr (tandem (t)BRCT domains from BRCA1 or ECT2) or pTyr (theSH2 domain from GRB2) have been expressed, purified and structurally characterized in their apo- or ligand-bound forms using computational modeling and X-ray crystallography. This work has identified key features underlying molecular recognition by the tBRCT domain family, which provides insight into the discrimination of pSer versus pThr, and exposes characteristics underlying selective

substrate recognition by different family members.

- A focused chemical library comprising ~130K elements has been designed, sourced and organized in an appropriate LIMS system. High-throughput primary screening assays (using fluorescence polarization) with Z scores $e^{0.6}$ against different domain targets were developed, and over 1 million *in vitro* screening reactions have been completed. Over 400 active compounds that selectively inhibit molecular recognition by either the BRCT or SH2 domains were identified, and taken forward into hit validation through orthogonal assay development for different domain targets.

The overall outcome of these programmes has been to deliver, in a stepwise fashion, a palette of novel chemical probes that selectively modulate the molecular recognition of pSer, pThr or pTyr-containing substrates in order to systematically explore how this mechanism contributes to intracellular signalling. These programmes also establish a powerful interdisciplinary capability for chemical biology and therapeutics development in the inStem/NCBS campus.

Collaborations:

- A new target that inhibits the liver cycle of the malaria parasite *P. vivax* – The inter-disciplinary capability for chemical biology and therapeutics development developed in the CCBT has spawned collaboration with NCBS.
- Molecular recognition of phosphopeptide substrates – The availability of novel, selective inhibitors of phosphopeptide substrate recognition by the BRCA1 tBRCT offers an exciting opportunity to systematically explore the contribution of this mechanism to DNA replication and repair. The CCBT is embarking for collaboration with ETH, Zurich in which

approaches in protein mass spectrometry will be used to provide systems-level understanding of the function of specific tBRCT ligands during these biological processes.

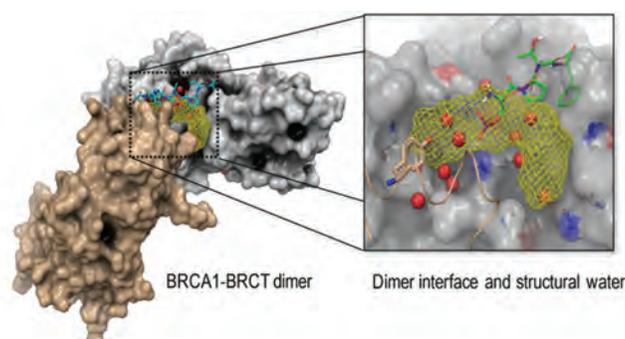


Figure 4. Structure-guided lead discovery of a protein-protein interaction (PPI) inhibitor. The schematic shows the structure of the tandem (t)BRCT domain of BRCA1 (left panel) and an enlargement (right panel) of the dimer interface with structural water (red dots). The yellow wires depict the novel binding pocket that has been explored through structure-guided lead discovery to develop Bractoppin, a first drug-like inhibitor of phosphopeptide recognition by tBRCT domains, with nanomolar potency *in vitro*, that selectively engages its target to modulate intracellular signalling

- Reversing inactivation of the FOXO3 tumor suppressor during carcinogenesis – The CCBT’s capabilities for structural biology and chemical library screening have led to a new collaboration with the MRC Cancer Unit, Cambridge and the Cambridge University spin-out company, PhoreMost, to characterize a potential new target in this pathway.

CENTRE FOR NEURODEVELOPMENTAL SYNAPTOPATHIES (CNS)

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-behaviour.

The Centre continue to generate new rat models of

highly penetrate single-gene causes of ASD/ID to better model autistic and cognitive behaviours that can accurately reflect autistic features in humans. The focus is on Fragile X Syndrome (FXS) as well as mutations in key glutamate receptors and their primary signalling pathways as prototypic causes of ASDs. A detailed characterisation of post- and pre-synaptic defects in the amygdala of the rat models of Fragile X Syndrome (FXS) has led to identification of deficits in activity-dependent synaptic plasticity in the amygdala. Researchers are also exploring the possibility of rescue of deficits, using oral treatment with Lovastatin, in the developmental acquisition of associative memory in the rat model of FXS. The results demonstrated that Lovastatin administration restores normal associative memory which is maintained 4-months after treatment cessation. This behavioural rescue is associated with a rescue of plasticity and protein synthesis deficits, providing proof-of-concept evidence that neurodevelopmental disorders may be amenable to transient, early intervention to restore the normal brain developmental trajectory. These results are of therapeutic significance because Lovastatin, which reduces the amount of cholesterol made by the liver, is already approved for use in humans. Further an *in vitro* system based on human induced pluripotent stem cell (iPSC) has also been established to study cellular and synaptic mechanisms underlying ASD/ID and is also used for potential high throughput screening of pharmaceutical compounds. Using a combination of whole-cell patch clamp recordings and microscopy, the scientists at CNS are trying to understand whether human cortical neurons recapitulate known physiological and anatomical milestones and, if so, whether these milestones are reached in human iPSC-derived neurons from affected individuals.

Using the rat models, the Centre demonstrated that several key cellular deficits in hippocampus that result from *Fmr1* deletion, are conserved between

species that separated in evolution more than 12 million years ago. The study also suggested that the loss of FMRP selectively affects a subset of hippocampus-dependent processes that include memory/binding of complex associations. Behaviourally, *Fmr1*-KO rats show deficits in hippocampal-dependent, but not hippocampal-independent, forms of associative recognition memory indicating that the loss of FMRP causes defects in episodic-like memory.

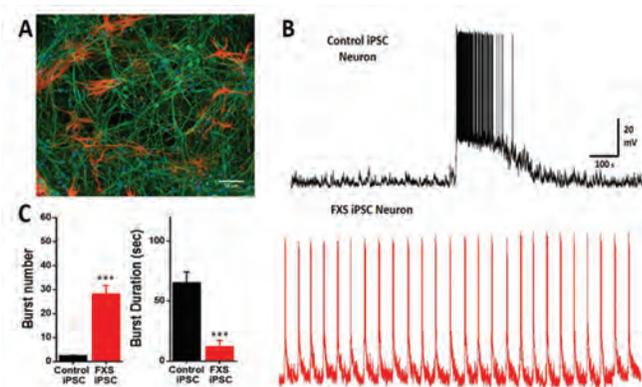


Figure 5. (A) Human iPSC-derived cortical neurons (green, *Map2ab*-positive) from a FXS patient co-cultured with rodent cortical astrocytes (orange, *GFAP*-positive) for 8 weeks in vitro. (B) Top: Burst of action potentials fired by control cortical neurons. Bottom: Burst of action potentials fired by FXS cortical neurons. (C) Quantification of action potential burst properties recorded from control and FXS cortical neurons.

NATIONAL MOUSE RESEARCH RESOURCE (NaMoR)

The National Mouse Research Resource (NaMoR) has been established at NCBS, Bangalore by the Department as a 'National Facility' for providing cutting edge technology, space and services to scientists using a range of laboratory animal based models in biomedical research.

NaMoR has a state-of-the-art facility with two different levels of Specific Pathogen Free (SPF) environments in the high barrier animal facility (SPF1-highest pathogen exclusion level; and SPF2-intermediate pathogen exclusion level). This allows the flexibility to have a more accessible SPF2

environment for dedicated breeding and experimental procedures on standard animals while maintaining the foundation stocks and certain high-end animal procedures in the highest SPF1 standards in a much more restricted and controlled environment. One animal room has also been redesigned to host Animal Biosafety Level-2 work (for dedicated risk-2 pathogenic or chemical work on animals). Staff and users are being trained to work in these different SPF level and Biosafety level environments. There are two microinjection stations in the facility for performing the transgenic techniques. The embryo transfer procedures have been standardized using a series of dissection stereomicroscopes with a camera and monitor. These micro-surgery platforms are also being used when doing demos/trainings/workshops for other staff members or trainees across the country.

04

**Research &
Development**

BASIC RESEARCH IN MODERN BIOLOGY

Basic research is essential for fostering the expansion of knowledge. The Department through Basic Research in Modern Biology has been funding basic research in a variety of biological science fields with a goal of exploiting new knowledge to enhance- and wherever possible, transform-future capabilities. During the period, thirty new projects were implemented. Further, support to on-going projects resulted in publication of several research papers in high impact journals. In addition, the division has also supported centres of excellence that provide long-term support to outstanding scientists with specific goal to enhance the innovative ability of the institutions and investigators in specific areas of biotechnology. Noteworthy achievements of some of the projects are presented below:

Study initiated on CS- induced atherosclerosis at the molecular and cellular level at University of Calcutta, Kolkata for the first time describes the preventive role of melatonin in combating CS-induced atherosclerosis in Guinea pigs that were fed with melatonin supplemented diet (Fig.1). The insights gained in this study may help for the better management of public health.

CS	-	+	+
Melatonin	-	-	+

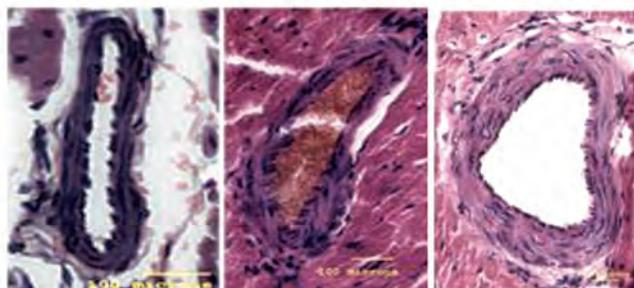


Figure 1. Melatonin prevents CS-induced atherosclerosis in guinea pig. Figure presents H&E stained guinea pig aortal sections obtained from differentially treated animals.

In a study carried out at IIT Bombay, hydrogen peroxide (H_2O_2) was identified as an important pneumococcal virulence factor, enabling their improved survival within the Blood-Brain Barrier (BBB) endothelium. Identification of virulence attributes crucial for pathogenesis and is expected to help in the development of novel treatment strategies to combat pneumococcal infections.

The tumor suppressor *TSC1* is down-regulated in oral cancer. Therefore, upregulation of *TSC1* could be a key therapeutic strategy to ablate/reduce oral tumor size. Researcher at IISc Bangalore, using bioinformatics approaches, have identified miR-130a as a potential post-transcriptional regulator of *TSC1*, suggesting that *TSC1* could be upregulated by a synthetic anti-miR-130a. .

RAF kinases participate in MAPK signaling pathway aided in cell growth, proliferation, and differentiation. CRAF mutations activate this pathway that leads to various diseases including Noonan syndrome, cardiac hypertrophy and cancer. Research work being carried out at Bose institute, Kolkata established the role of Hsp90 and its co-chaperone Cdc37 in maintaining CRAF kinase stability and activity by facilitating Ser-621 phosphorylation of CRAF. Moreover, it was found that Hsp90 facilitates CRAF activation during growth factor mediated stimulation. It was also found that co-chaperone HOP is not required for CRAF stability, but it is crucial for maintaining CRAF activity suggesting that HOP could be a potential target instead of Hsp90 to combat RAF mediated rasopathy.

Sphingolipids are a class of lipids present in all living systems. They play several important roles in normal physiological functions. However, mutations affect genes involved in the metabolism of sphingolipids and change in their levels observed during disease conditions. In ongoing research at RGCB, Thiruvananthapuram a molecule (FTY720) which affects sphingolipid metabolism and inhibits the

growth of pancreatic cancer in mouse models have been identified. Combining FTY720 along-with currently used chemotherapeutic drugs was found to be more effective.

Studies being carried out at IIT, Bombay, Mumbai to understand the effect of p38 signaling pathway on cell cycle regulation have produced permanently FUCCI transfected (by using Lenti-Viral constructs) cell lines (Hela and MCF-7) to observe cell cycle phase distributions and the overall cell cycle time change in proliferative as well as in a serum starved situation continuously for 2-3 days under the microscope at the single cell level (Fig.2).

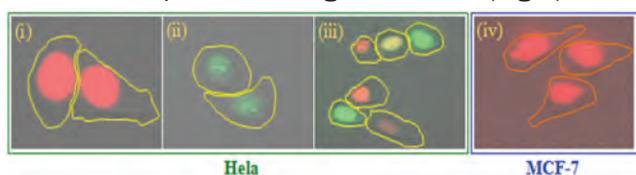


Figure 2. Single cell images under the microscope of HeLa cells((i)-(iii)) and MCF-7 cells (iv) are shown. (i) RFP and GFP fluorescence are observed mostly in the nucleus of 2 individual HeLa cells when cells are excited separately to red and green laser sources. (iii) 3 individual HeLa cells (on top of the figure) are captured in G1 phase (leftmost, red), S-G2-M phase (rightmost, green) and while transiting from G1 to S phase (middle one, yellow) having different coloured nucleus. (iv) RFP fluorescence is observed mostly in the nucleus of 3 individual MCF-7 cells when cells are excited with only red laser source. (All the images are taken at 40X magnification and each with 15 minutes interval and In all the frames, yellow (for HeLa cells) and orange (for MCF-7 cells) lines are drawn just to give a rough idea of the cell morphologies)

Hepatitis C Virus (HCV) infection is one of the major liver diseases and is a global health concern. One of the potential targets for HCV inhibitors is the highly conserved 5'-untranslated region (5'-UTR) of the viral genome which harbors IRES (internal ribosome entry site). Researchers working at IICB, Kolkata have successfully designed HCV IRES inhibitors based on quinoxaline molecules which are effective in reducing the viral cap independent translation in low micromolar range. In future these compounds can be used as effective therapeutics and diagnostics.

Centre for Excellence/ Institutional Programme Support-Basic Research: The salient achievements in some of the ongoing programme support are as follows:

Protein Misfolding In Neurodegenerative Disease: Prion diseases, also known as transmissible spongiform encephalopathies, is a group of fatal neurodegenerative disorders linked with the misfolding and aggregation of the prion protein (PrP). The ongoing research in the area at NCBS, Bangalore has led to the characterization in unprecedented details of how misfolding and aggregation of the prion protein commences. Results have led to a simple biophysical explanation for why a specific mutation in the disordered region of the prion protein is protective against prion infection. **Integrative Approaches to Understand Structure, Stability and Function of Bacterial Toxin-Antitoxin Systems:** Under this institutional programme support project being implemented at IISc, Bangalore, comprehensive fold recognition of toxin-antitoxin (TA) complexes has been used to construct structural models for several TA complexes and to identify novel TA systems in *Mtb* and *E. coli*. Novel saturation and saturation suppressor mutagenesis methodology has been developed to identify residues present at protein:ligand interfaces.

AGRICULTURAL BIOTECHNOLOGY

The mandate of Agriculture Biotechnology program is knowledge generation, technology and product development for productivity gains, enhanced nutrition and ensuring quality, resistance to drought salinity, high temperature, resistance to pests and diseases, input use efficiency, climate resilience and biosafety. The nature and types of programs include product oriented basic research, translational R&D projects, national networks, autonomous institutions, grand challenge program, centers of excellence, international collaboration, public-private partnership etc.

Under major initiatives, during the period the

department has supported new projects on improving oil quality and productivity in Groundnut, genome wide association study in *Phaseolus vulgaris* – *Colletotrichum lindemuthianum* pathosystem, development of genetic stocks for maturity and growth habit genes in Soyabean. Network programs were supported on double haploid platform for accelerated maize breeding, hybrid development and enhanced genetic gains in South Asia, marker-assisted breeding and mapping of QTLs for drought tolerance in wheat, genomics-assisted introgression and field evaluation of rice varieties with genes/QTLs for yield under drought, flood and salt stress, characterization, race profiling and genetic analysis of wheat powdery mildew pathogen in India. In order to establish a centre/facility for Molecular Characterization and Genomics Services for Marker Assisted Breeding and Crop Genome Characterization, a group discussion with experts was also conducted to discuss proposal. Major achievements during the period are as follows:

Cereals:

a) Rice: A herbicide tolerant mutant of Nagina 22, (named as *Robin*) identified, mapped and characterized earlier is being used in marker assisted backcross breeding program to introgress herbicide tolerance in 10 varieties of rice viz. PB1121, PB 1509, Sahabghagidhan, Naveen, Pooja Swarna-Sub1, CO 51, Anna, CB 06803 and CB 08702. The rice variety PB1121 NILs with stable herbicide tolerance, 98% genome recovery and Basmati cooking quality is in BC₄F₃ generation and its field trials is expected by June 2018 through AIRCP. Promising mutants identified for better phosphorous use under low P conditions were characterized with highest grain. Three promising mutants identified for sheath blight tolerance. Whole genome sequence of Nagina 22 has been generated to the tune of 170x depth, comprising of both long and short reads. A genome browser to enable both forward genetics and reverse genetics is under development.

The functional impact of the genes showing variety specific drought response in various tissues of rice varieties viz. Nagina 22 and IR64 was analysed at UDSC, New Delhi. It was observed that drought mediated dynamism in rice variety-specific indicating that rice varieties do maintain a distinct and dynamic epigenetic profile wherein histone modifications play an important role. Further analysis and integration is being done to establish the impact of epigenetic modifications in regulating variety specific responses.

b) Maize: In an attempt to enhance nutritional quality of maize through molecular breeding, backcross populations of HKI193-1 and HKI163 (parental inbreds of HQPM-1) targeted for introgression of favorable allele of *crtRB1* and *lcyE* for enrichment of provitamin-A in QPM background. Progenies with >90% recurrent parent genome (RPG) were recovered. The mean provitamin-A content in MAS-derived progenies was 13.34 µg/g and 14.11 µg/g, compared 2.46 µg/g and 2.06 µg/g in HKI163 and HKI193-1, respectively.

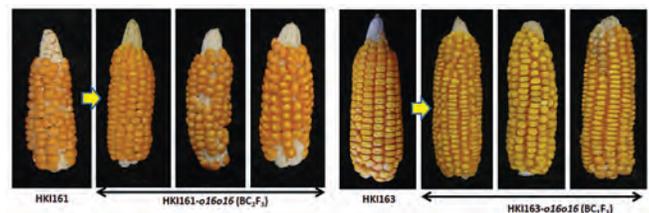


Figure 3. Ear and grain characteristics of o2o2/o16o16 progenies in comparison to o2o2 parents.

c) Wheat: At Directorate of Wheat research, Karnal, a project was initiated for improving biscuit making quality of wheat in North Western Plains using MAS. Prebred PBW373 and UP2425 lines developed by crossing Nap Hal as source of Glu-D1 double null during 1st phase of the project were used for Glu-D1 donor as main activity. Micro level tests for gluten strength (micro sedimentation test) and grain hardness were also employed for selecting desirable segregants for weak gluten and soft grain characteristics for advancing into higher generations. Advanced materials were also evaluated for baking

tests and desirable lines with high biscuit spread factor were identified for further testing under station and national trials.

d) Barley: In a study carried out by scientists at Punjab Agricultural University, Ludhiana for characterization and molecular mapping of aphid (*Rhopalosiphum maidis* Fitch.) resistance in barley, advanced filial generation of a cross between BK 9816 (aphid resistant) X PL 426 (aphid susceptible) has been maintained. The results of studies on mechanism of aphid resistance revealed that resistant lines markedly altered the behavior, reproduction and development of aphid and possess both antixenosis and antibiosis type of resistance.

Oil Seeds:

a) Groundnut: In an effort to biofortify long chain polyunsaturated fatty acids in peanut by metabolic engineering of fatty acid biosynthetic pathway the bi-cistronic construct with two *FAD* genes under a single oil-body specific gene promoter was prepared and used for transformation.

b) Mustard: In an attempt to develop low sinapine mustard (*B. juncea*) lines through antisense and RNAi technology, scientists at Delhi university have adopted transgenic approach for gene silencing by targeting two genes involved in the final two steps of sinapine biosynthetic pathway. These two genes were isolated from *B. juncea* and eight silencing constructs were developed using three different RNA silencing approaches. Reduction of seed sinapine content in these lines ranged from 15.8% to 67.2. Two low sinapine transgenic lines (homozygous) DSW have been established which can be used as product.

Pulses:

a) Chickpea: The Challenge Programme on Chickpea Functional Genomics (CPCFG) has been undertaken as a sequel to the completed whole genome sequencing of chickpea with the objective of applying

the available sequence information for crop improvement. Identification of long non-coding RNAs has been optimized and 2248 lincRNAs have been identified during flower development. The sequencing of transcriptomes of four chickpea cultivars with contrasting response to *Fusarium* infection has identified 303 polymorphic microsatellites, 14,462 SNPs and 1864 insertions/deletions (InDels). From the dehydration-responsive secretome, a leaderless Bet v 1-like protein, designated CaRRP, was identified and shown to participate in multivariate stress responses. Moreover, genome-wide identification of members of Transcription Factor gene families including CCCH Znf, B3 domain containing, Aux/IAA and ARF genes was carried out for structural, differential expression, evolutionary and phylogenetic studies.

Commercial Crops:

a) Sugarcane: Scientists at Sugarcane Breeding Institute, Coimbatore have transformed popular tropical sugarcane variety Co 86032 with abiotic stress related genes viz., EaDREB2, EaHSP70 and PDH45VEGETABLES

b) Tomato: In order to develop resistance to begomoviruses in tomato, translational fusion constructs containing nuclear localization signal and the single strand binding protein encoded genes were developed which have shown ability to reduce geminivirus replication. Transgenic nature of the plants has been confirmed by PCR using gene specific primers. Transgenic tomatoes (T1) are being raised for challenge inoculation for further analysis.

c) Chilli: The scientists of JNU have identified role of a chilli leaf curl virus (ChiLCV) responsive nucleotide-binding site-leucine-rich repeat NBS-LRR in conferring resistance in chilli. This study has also for the first time deciphered the molecular mechanism behind resistance breakdown in chilli.

d) Potato: To address the issues of sexual

incompatibility of wild species with common potato, four interspecific somatic hybrids between *S. tuberosum* dihaploid C-13 and *S. cardiophyllum* were developed via protoplast fusions. These four hybrids were confirmed as true somatic hybrids containing both parental genomes based on molecular markers and phenotypes. Late blight resistance of the hybrids was assessed by challenge inoculation of *P. infestans* under controlled conditions. The best somatic hybrid line 'Crd-6' have been applied for registration with NBPGR, New Delhi.

Program Support: Under Programme Support for R&D in agricultural Biotechnology at G.B. Pant University of Agriculture and Technology, Pant Nagar, transgenic *Brassica juncea* overexpressing MAPK3 gene has been developed and disease scoring has been done of these transgenic plants. 5 SNP markers linked to grain yield and its component traits in finger millet were identified and expression and transformation gene constructs harboring EcCaM, EcCaX1, EcCaX3, EcCBL-4 and EcCBL-10 has been developed and *in vitro* calcium uptake studies using mammalian cell culture (caco-2) has been standardized.

BASIC PLANT BIOTECHNOLOGY, AGRICULTURE AND FRONTIER AREAS

Basic research has been a major thrust area under plant biotechnology with special emphasis on understanding biotic and abiotic stress mechanisms, elucidating the signal transduction pathways during plant development, host pathogen interaction etc. Application of genomic tools also received impetus with respect to functional genomics for improvement of crop specific traits. In addition, the thrust has been on biotechnological interventions in forestry, horticulture and plantation crops; germplasm characterization and improvement of crops using molecular biology tools. Support continued on various network projects on metabolomics, saffron and projects under Solanacea Genome Initiative-

Phase-II.

Apart from the above mentioned, new priority areas identified through discussion meetings included accelerated domestication of underutilized crops; plant microbe interactions; integrated metabolomics, role of transcription factors in regulatory networks etc. Major programs were initiated on accelerated domestication of underutilized crops and plant microbe interaction.

Priority areas were identified under “Accelerated domestication of underutilized crops and Plant microbe interactions” and 6 major under-utilized crops, i.e.; Chenopodium, grain amaranth, rice bean, buckwheat, foxtail millet and proso-millet have been identified as priority crops under accelerated domestication. The main focus is on genetic improvement of these crops so that these crops could be brought into mainstream agriculture.

Basic Research: Another study was supported at National institute of Plant Genome Research (NIPGR), New Delhi to elucidate the role of glucose and its interactions with other hormones during the shade avoidance response (SAR) in *Arabidopsis* and Tomato. The results obtained indicated that Glucose affects shade avoidance response in dose dependent manner. Cytokinin and ethylene were found to have a negative effect on shade induced hypocotyl elongation. Future studies are going on for identification and characterization of genes playing role in shade avoidance response.

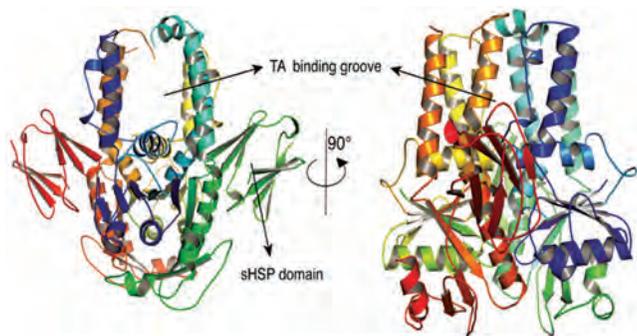


Figure 4. Overall crystal structure of *Arabidopsis* Chloroplast Get3 with all the domains.

A study is being supported at Punjab Agricultural University (PAU), Ludhiana for identification of different cyclophilin genes and their role in heat stress tolerance in wheat. The mechanism of regulation of PPlase activity of TaCYPA-1, one of the heat regulated cyclophilins has been elucidated. Expression analysis of identified cyclophilins is underway currently so that the genes responsible for thermo-tolerance in wheat will be identified.

Host Pathogen Interaction: A study was supported at Tamilnadu Agricultural University (TNAU), Coimbatore, to understand the *Thrips* and *Tospovirus* interactions in tomato and watermelon pathosystems. Virus infected host plants (tomato and watermelon) showed increased total protein, carbohydrates and fat content compared to non-infected plants. Further, vector interactions and characterization of virus infected and non-infected host plants in response to vector interactions are being studied.

At Institute of Life Sciences (ILS), Bhubaneswar, study is going on to understand the molecular and functional interactions of TGA and WRKY transcription factors in *planta*. It has been found that TGA3 and WRKY53 co-localize and physically interact in the nucleus and only N-terminal domain of TGA3 is sufficient for interaction with WRKY53. Both these transcription factors act synergistically to regulate the activity of CmYLCV promoter

Solanaceae Genome Initiative (Phase II): Support continued for various projects under SOL Phase 2 program involving network partners. At University of Delhi South Campus, Delhi (UDSC), Delhi study is being supported on characterization of ripening-associated ERFs of tomato. The study focused on transformation of tomato var. Arka Vikas with LeERF9, 11, 72, and 81 for down regulation as well as over-expression of these LeERF's. Vectors for overexpression and silencing of these genes have been constructed. 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 fruit ripening and productivity. Transgenic tomato with constitutive expression of *SIERF6* expression show delayed ripening while those with suppression of *SIERF6* show early ripening. Transformation with fruit specific constructs is in progress.

At University of Hyderabad, Hyderabad, research is being undertaken to understand how phototropin genes affect tomato fruit quality and shelf life. High carotenoid content of *Nps1* mutation was successfully introgressed into Arka Vikas. Silencing of phototropin genes has been achieved. It was observed that, few lines exhibited good silencing of phototropin 2 gene and these have been forwarded to T1 generation. In addition, CRISPR constructs of *phot1* and 2 were transformed into tomato. Crispr *phot1* plants are in greenhouse and crispr *phot2* plants are in rooting medium. Confirmation of gene editing is in progress.

At Jawaharlal Nehru University (JNU), New Delhi tomato transformants have been generated with three *Rep* mutant constructs (D261A, D262A and K272A) of ToLCV. The synthetic *Rep* and the dominant lethal *Rep* mutants (D261A, D262A, K272A) have been cloned into plant transformation vector and transformation of tomato cv. Pusa early dwarf has been carried out with Synthetic *Rep*, *Rep*-D261A, *Rep*-272A, wt *Rep*. Putative transformants (more than 300) are at present in the shooting media. In planta, efficacy of the constructs have been evaluated. Further, molecular characterization of these plants will be undertaken.

In the phase-II of TILLING project supported at University of Hyderabad, Hyderabad NGS-based strategy was used for high throughput identification of mutations. An EMS-mutagenized tomato population of 768 individuals pooled in three-dimension was analyzed for mutations in 25 genes

by NGS-based TILLING. A total of 64 mutations were identified in 19 genes out of 25 genes examined. From NGS-identified mutant lines, a mutant line defective in 9-cis epoxy carotenoid dioxygenase 1 (NCED) gene showed deficiency in plant hormone ABA and is now being characterized further. Interestingly NCED mutant lines demonstrated higher lycopene levels in fruit but have a very small seed size (Figure 5).

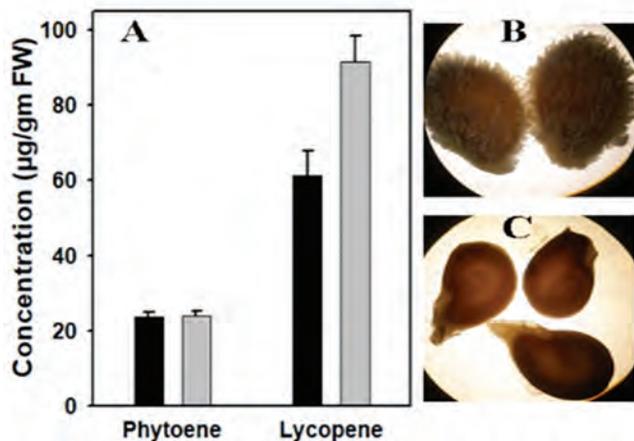


Figure 5. The tomato NCED mutant was isolated by NGS-Based TILLING. A. NCED Mutant shows higher levels of lycopene (Gray bars) compared to its wild type Arka Vikas cultivar (Black bars). B. Seed phenotype of wild-type Arka Vikas. C. Seed phenotype of NCED mutant.

Metabolomics: Project was supported at School of Computational and Integrative Sciences, Jawaharlal Nehru University (JNU), New Delhi and at International Institute of Information Technology (IIIT), Hyderabad for developing a promising database tool for storage, retrieval and analysis of large scale metabolomics data. During the current year an enhanced version v4.4 with features such as bulk raw data upload option, fixing peak alignment has been developed and released.

At University of Hyderabad, Hyderabad, a project was supported on delineating metabolome networks during tomato fruit ripening. A high β -carotene line has been identified from natural accessions of tomato that has about $40\mu\text{g}$ β -carotene per gm of tomato fruit tissues. Molecular analysis of this line

showed that higher β -carotene results from very high expression of fruit-specific lycopene β -cyclase (CYCB) in red ripefruit. In addition, a trifoliolate (*tf*) mutant has been obtained that has fourtimes higher folate level in tomato fruits than the parent cultivar. The mutant showed higher expression of genes *ADCS* and *GTPCHI* which are responsible for the formation of folate biosynthesis precursor PABA and pterin.

Saffron Network Programme: Support 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; and School of Life Sciences, Jawaharlal Nehru University, New Delhi towards understanding the regulation of synthesis and accumulation of apocarotenoids. Transcriptome profiles have been developed for stigmas at three stages of development for correlating apocarotenoid biosynthesis with gene expression patterns. A complete profile of changes in abscisic acid in the corms during dormancy and onset of renewed bud growth has been developed. A marked decrease in the level of abscisic in the buds was observed during transition from dormancy to active growth. Pretreatment of corms with low temperature treatment had no effect on flower bud development. Genes upregulated by GA3 treatment included Agamous like MADS box AGL9 homolog, MADS box transcription factor 2 like isoform, MYB 306, APETALLA2. Signature metabolites as responses of corms to GA3 treatment have also been identified.

Forestry, Horticulture and Plantation Crops: Support continued on some important forestation and plantation crops during this year. In a study supported at Institute of Forest Genetics and Tree Breeding (IFGTB); Coimbatore for identification and Tagging of QTLs/Candidate genes for wood property and adventitious rooting traits in Eucalyptus and also for establishment of phenomics facility for water stress tolerance studies; A rapid micro protocol was

optimized for estimation of total lignin from Eucalyptus wood samples. The protocol was tested and validated on 75 wood samples. Genetic linkage map for two inter-specific crosses of eucalypts was generated with 538 markers (SSRs, ISSRs and SRAPs) with the map length of 1326.2cM.

A collaborative project including Institute of Forest Genetics and Tree Breeding (IFGTB), Coimbatore, Kerala Forest Research Institute (KFRI), Kerala and College of Forestry, University of Agricultural Sciences, Dharwad (UAS) has been supported on conservation of natural teak genetic resources (TGRs) population structure. In the states of Tamil Nadu and Kerala several remnant natural trees of teak were identified. A draft genome assembly was made by whole genome sequencing. *De novo* contig assembly and gene annotation was carried followed by the discovery of SSRs. In total 1,82,712 microsatellites were identified for primer designing. This information generated will be utilized for evaluating the genetic diversity existing across populations in Southern India and to estimate the population demography.

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 Medicinal and Aromatic Plants Initiative in Bundelkhand Region was organized on February 17-18, 2017 at Bundelkhand University, Jhansi with an aim to develop a network programme on end-to-end demonstration of medicinal and aromatic plants cultivation in Bundelkhand leading into future start-ups in the region. A new programme on Phytopharmaceuticals Mission for North East Region is being formulated. The salient achievements of the

programme during the year are as follows:

Characterization, Multiplication and Agrotechnology: Vegetative propagation of *Symplocos racemosa* and seed propagation of *Pterocarpus marsupium* and *Saraca asoca* have been standardized at Sikha-O-Anusandhan (SOA) University, Bhubaneswar. About 2000 saplings of *S. asoca* and *P. marsupium* have been reintroduced into their natural habitats. Out of all populations studied so far, Thakurmunda population of *S. racemosa*, Olaba population of *P. marsupium* and Dhani population of *S. asoca* have shown highest genetic diversity.

Work has been continued to develop microbial inoculants for high-value agarwood oil production in *Aquilaria* tree at Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow. Twenty two different microbes were isolated from infected wood. Out of these, four fungi which could produce appreciable rotting in lab experiments were selected for field studies. Two locations in Hojai, Assam and Agartala, Tripura were selected and 10 trees in each location were inoculated with these fungi. Two fungi F5 and F7 could produce some rotting in agarwood trees.

Work has been recently initiated on chemotyping, quality assessment and post-harvest technology development in some important medicinal plants (*Bacopa monieri*, *Andrographis paniculata* and *Withania somnifera*) for elite selection, drug yield optimization and quality retention jointly at SOA University, Bhubaneswar and Ramakrishna Mission Vivekananda University, Kolkata.

Novel Bioactive Agents and Herbal Formulation: Out of six medicinal plants evaluated for anti-leishmanial activity, three plants (*Agave americana*, *Piper nigrum* and *Trachyspermum ammi*) have shown significant anti-leishmanial activity jointly at Jadavpur University, Kolkata and Balaji Utthan Sansthan, Patna. Among them, *T. ammi* extract and

isolated compound – thymol have shown maximum anti-leishmanial activity.

Efforts have been continued to scientifically validate the use of *Asparagus racemosus* (Shatavari) as substitute for rare and rejuvenative plant drugs, *Meda-Mahameda* – the members of *Ashtavarga* group of Ayurvedic drugs at Foundation for Revitalization of Local Health Traditions (FRLHT), Bangalore.

Aqueous extracts of *Solanum xanthocarpum* and *Albizia lebeck* have shown potential to attenuate the bronchial hyper-responsiveness in OVA-induced model of airway inflammation at V. P. Chest Institute, University of Delhi, Delhi. The sub-acute toxicity study of standardized extracts of *S. xanthocarpum* and *A. lebeck* showed no remarkable toxicity sign and showed body weight gain as compared to control rats. Standardized extracts of *S. xanthocarpum* and *A. lebeck* have anti-inflammatory, immunomodulatory, anti-remodelling, anti-oxidant and anti-hyper-responsive activity, in the models of airway inflammation, remodeling and hyper-responsiveness.

Based on animal studies, the anti-dermatophytic herbal formulation using essential oil of *Trachyspermum ammi* (Ajwain) has been further improved jointly at Dolphin Institute of Biomedical and Natural Sciences, Dehradun and Centre for Aromatic Plants (CAP), Dehradun. Significant results obtained against *Microsporum canis* and *Trichophyton mentagrophytes* suggests its utility in treating animal dermatophytes, common in pets. Genomics and biosynthetic pathways

Efforts have been continued to induce santalol biosynthesis in sandalwood cell suspension cultures by simultaneous overexpression of three genes of the lower mevalonate pathway namely *farnesyl diphosphate synthase* (FDS), *santalene synthase* (SS) and *p450 hydroxylase* under control of constitutive promoters at Vittal Mallya Scientific Research Foundation, Bangalore.

Under a Programme Support being implemented jointly by Jaypee University of Information Technology (JUIT), Solan and Himalayan Forest Research Institute (HFRI), Shimla, novel strategy has been formulated and implemented wherein natural chemotypes of *Picrorhiza kurrooa* were used in ascertaining and validating the biosynthetic routes of both the picrosides (Picroside-I and II). Multi-location testing of genetically superior chemotypes (PKS-1 and PKS-5) of *P. kurrooa* has been undertaken in farmers' fields in high altitude areas. About 10,000 plants of selected elite chemotypes have been multiplied for field plantation and demonstration trials.

Herbal Formulations for Veterinary Healthcare:

A network project on development of phytopharmaceutical product for bovine mastitis has been recently initiated jointly at CSIR-Indian Institute of Integrative Medicine, Jammu, ICAR-Central Institute for Research on Goat, Mathura and ICAR-National Dairy Research Institute, Karnal. A topical formulation for antibacterial and anti-inflammatory has been developed using combination of four plant extracts (*Terminalia bellerica*, *Piper betle*, *Boswellia serrata* and *Bergenia ciliata*).

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 Biotechnological Applications in Muga and Eri Culture” was jointly organized by DBT and Central Silk Board (CSB) on May 26, 2017 at Central Muga and Eri Research and Training Institute (CMERTI), Jorhat with a view to identify the priority areas and develop a network programme on biotech applications in muga and eri culture. Significant achievements are summarized below:

Development of improved races of silkworm for enhanced productivity: Efforts have been continued to introduce sex-limited foundation crosses for cocoon colour as a male component for the production of commercial cross breed at APSSRDI, Hindupur. Under a network project on use and validation of DNA markers in silkworm breeding programme for NPV resistance along with multi-location field trials being implemented jointly by Seribiotech Research Laboratory (SBRL), Bangalore; Central Sericultural Research & Training Institute (CSR&TI), Mysore; CSR&TI, Berhampore and CSR&TI, Pampore, J&K, the continuous maintenance of lines generated through marker assisted selection for NPV resistance (MAS-N) with larger cocoon traits has been continued. Marker analysis showed presence of the NPV tolerance-associated markers in the evolved lines, whereas expression of genes encoding host-response proteins showed differential expression in MAS-N lines from parental races.

Development of Disease and Pests Control Measures: Efforts have been initiated towards developing a diagnostic kit for early detection of tiger band disease in oak tasar silkworm (*Antheraea proylei*) jointly at SBRL, Bangalore and Regional Tasar Research Station, Imphal, Manipur. The causal agent has been purified and characterized through partial viral genome sequence and its phylogenetical analysis revealed that the virus belongs to the alpha baculovirus and sequences were similar to *Antheraea pernyi* nucleopolyhedrovirus. The mode of transmission was investigated and found the eggs laid by infected gravid female carrying the viral particles. The development of appropriate PCR based diagnostic technique for early detection of the virus is in progress.

Improvement of Host Plants: Thin transparent silk films from *Antheraea mylitta* have been developed as biocompatible promising scaffold for corneal regeneration jointly at West Bengal University of Animal and Fishery Sciences, Kolkata, IICB, Kolkata

and IIT, Kharagpur. The scaffolds have also supported healing of corneal defects in the rabbit eye. Work is in progress to develop functionalized silk films for corneal regeneration. An Indian patent has been filed. An initiative to translate the discovery for veterinary applications is being pursued actively.

Studies on design and development of silk fibroin coatings for biomedical application have been initiated at CSIR-National Chemical Laboratory, Pune. Novel process combining two conventional coating techniques (dip and electrospinning) has been developed that results in the formation of crack resistant, stable silk fibroin coating on primarily polydimethylsiloxane (PDMS). Functional coatings of silk fibroin using glycolipid as a bioactive biomolecule have been prepared that exhibit crack resistance, antibiofilm and quorum quenching activity.

Utilization of By-Products: Silkworm pupae residue degrading microorganisms (bacteria, fungi, yeast and actinomycetes) were isolated and tested for their ability to produce enzymes such as protease, pectinase, cellulase, chitinase and ligninase etc. at UAS, Bangalore. A protocol has been standardized for isolation of alpha-linolenic acid (ALA) from silkworm pupae residue. Biocontrol and plant growth promotional attributes of silkworm pupal residue-biosoft descent has also been studied.

Efforts have been continued on isolation and characterization of sericin from tasar silk fibre waste at CTR&TI, Ranchi. Separation of residual sericin from silk fibre waste was confirmed by scanning electron microscope (SEM). In tasar fiber waste sericin, the amount of serine, aspartic acid and glycine were found to be 55.99%, 60.49% and 54.34%, respectively in basin, diflossing and reeling wastes.

ANIMAL BIOTECHNOLOGY

Animal Production: Animal Production is an important part of national economy of our country which effects the economy in the form of

employment; rural development; agricultural production and allied areas. During this period, projects on applied areas of animal reproduction and related techniques, development of transgenic animal, molecular characterization of indigenous breeds, various aspects of animal nutrition and utilization of animal byproducts were actively pursued. In an attempt to diagnose early pregnancy in buffalo, the potential pregnancy associated glycoproteins and novel urinary proteins as possible biomarkers having significance in pregnancy were identified and possible role of neutrophils in maintenance and diagnosis of early pregnancy in buffaloes were taken up. During the period brainstorming meeting on development of bovine sex semen sorting technology and genomic characterization of indigenous breeds of cattle were organized and efforts are on to develop network project on priority basis.

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:

a) Reproduction: Availability of quality semen is a major constraint in 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. The transcripts (121 transcripts) regulating sperm functional parameters such as motility, membrane integrity, mitochondrial function were identified. This study will help in developing fertility diagnostic and identifying quality of semen of bulls selected for breeding purpose.

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, measured during day 12 to day 20 post insemination, and play an important role during peri-implantation period of embryo. The up-regulation of interferon stimulated genes like ISG15, OAS1, MX, IFI16 in pregnant cows suggest their possible role in successful implantation. The preliminary results indicate 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.

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 improves 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. The study suggests that exogenous melatonin at optimum dose (3mM) helped in preservation of semen and also enhancement of fertility rate of mithun.

b) Transgenic: A novel non-invasive technique for generation of transgenic rat model was developed at National Institute of Immunology, New Delhi. The transgenic rat line was developed by integrating transgene into the genome of the spermatogonial cells by testicular injection of DNA followed by electroporation. A transgenic disease model displaying alpha thalassemia was successfully generated.

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 TRL4 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.

c) 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. A total 72 DNA samples (18 random samples/breed) were genotyped using 777K SNP chip and analyzed. A total 1000 specific markers were identified having potential to differentiate these cattle populations. These 1000 markers account 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). The genomic regions containing highly differentiated SNPs with F_{ST} ($e^{-0.25}$) 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.

d) 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. It was noted that the supplementation of Se nanoparticles 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. Further, studies on supplementation of nano formulations in the feed of ruminants are underway.

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.

e) 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.

f) 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). Pre-dipping of skin or carcass in acidified sodium chlorite (ASC) or carvacrol before thermal treatment resulted in the rapid decontamination of skin or carcass surface. The results obtained were used for the thermal death time modeling of hardy *S. 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 effect on sensory attributes and organoleptic quality of meat.

Animal Vaccine and Diagnostics: The mandate of 'Animal Health Division' which is also called as Animal Vaccines and Diagnostics division is to establish collaborative research for development of new generation vaccines and diagnostics along with translation of existing candidate vaccines and diagnostics for field use around major animal diseases of national importance to make product affordable to small and marginal farmers. The emphasis of the Animal Health program is on the collaborative translational research, consolidation of existing projects with potential leads and generation of network programmes around major animal diseases. The division supports and implements research projects in form of networks as well as individual investigator driven projects. The division has supported 5 new and 24 ongoing projects during 2017-18.

During the period 10 products were generated, 5 technologies were developed, 2 technologies were

commercialized, 1 patent was granted, 6 patents were applied and a total of 43 research papers have been published with an average IF of 1.5 in the area of Animal Health research. Also about 75 manpower were trained in R&D projects of Animal Health programme during 2017-18

During the year, several new projects on development of vaccines for *Leptospira interrogans*, development and evaluation of a genetically engineered vaccine against Newcastle disease and chicken infectious anaemia infection of chickens, validation of molecular diagnostics and vaccine for Classical Swine Fever, development and evaluation of humanized rabies monoclonal antibody in transgenic chicken bioreactors for post-exposure prophylaxis and studying the mechanism of host adaptation by *Campylobacter jejuni* to control enteric commensalism in chicken have been supported.

The Department has organized a Brain Storming meeting on "Bovine Tuberculosis and Paratuberculosis" to identify priority areas for initiating a network programme inviting several Indian and foreign experts.

Under Animal biotechnology Career Enhancement Program (ABCEP) 30 students were trained in various areas of animal biotechnology. Five technologies were developed; LEPTOLAT for the detection of leptospirosis, LFA kit for the detection of CPV maternal antibody level in pups, Egg yolk semen extender for the cryopreservation of bull semen, KETOCHECK for the detection of Ketosis (Fig. 6), and conductivity meter for the detection of Subclinical mastitis. Apart from these two technologies, the devices Photolyser, and Portable incubator and LAMP device were commercialized to M/s. Endhiran Innovations LLP, Chennai



Figure 6. A) Lepto LAT for diagnosis of Leptospirosis, B) Rapid Parvo detect kit, C) Egg yolk semen extender for the cryopreservation, D) Classic shampoo for dogs, E) Keto check for diagnosis of Ketosis, F) Scrub kit for surgical wounds and G) Nano spot on, Nano IVMEC shampoo

Scientists from IVRI, Izatnagar successfully demonstrated the induction of high levels of antiporin antibodies and enhanced cell mediated immunity by developing a cocktail vaccine for poultry salmonellosis. The vaccine could afford satisfactory protective response and organ clearance against virulent *Salmonella typhimurium* and *Salmonella enteritidis* challenge in poultry birds.

Another group of scientists from IVRI, Bareilly have developed sub viral particle (SVPs) based infectious bursal disease virus (IBDV) vaccine for immunization in chickens. It induces protective immunity in specific pathogen free chicks against very virulent IBDV challenge. SVPs completely protect the broiler birds in presence of maternally derived antibodies at day old vaccination. The vaccine does not cause immunosuppression as characterized by an intact histological architecture of the bursa of Fabricius. The vaccine has also been validated in a poultry vaccine company M/S Globion Pvt. Ltd., Hyderabad.

For developing recombinant antigen based diagnostics and chimeric plant virus-like particle based vaccine for infectious bursal disease virus, the scientists from Sri Venkateshwara University, Tirupati have optimized Indirect ELISA and LFA tests using chimeric VLP-based antigens for the detection of IBDV.

A real time PCR based assay for detection of *Mycobacterium* species including *Mycobacterium*

tuberculosis complex with a specificity and sensitivity of >95% has been developed by scientist from JNU, New Delhi which is ready for 3rd party validation. This test costs approx. Rs. 206/sample, which is 12.5 times lesser than conventionally available test by GeneXpert system.

- *Translational Research Platform for Veterinary Biologicals*: The platform has obtained NABL accreditation (IS/ ISO 17025:2005) for diagnosis of Bovine Trichomonosis & Brucellosis & Initiation of cGMP licensing. Among various services, the platform is also offering OIE approved diagnostic services of Breeding Bulls for Brucellosis, Trichomonosis and IBR in lieu with regulatory needs. Five research papers have been published during the year in international journals. Other major research accomplishments are Development of Baculo virus expression system to generate VLPs as a production platform for veterinary vaccine and diagnostics, development of PPRV vaccine in BHK21 cells (suspension) as an alternate, nanotechnology based therapeutics for veterinary clinical applications and efficacy studies of Canine ParvoVirus-virus like particles in Beagle dogs.

TRPVB also produced new innovative products like *Lepto* LAT for diagnosis of Leptospirosis, Rapid Parvo detect kit for Canine Parvo Virus, Conductivity meter for Mastitis detection, TANUVAS Scrub kit for surgical wounds, Ketocheck for diagnosis of Ketosis, Nano spot on, Nano IVMEC shampoo and TRPVB Classic shampoo for dogs.

Network program on Brucellosis: During the period, the six centres involved in epidemiological studies continued the surveillance program and isolated more than 248 *Brucella* isolates. The recombinant antigen based ELISA kit developed by centre involved in development of diagnostics for diagnosis of bovine brucellosis was sent to TRPVB, TANUVAS, Chennai for external validation. Another centre prepared sLPS based ELISA and LFA kits and sent to TRPVB,

TANUVAS, Chennai for validation. The prepared rapid and ELISA kits were used to screen Gosalas and field samples.

AQUACULTURE AND MARINE BIOTECHNOLOGY

Aquaculture plays a very important role in Indian agricultural economy. The programme is being implemented for enhancing aquaculture production and productivity increase and development of useful product and processes from marine resources. Under this programme several projects are being supported to benefit the aquatic and marine sectors by addressing broad areas on fish genomics and transcriptomics, fish and shellfish disease, immunostimulants and antimicrobial peptides. Projects on development of bioactive molecules biomaterials, bio-surfactants, marine actinobacteria, DNA barcoding and molecular taxonomy, cell lines and diagnostics were also pursued through adoption of molecular tools and techniques. Some of the major achievements of these projects are as follows:

Fish Genomics and Transcriptomics: A network programme on whole genome sequencing and development of allied genomic resources in two commercially important fish *rohu* (*Labeo rohita*) and catfish (*Clarias batrachus*) is being continued at NBFGR Lucknow, CIFA Bhubaneswar, IASRI New Delhi and AAU Gujarat. In rohu genome assembly and scaffolding using MaSuRCA and SSPACE has been done using 13477 scaffolds with maximum scaffold size of 15.2 Mb covering about 95% of the genome with predicted 40,099 genes which were annotated with Blast2Go resulting in 24,525 genes. Similarly, catfish genome using 35,313 scaffolds with maximum scaffold size of 5.2 Mb covering about 94% of the genome resulted in 81,000 genes. Whole gonadal transcriptome and small RNA dynamics of male and female gonads of catfish resulted 54,061 and 1,09,204 transcripts in ovary and testis, respectively. A total of 1,07,495 non-redundant

gonadal unigenes have been identified which contains 39,147 candidate coding regions within transcripts, and of which 35,777 have been annotated against the fish proteins in UniProt. Among the annotated unigenes, 27,130 and 12,661 were assigned to gene ontology categories and clusters of orthologous groups. Additionally, 14,972 unigenes were mapped to 374 pathways in KEGG Pathway database. Differential gene expression analysis of male testis verses female ovary resulted in 6,034 upregulated and 5,314 down-regulated genes with the presence of 18,166 male and 2,015 female specific genes. Mining of the gonadal miRNAs resulted in 166 and 224 conserved miRNAs, along with 4 and 20 novel miRNAs in ovary and testis, respectively. The interaction between miRNAs and genes that regulate immunity performed using miRanda target prediction tool revealed miR-462, miR-731, miR-146, miR-181 and miR-223, associated with the immune response.

Transcriptome profiling of immune responsive genes in golden mahseer (*Tor putitora*) was pursued at ICAR-DCFR, Bhimtal. Six tissue specific transcriptomes were initially sequenced and assembled into a reference transcriptome followed by identification of various tissue specific genes. About 24 putative solute carrier (SLC) genes falling in 15 solute carrier families were characterized from kidney transcriptome. Transcriptome of *T. putitora* challenged with *A. hydrophila* revealed 61,042 unigenes which after Gene ontology annotations resulted in allocation of 46.16% in biological process; 16.39% in molecular function and 37.46% in cellular components. Differential gene expression analysis revealed 1,104 upregulated and 1,304 down-regulated unigenes known to be mainly involved in cell surface receptor signalling. Twelve unigenes were found to be differentially expressed in accordance with *in silico* expression analysis. From the RNA-Seq and qRT-PCR analysis, it was observed that the immune responsive acute phase proteins and other

stress-related proteins trigger the adaptation mechanism to face the initial bacterial infection in golden mahseer as well as complement system of fish also plays an integral role during the pathogenesis.

Fish and Shellfish Disease: A study on virulence factors identification in fish disease Epizootic Ulcerative Syndrome (EUS) causing fungus *Aphanomyces invadans* by transcriptome approach was carried out at SRM University, Chennai & CSIR-CDRI, Lucknow. Infected *Channa striatus* with severe ulcers (Fig. 7) collected from different natural aquatic environment lead to isolation of five morphologically different fungal pathogens with two of them being prevalent in most of the ulcers. Sequencing of 18S ITS region confirmed one of the isolate as *A. invadans* which was further subjected to RNA sequencing for identification of virulence factors.



Figure 7. *Channa striatus* with severe ulcers

A study on development of quorum sensing inhibitors and anti-infectives from marine microorganisms for the control/prevention of pathogenic *vibrios* in shrimp aquaculture was implemented at Pondicherry University. A new secondary etiological agent *Aliivibrio fischeri* associated with white spot syndrome virus (WSSV) outbreaks during 2015 in shrimp farms located in southeast coast of India was identified (Fig. 8a & b). The bacterial isolates from the hepatopancreas of diseased samples screened for extracellular virulence identified isolate SK11 as highly virulent and pathogenic with LD_{50} of 10^3 CFU/ml. The mortality rate and pathogenicity index was reported very high in challenged shrimp. This is the first report on the emergence of *Aliivibrio fischeri* in

WSSV outbreak as an opportunistic etiological agent in Indian shrimp farms.

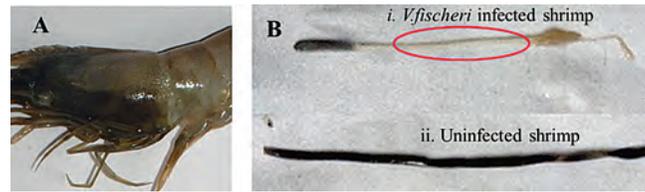


Figure 8. A. Shrimp infected with *Aliivibrio fischeri* showed black spots on the exoskeleton region and dark hepatopancreas. B. i. Empty midgut observed in *A. fischeri* infected shrimp; ii. Uninfected shrimp - Full midgut observed in uninfected shrimp (shrimp without infection)

Fish Nutrition: A project on development of pelleted Diet for *Labeo rohita* and *Clarias batrachus* using *achyranthes aspera* and evaluation of its immunostimulatory properties in pond culture system was continued at University of Delhi, Delhi Technological University, Delhi and Central Institute of Fisheries Education Centre, Rohtak. The immunostimulatory and disease resistance properties of seeds of *Achyranthes aspera* was evaluated in both laboratory and field conditions. Challenged study with pathogen *Aeromonas hydrophila* showed that the weight gain of rohu was influenced by the supplementation of plant ingredients and enhanced growth rate helps the fish to overcome the adverse environmental conditions for productivity increase in the culture system due to altered expression pattern of various immune-related genes viz. pro-inflammatory genes encoding IL-1 β and anti-inflammatory IL-10, antimicrobial gene encoding lysozyme C and lysozyme G in hepatopancreas and kidney.

Immunostimulant and Antimicrobial peptides:

A study on herbal immunostimulant formulated feed to protect shrimp (*Penaeus monodon* and *P. vannamei*) from WSSV infection is being continued at C. Abdul Hakeem College, Melvisharam. Aqueous extract prepared from a plant material showed anti-WSSV activity at laboratory as well as in shrimp farm. Similarly ethyl acetate extract also showed a strong anti-WSSV activity and therefore subjected to

chromatography resulting in detection of strong anti-WSSV activity in two fractions. The shrimp were fed with plant extract formulated feed continuously with a gap of seven days till completion of the culture and sampling was done regularly. After using the plant extract, the production was about 18 tonnes in first crop and 21 tonnes in second crop with survival rate of 80 to 90% without WSSV infection even though nearby untreated ponds were affected by WSSV. Field trial and study on identification of bioactive compound is being pursued.

Studies 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. Pattern recognition molecule β -GBP was isolated and purified from the haemolymph of rice field crab *Paratelphusa hydrodromus* and Indian white shrimp *Fenneropenaeus indicus*. Purified β -GBP was confirmed to be an anti-inflammatory and antioxidant agent. It was thermostable even at 100°C as well as involved in the activation of proPO at pH 7-8 in the presence of Ca^{2+} and Mg^{2+} . β -GBP protein based zinc oxide and silver nanoparticles were synthesized and the antibacterial activity of were determined by live/dead Baclight assay. The antibiofilm potential of β -GBP based nanoparticles observed under confocal laser scanning microscopy showed that it effectively inhibits the biofilm architecture of both Gram positive and Gram negative bacteria.

Isolation of antimicrobial peptides from brachyuran crabs and its perspective antigen based molecular docking studies was pursued at Annamalai University, Tamilnadu and National Institute of Oceanography, Goa. Brachyuran crabs were collected from the selected stations along the east and west coast of India and healthy male and female crabs at different stages of development were used for study. To identify potential brachyuran crab showing antimicrobial activity, hemolymph extracts of ninety

six crab species were collected and investigated by disc diffusion method. The results clearly demonstrated that the hemolymph of *Dromiadehaani* exhibited broad spectrum activity against microbial fungal. The antimicrobial peptide has been characterized is being further studied.

Bio-prospecting: A project for molecular characterization of bio-film produced by coral associated bacteria isolated from Andaman Sea was carried out at Institute of Life Sciences, Bhubaneswar. A halostable, solvent tolerant novel α -endoglucanase has been identified from a marine bacterium *Photobacterium panuliri* LBS5T (DSM 27646T) in addition to two novel SXT/R391 integrating conjugative elements ICEMfuInd1a and ICEMfuInd1b, in the genomes of *Marinomonas fungiae* JCM 18476T. The existence of such ICEs in marine bacteria reveals the dissemination of multidrug resistance genes and their impact in natural populations.

Study on construction of polyketide synthase, non-ribosomal synthetase gene library and natural product library from cultivable and uncultivable marine actinomycetes was carried out at VIT University, vellore. The isolation of extremophilic actinobacterial was carried out by mimicking its natural growth environment along with inducing certain extreme growth conditions. Diversity studies for the cultivable marine actinomycetes were performed using polyphasic taxonomy approach combining phenotypic and genotypic studies. Six unique actinomycetes strains isolated from Marakkanam, Muthupet, and Tuticorin subjected to 16S rRNA gene sequence analysis were identified as *Jishengell aendophytica*, *Verrucosispora andamanensis*, *Streptomyces rubidus*, *Streptomyces variabilis*, *Actinopolyspora alba*, and *Saccharopolyspora salina*. These strains are rare *Actinobacteria* sp. reported for the first time from Indian coast.

Comprehensive analysis on cyanobacterial Glutathione S-Transferases: new insights and perspectives were carried out at Bharathidasan University, Tamilnadu. A pesticide tolerating and degrading marine cyanobacterium *Anabaena* sp. BDU41811 identified from the repository of National Facility for Marine Cyanobacteria (NRMF) was tested on commonly used pesticide acephate, carbendazim and glyphosate at optimum concentrations. Pesticide exposed *Anabaena* sp. BDU41811 exhibited enhanced level of Glutathione, Glutathione-S Transferase (GST) and Glutathione Reductase (GR) in the organism. *In silico* studies of the second line of defense (degrading) enzymes revealed 12 types of new GST isoforms and based on the activating residues in the N-terminal end, cyanobacterial GSTs were categorised into three types namely; S/C-, S/Y- and Y-types. Through experimentation based on the interaction with pesticides, expression of S/Y- and Y-type GSTs was found only in higher order Nostocales and also proved to be the most active form of GSTs compared to lower and middle order cyanobacteria as supported by RT PCR studies. S/Y- and Y type could be a highly evolved GST isoforms among cyanobacteria with a potential of its use in bioremediation.

A collaborative project on investigation of chemical nature of bioactive compounds from *Turbo brunneus* extract and its mode of action in regulation of osteoclastogenesis was carried out at ACTREC, Navi Mumbai and D. G. Ruparel College (DGRC), Mumbai. The anti-osteoporotic effect of marine mollusc *Turbo brunneus* extract (TME) and its fractions were evaluated for its chemical nature and mechanism of action in regulation of osteoclastogenesis. *In vitro* osteoclastogenesis by resorption pit assay, TRAP and F-Actin staining showed significantly inhibited RANKL induced osteoclastogenesis. Oral administration of hexane fraction of *Turbo brunneus* (HxTME) resulted in increased percentages of Treg and CD8+ IFN- γ cells with a marked decrease in pro-osteoclastic

cytokines IL6 and TNF- α in OVX mice. On stimulation with PHA, PMA/IO and ConA, a significant decrease in proliferative response in the splenocytes of OVX mice was observed. Similarly, Raman spectroscopy and MicroCT analysis revealed that bone architecture was preserved in treated OVX mice. GCMS analysis showed the presence omega fatty acids, mono-unsaturated fatty acids as well as terpenoids which were supposed to be involved in bone metabolism. Therefore, Hexane fraction of *Turbo brunneus* extract may play an important role in reversal of bone loss in OVX mice and may be pursued as a potential candidate for an anti-osteoporotic drug.

A project on improving therapeutic efficacy of antifungal drugs using marine microbial chitinase was implemented at Manipal University, Manipal. Seventeen marine and terrestrial soil and water samples of fungi and 129 microorganisms were isolated and screened for chitinase productivity. Out of 129 microorganisms screened for chitinolytic bacteria 14 bacterial, 3 actinomycetes and 4 fungal species which produced extracellular chitinase and inhibit pathogenic fungi were identified. Three actinomycete isolates showed better chitinolytic activity than *Streptomyces griseus* (MTCC4734) and *Streptomyces violaceusniger* (MTCC 3959). Four bacterial isolates (PB1, PM1, FMO and FM3) and four fungal isolates (PF3, MB1, MB2 and MB3) showed antifungal activity against *Aspergillus niger*. PB1 also showed a good inhibition of *Candida albicans* by modified cross streak assay. A simple, improvised method was formulated for isolation of chitinolytic actinomycetes.

A project on Purification and Chemical Characterization of Bioactive compounds from a Marine Bacterium was continued at Vikrama Simhapuri University, Andhra Pradesh. An antioxidative extra cellular polysaccharide (ECP) with emulsifying activity was isolated, purified and analyzed from a marine bacterium (*Acinetobacter* sp). The polymer produced has shown significant

emulsification and surfactant activities comparable to some of the commercial emulsifiers. The isolated *Acinetobacter sp* was proved to be producing a novel alkaline laccase amenable to various industrial applications. A patent related to the novel alkaline laccase discovery was filed (Patent Application number: 01741012684).

A project on mining the genome and metagenome of marine microbiome for pks-nrps biosynthetic gene clusters and bioactive small molecules was implemented at Pondicherry University, Puducherry to investigate microbial communities associated with apparently healthy coral *Favites abdita* and actively progressing *Terpios* over corals in a coral reef ecosystem using genomics. It was evident from 16s RNA analysis that due to altered microbiome, coral lost its core symbionts, while sponge gains microbial associates and niche from coral tissue during invasion (Fig 9.).

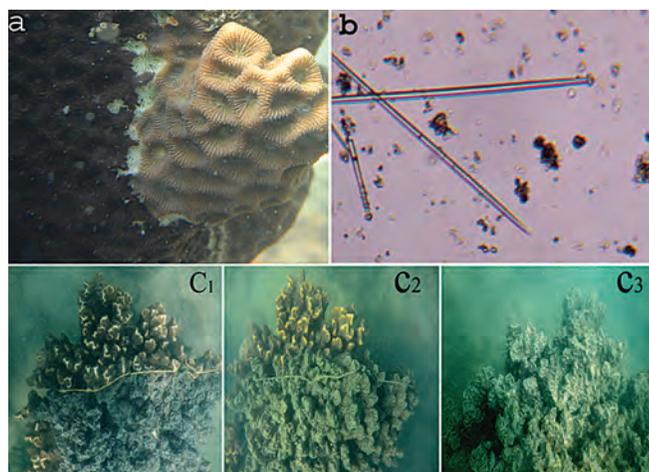


Figure 9. Invasive growth and progression of marine sponge *Terpios* over coral colonies. a. Close up view of the sponge invasion over coral. b. Microscopic view of spicules in the sponge tissue sample. C₁. Progression of *Terpios* over marked portion. C₂ and C₃ Progression after 2 months and one year respectively.

Molecular Taxonomy and DNA Barcoding: Studies were carried out to develop database using barcoding technique at Berhampur University, Odisha. To identify fish species of Odisha coast, Bay of Bengal, India morpho-taxonomy followed by

molecular analysis was performed. The partial gene sequence of *Ulua mentalis*, *Pinjalo pinjalo* and *Tylosurus crocodiles* were generated and analyzed through construction of phylogenetic relationships.

Study on molecular and pattern identification of Indian mariculture fauna using DNA barcoding and soft computing techniques was carried out at Sri Padmavati Mahila Visvavidyalayam, Tirupati. The project was undertaken to develop Biometric analysis and construction of unique DNA Barcode profiles for mariculture fauna by using image processing & soft computing techniques and DNA Barcoding. Mariculture specimen tissues and capturing images were collected from various Aquaculture Centers in Vizag, Kakinada, Kolkata, Mumbai, Gudur, Ongole, Chennai and thinning process such as image resizing, noise removal and edge detection techniques and extracted features like mantle length, mantle width, head length, head width and fin width by using image processing techniques was performed. Artificial Neural Network (ANN) and Fuzzy Inference System have been used to classify the species based on extracted morphometric features. MATLAB software was used to implement the procedures and new algorithms for Species Recognition are being developed.

Development of Cell Lines: A project on derivation and characterization of embryonic stem cell lines from the marine ornamental maroon clownfish *Premnas biaculeatus* and induced pluripotent stem cell lines from the humpback grouper *Cromileptes altevelis* was carried out at Central Marine Fisheries Research Institute, Kochi. Embryonic stem (ES) cell cultures derived from midblastula stage embryos of *P. biaculeatus* were cultured, passaged and characterized for presence of pluripotency genes as well as for stem cell specific markers. Strong signals of GFP expression by fluorescence microscopy as well as formation of putative iPS colonies by phase contrast microscopy were recorded. The effect of various pathway inhibitors and supplements are

being evaluated for improving reprogramming efficiency.

A project on development of shrimp cell lines was implemented at Cochin University of Science & Technology. Studies on immortalization of lymphoid cell culture from *Penaeus monodon* by transduction with oncogenes, ectopic expression of telomerase reverse transcriptase using shrimp specific expression vectors and hybridization aspects were carried out. Two shrimp specific vectors were constructed respectively, Bac le1-GFP and Bac P2- GFP. Transcriptional activities of these vectors were confirmed in the primary lymphoid cell culture. Using these expression vectors an oncogene H-Ras successfully expressed in primary lymphoid cell culture indicated enhanced multiplication of cells compared to normal cells. Shrimp lymphoid cells were fused with Sf9 insect cell line and a hybrid cell line was developed and presence of both (shrimp and Sf9) genome in confirmed using various studies. The hybrid cells exposed to shrimp virus WSSV showed nucleus enlargement and granular formation after 72 hours. RNA isolated from the floating cells and VP28, DNA polymerase, WSSV le1, WSSV protein kinase-1 and WSSV endonuclease were amplified which indicated that Hybrid cell line supported the growth of shrimp virus WSSV. The validation of the new hybrid shrimp cell lines is in progress with its safe maintenance at NBFGR, Lucknow. The technology of hybrid cell line production is being patented.

Development of Diagnostics: A project on development of field level nano-particles based immunodiagnosics for viral pathogens of shrimp and prawn is being continued at C. Abdul Hakeem College, Melvisharam in collaboration with Agharkar Research Institute, Pune. Lateral flow immunoassay (LFIA) which employs polyclonal anti-WSSV serum conjugated with gold nanoparticles that aid the visual detection of WSSV was developed. The LFIA could rapidly (~20 min) detect the virus in different tissues after 3 h (hemolymph), 6 h (gill tissue) and 12 h (head

soft tissue, eye stalk, and pleopod) of infection. In a validation, performed using 75 field samples, the LFIA results compared with the conventional one-step PCR was found to be highly sensitive (100%) and specific (96.77%) for detection of WSSV. Development of similar assays for detection of MrNV (*Macrobrachium rosenbergii* Noda Virus), causing white tail disease and IMNV (Infectious Myonecrosis Virus) is being carried out. The assay can be used by fish farmers and hatchery operators to screen brooders and seed; monitoring of stock on farm site and for disease surveillance.

A project on development of novel methods for the sensitive detection and enumeration of *Vibrio parahaemolyticus* was implemented at Nitte University Centre for Science Education & Research (NUCSER), Nitte University, Deralakatte, Mangalore. Development of loop-mediated isothermal amplification (LAMP) assay was performed for detection of total *V. parahaemolyticus* targeting *tlh* gene. Standardization of assay was carried out using both simple heat block and real-time turbidimeter. LAMP assay standardized for *tlh* gene were 100 % sensitive and specific as well as 1000-fold more sensitive compared to conventional PCR and showed amplification of *tlh* gene even at 10 fg concentration. The positive amplifications of LAMP were also visualized by naked eyes as well as under ultraviolet light after the addition of fluorescent dye into the reaction mixture. Further, LAMP primers were designed for the detection of pathogenic strain of *V. parahaemolyticus* (targeting *tdh* and *trh*) and standardization of these pathogenic genes and preparation of enzyme labeled probes for enumeration of *V. Parahaemolyticus* using colony hybridization is in progress.

NATIONAL BIORESOURCE DEVELOPMENT PROGRAMME

Bioresource Development & Utilization: Focus areas of this programme includes inventorization and

characterization on bioresources, prospecting of bioresources for novel genes and genes products, biomolecules and compounds, improvement of economically important bioresources, and capacity building public outreach on bioresources development & utilization. Department took initiative towards development of network project on exploration, discovery, and utilization of biological resources for sustainable development in North East India. Efforts are also being made to develop programme on bioresource documentation and utilization of Western Himalayan region of India.

During the period, research projects on bio-prospecting of anti-microbial peptides from Hymenopteran (*Ants, Bees and Wasps*) insects, development of herbal formulations from Seabuckthorn, Phase II of microbial culture collection centre in North East region of India, mapping and quantitative assessment of plant resources and its distribution in Madhya Pradesh, Central India, and validation and optimization of artificial infection method for agarwood production and its use in economic development of local tribes of North Eastern India etc. have been initiated. Some of the salient achievements of the ongoing projects are summarised below:

In a network project on lichens for bioprospecting its secondary compounds and establishing cultures collections implemented at MSSRF, Chennai; Cancer Institute, Chennai; TRI, Chennai; CSIR-NBRI, Lucknow; and ARI, Pune, investigators successfully bring 31 species to culture. Investigators using a variety of separation techniques could isolate 25 different compounds, some of which displayed anti-cancer, antimicrobial, anti-mycobacterial and hepatoprotective activities. One potential compound showed promising activity against MDR TB strains.

Under a project at Delhi University, Delhi, investigators have cloned, expressed and carried out

biochemical characterization of various lipases from *Yarrowia lipolytica*. Maximum expression of YLIP9 was obtained by fusing the protein with SUMO tag using pETSUMO vector. Targeted lid and binding pocket mutations were performed in YLIP9 resulting in a double mutant, YLIP9L1Bp3. This double mutant showed significant shift in substrate specificity towards long-chain pNPesters. Its application as a biodiesel enzyme was also validated by transesterification of palm oil in presence of methanol where it showed ~70% conversion of oil to methyl esters.

Studies on chemical profiling of turmeric from different agro-climatic regions and optimization of environmental parameters for high curcumin yield have been carried out at SOAU, Bhubneshwar. Total 453 turmeric germplasm accessions covering 10 agro climatic regions of Odisha have been collected. The curcumin content varied from 0.5% to 9.2%. Highest curcumin content (9.2%) was observed in accession Su 3 of Sundergarh. A total of 19 elite genotypes with high curcumin content (e"7%) were selected for further work. Artificial Neural Network (ANN) models, were developed for prediction and optimization of yield of curcumin and MLFN-8 was selected as the best model. The result of the present work of ANN modelling has shown that curcumin content of turmeric can be improved by changing the input parameters.

Molecular analysis of fruit development and ripening of *Hippophae salicifolia* of Sikkim Himalayas using high throughput sequencing-based gene profiling has been carried out at TERI-NE, Guwahati. In-silico mining of microsatellites for unigenes from all the five libraries resulted in identification of SSRs. Investigators have also identified *H. salicifolia* genes involved in omega-3 and omega-6 fatty acid biosynthesis, phytosterol biosynthesis, carotenoid biosynthesis, ascorbic acid biosynthesis, phenylpropanoid biosynthesis.

Efforts have been continued towards in-vitro production of doubled haploids in tea at IIT, Guwahati. Haploid embryos and nodal segments from haploid shoots, developed from anther cultures of *Camellia assamica* sp *assamica* and *Camellia assamica* sp *lasiocalyx*, were treated with anti-mitotic agent at various concentrations and at different time duration. So far about 700 doubled haploid embryos have been generated, which are germinating into clusters of shoots. Once sufficiently elongated, the shoots will be multiplied using nodal segments to achieve targeted 1000 doubled-haploid plantlets.

In Phase II of network project on morphometry and phylogeography of Indian Honey bees and Stingless Bees, diversity of honey bees (*Apis dorsata*, *A. florea*, *A. cerana*) and stingless bees from different agro-climatic zones of Gujarat, Rajasthan, Haryana, Punjab, Himachal Pradesh, Uttarakhand, Uttar Pradesh, Bihar, Jharkhand, West Bengal, Chhattisgarh, Orissa, Andaman, Nicobar and Lakshadweep islands through morphometric and reproductive tools are being documented. Studies are also undertaken to determine genetic diversity and phylogenetic relationships among populations of honeybees occurring in these states using microsatellite markers and mitochondrial genes.

Under the network project on enrichment and update of plant chromosome database for *Spermatophytes* and *Archegoniate*, checklists for Bryophytes, Pteridophytes, Gymnosperms and Angiosperms have been prepared by consulting relevant literature on the groups. Data sheets on species and genus, containing 29 and 22 parameters also include all aspects of 'Genome(s)' including information w.r.t. taxonomic nomenclature and taxonomic classification. Data sheets of ~4000 species / subspecies / varieties and 781 genera belonging to Spermatophyta and Archegoniatae covering 119 families have been prepared.

Attempts have been continued towards production

of prebiotic bifidogenic molecules from antarctic fungus for nutraceutical industries at IIT, Kharagpur. The scale up study in airlift bioreactor has shown that EPS concentration is significant to explore industrial application of the molecules.

Efforts continued on development of sustainable production technology for Camptothecin (CPT) from newly identified plant and fungal sources jointly at UAS, Bangalore; IISc., Bangalore and UAS, Dharwad. Biomass of *Pyrenacantha volubilis* could be significantly increased by growing them under partial shade and bio-fertilizer which lead to increase in production of CPT. Mass propagation methods have been developed for *Pyrenacantha volubilis* and *Miquelia dentate*. It has also been concluded that CPT production in endophytic fungi is under epigenetic control. Two epigenetic regulators, doxycycline and isotretinoin, were found to elicit CPT and other metabolites.

Under a network project on characterization and consolidation of *Hippophae* genetic resources and propagation of elite genotypes for varietal evaluation, a total of 805 accessions of sea buckthorn have been maintained at the IHBT High Altitude Centre at Lahoul, H.P., comprising 95 accessions from Ladakh region, 102 accessions from Sikkim, 110 accessions from Uttarakhand, 81 accessions from Himachal Pradesh, 200 accessions from Arunachal Pradesh. This Germplasm Resource Centre also housed over 200 accessions procured from China and Russia. Research work related to development of descriptor records for fruit character, revival of *Hippophae* accessions from Uttarakhand, standardization of raising soft wood cuttings in nursery, chemical characterization of *Hippophae* from different regions and genetic diversity analysis of *Hippophae* are 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 institutes, thirty new swamps were located in Northern Kerala from completely isolated regions (the sacred groves) in a fully fragmented condition. The detailed ecological and vegetation studies were conducted in 70 swamps and completed the mapping of 60 swamps using Q-GIS and ARC-GIS. Twenty three plants were collected from Western Ghats, extracted and screened for their antiviral activity. Out of these, extracts from six plants showed promising antiviral activity. These active extracts were further subjected to activity-guided fractionation which led to isolation of a potent molecule A1B1 from JNTBGVR14, which consistently showed very significant activity against Chikungunya virus.

Bioresource: Conservation and Digitized inventorization:

a) *Centre of Excellence for National Centre for Microbial Resource (NCMR)*: Department has established a Country's largest Microbial Culture Collection Centre (MCC) at National Centre for Cell Sciences, Pune in 2008 and since then it is preserving nations precious microbial resources. The main aim of MCC is to establish world class infrastructure with the aim to preserve India's rich microbial resource to provide authenticated microbial cultures for research and education and high quality services for microbial preservation, characterization and authentication to industry and academic institution.

It has acquired the status of '*International Depository Authority (IDA)*' under the Budapest Treaty and is also designated as '*National Repository*' under the Biological Diversity Act, 2002. It has recently been renamed as the "National Centre for Microbial Resource (NCMR)". With more than 180,000 microorganisms (archaea, bacteria, fungi including yeasts) in its collection at present, the centre is the single largest culture collection in the world, and has put India in the top three countries with the largest

collections after USA and Japan.

NCMR provides a variety of culture deposition (including deposits under Budapest Treaty), supply and identification services. In addition, the scientists are also actively involved in the research in the area of microbial ecology and taxonomy. In its attempts to characterize nation's microbial diversity MCC scientists described thirteen novel taxa from diverse ecological habitats which are depicted as below:

Table: New taxa described by NCMR scientists

Sr. No	Taxa	Scientist	Year
1	Reclassification of <i>Phycicola gilvus</i> and <i>Leifsonia pindariensis</i>	Dhiraj Dhotre	2017
2	<i>Mangrovibacter phragmitis</i>	Neetha Joseph	2017
3	<i>Candidatus</i> <i>Phytoplasma asteris</i>	Amit Yadav	2017
4	New subgroup 16SrXI-F phytoplasma	Amit Yadav	2017
5	<i>Lysinibacillus telephonicus</i>	Praveen Rahi	2017
6	<i>Aliinostoc morphoplasticum</i>	Prashant Singh	2017
7	<i>Westiellopsis ramosa</i>	Prashant Singh	2017
8	<i>Auricoccus indicus</i>	Om Prakash	2017

This Centre has already begun to provide services to academic and industrial establishments for microbial identification. Currently, it offers 16S rRNA based identification, FAME and MALDI profiling.

b) *Indian Bioresource Information Network*: Department has been promoting the development of a National level database on biological resources, vegetation cover and biological diversity of the

country through support to several such activities. DBT along with Department of Space has been supporting database development on spatial and non-spatial characterization of bioresources and vegetation of the country. It also led to development of a web enabled portal system, “Indian Bioresource Information Network (IBIN)” consisting of spatial and species data. It is a de-centralized bio-resource database based on distributed architecture. All the distributed data providers are now retrievable through a single window (www.ibin.gov.in).

The IBIN mobile app is designed and developed based on crowdsourcing approach. The Apps can be used by the field workers for identifying the Endangered plants of Western Ghats, Butterflies and also for developing database on the Distribution of plants and animals.

During this year, following three Android Apps have been developed.

Android app for ‘Rare Endangered and Threatened Plants of Western Ghats’: This app enables the user to identify Rare, Endangered and Threatened (RET) plants of Western Ghats based on simple image based keys observed in the field. The application can be used by scholars, ecologists working on conservation of RET plants of Western Ghats.

Android app for Butterfly Identification- “*Pathanga Suchya*”- Version 2: This is an image based butterfly identification app for android smart phones and has grabbed the attention of many butterfly enthusiasts especially amateurs and children by enabling them to identify the butterflies in the field.

Android app- ‘Plant Place Picture’: This app has been developed to promote the participation of common man in generating data for the IBIN on the distribution, images and any useful data on plants and animals in the field through crowd sourcing. It provides a platform to snap and upload the images of species along with an instantaneous info on its

coordinates such that the central data unit automatically compiles and updates the distribution maps with the images.

Efforts are underway towards expansion of IBIN through connecting new Bioresource Information Centres and integration of IBIN services to Bhuvan Geoportal.



Figure 10. A) Android app for ‘Rare Endangered and Threatened Plants of Western Ghats’; B) Android app for Butterfly Identification- “*Pathanga Suchya*”- Version 2; C) Android app- ‘Plant Place Picture’

c) **National Certification System for Tissue Culture Raised Plants (NCS-TCP):** The Department has been implementing the “National Certification System for Tissue Culture Raised Plants (NCS TCP)” and notified as the Certification Agency under the Section 8 of the Seeds Act, 1966. 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. The overall impact of this unique quality management system, first of its kind in the world, is the mentorship and guidance to tissue culture companies with the aim to improve India’s agricultural production to ensure food security in the country. Since implementation of the system in the year 2006, NCS-TCP has played a significant role for facilitating production of quality planting material and certification of end products. For implementing the NCS-TCP in the country, DBT has established a well-defined operational structure. A high level Apex Committee and Project Monitoring & Evaluation

Committee (PMEC) have been constituted for review of the activities related to NCS-TCP. DBT also constituted a technical working group for developing Standard/Guidelines for Accreditation/ Recognition and developing Standard/Guidelines for production and certification of Tissue culture plants. At present, this certification system has standards for production of eight economically important crops namely potato, apple, banana, sugarcane, black pepper, bamboo, citrus and vanilla. 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. The logo of NCS-TCP has been designed and registered under the Trade Mark Act, 1999 of the Government of India.

Currently around 80 companies are recognized with gross installed production capacity of about 340 million plantlets per annum and 5 Test Laboratories are accredited under this system. A number of State Agriculture Departments have made certification of Quality Planting Material mandatory for their plantation programme.

This year 109.67 million tissue culture plants have been certified by ATLS and 98,620 labels were issued. So far more than 250 million plants have been certified under NCS-TCP and 229017 certification labels have been issued.

Department has organized a Stakeholder Meet on “National Certification System for Tissue Culture Raised Plants (NCS-TCP)” on November 14, 2017 at New Delhi to create awareness among all the stakeholders.

Energy Bioscience Programme: Department of Biotechnology has been promoting R&D for biofuel technology development recognizing the need for alternate energy for transportation. Many leads have been taken forward for potential translational value in the form Biofuel products or technologies. During

2017 various novel technologies identified and supported which are able to address the current challenges associated with solid and liquid waste management.

Energy Bioscience Division has been promoting cutting edge research in Biofuel areas through Centre of Excellence, extramural projects and fellowship schemes. DBT is also participating in the Swachh Bharat Mission through supporting research projects on generation of energy from waste.

R&D projects supported in the area of Virtual Enzyme Center, National Repository for Microalgae and Cyanobacteria, Feedstock Development for various Biofuels, Photobioreactors and Algal Mass Cultivation, 2G Ethanol – Pretreatment and Enzyme Development - Biodiversity

One of the major achievements of Department in this area is Transfer of Cellulosic Ethanol Technology developed by DBT-ICT Center for Energy Biosciences, Mumbai to Oil Marketing Companies (HPCL and BPCL). Also enzyme needed for 2G Ethanol is being developed at DBT-IOC and DBT-ICGEB Centres. While progress is being 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 strengthened by launching Bioenergy Awards in Cutting Edge Research (B-ACER) and continued support to Energy Bioscience Overseas Fellows. Also, Indian Biological Engineering Competition (iBEC) call was announced to support students teams to participate in an International contest iGEM 2017.

Under Partnership for Advance Clean Energy Research (PACE-R) between India and US DBT and DST have jointly supported Joint Clean Energy Research and Development Center (JCERDC) program for last 5 years in three mutually agreed priority areas; Solar Energy, Energy Efficiency of

Buildings and Second Generation Biofuels. Three projects supported in consortium mode to IICT, Hyderabad and University of Florida has successfully completed.

a) Bioenergy Centers: The Department has been supporting four DBT-Bioenergy Centers with specific goals and targets and Centre wise major achievements are mentioned below

a.1) DBT-ICT Centre for Energy Biosciences, Institute of Chemical Technology, Mumbai: DBT-ICT 2G Ethanol Technology a highly competitive technology for lignocellulosic ethanol production has been scaled up to demonstration plant at India Glycols Ltd., Kashipur, Utrakhnad, India. The Centre has signed MOUs with Bharat Petroleum Corporation Ltd. and Hindustan Petroleum Corporation Ltd. to scale up this technology to produce 100KL 2G ethanol/day at Bina, MP and Bhatinda, Punjab respectively.

The Centre Team has developed Municipal Solid Wastes to Bio-Oil Technology, a composite technology that is capable of handling the unsegregated MSW. The available carbon in the waste is to CTL-Oil- converted to Biogas and the demonstration of the technology using 1tonMSW/day is underway in collaboration with BPCL.

An innovative DBT-ICT ZeroD Technology has been developed for distillery spent wash processing to generate energy and fuel product while also producing clean water. The centre has successfully designed scalable algal photobioreactors wherein CAPEX and OPEX have been substantially reduced to improve commercial viability of algal based technologies.

a.2) DBT-IOC, Centre for Advanced Bioenergy

*Research, Faridabad:*DBT-IOC (the first partnership Bioenergy Centre) Centre has completed five 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, Membrane filtration system etc. Major achievements of this Centre in last year are as below

The centre team has developed tailored enzyme cocktail for each biomass feedstock and has done its scale up to 150 litres. This enzyme is benchmarked against world's best enzyme & its successive trails shall lead to large scale enzyme production at toll manufacturer site and supply to 2nd Generation Lignocellulosic ethanol plants for testing. This is first such attempt in country. 10 TPD demo plant on cellulosic ethanol to be commissioned soon shall have integrated enzyme production.

The centre team has carried out Life Cycle Analysis (LCA) studies for 2G ethanol process to ensure that the developed technology meets GHG reduction criteria. LCA vetting capability has been recognized as best available in country.

The centre has developed high performance phototrophic mutant algae strains producing high lipid content and have high temperature tolerance. Scale up of these mutant strains done in 20 L & 200 L to produce algae biomass for lipid production in sea water and recycled media.

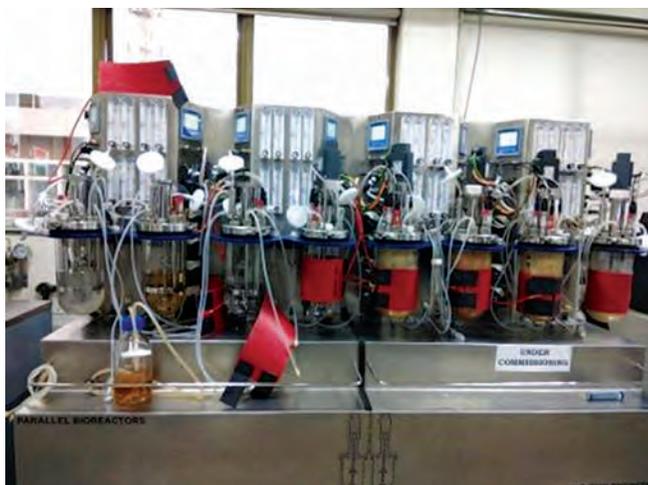


Figure 11. Parallel Bioreactor at DBT-IOC Centre

a.3) *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. The major achievements in this year are as below.

Enzyme Development-The efficiency of cellulase enzymes, named DICzyme-1 developed using engineered fungal strain also validated from third party. Industrial collaboration initiated for scaling up the enzyme production.

Yeast Engineering-Genetically engineered yeast strains developed for direct fatty acid ethyl ester (FAEE) production and identified high TAG accumulating yeast and fungal isolates. Algal metabolic engineering & Omics. Developed genetic engineered of marine alga strain for higher biomass and lipid for biofuel applications, remediation of urban wastewater and algae growth.

Systems Biology-Reconstructed the largest genome scale model till date for an alga. Utilized metabolic labeling to quantify precursor

contributions to polyhydroxybutyrate (PHB) in cyanobacterium. Software developed to conduct stationary ^{13}C -MFA using freely available tools, thus circumventing the need for MATLAB, a proprietary platform. Cellulase enzyme composition, named DICzyme-1, developed for effective biomass hydrolysis. Pilot scale technology developed to jet oil from modified algae and remediation of urban wastewater.

a.4) *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 IIT Mumbai facilitated with central equipment facility for molecular biology, fermentors and LCMS etc. for analysis purpose.

b) *The thematic group wise achievements:*

b.1) *Theme I: Cyanobacterial Biofuels*- A recombinant strain of cyanobacteria producing high titers of alkane has been constructed while some robust cyanobacterial strains have also been isolated and are being characterized genetically, proteomically and metabolically.

b.2) *Theme II: Algal biofuels* - Engineering of *Chlorella vulgaris* cells to produce either bio-ethanol or lipids are being attempted successfully through genetic engineering attempts for generation of sustainable sources of bio-fuel.

b.3) *Theme III: Algal Bioenergy*- process engineering - The use of algal biomass for hydrogen production is currently underway with great success. In order to optimize the production of high density algal cultures for maximal biomass production several parameters such as growth at different CO_2 regimes were successfully undertaken and

conditions optimised from lab scale reactors, which when scaled up in the pilot plant with improved biomass yield which exceeded the set target. Dual (Air-lift and Bubble-Column) 25L Photobioreactor, with a working volume of 20L was installed. Algal yield increases linearly with reactor volume and external surface area. Electro-harvesting of microalgae using stainless steel as an electrode improved the biomass recovery to 98%.

b.4) Theme IV: Biochemical, Thermochemical and electrochemical conversion - New cost-effective and green Ni/Co-intercalated natural clay catalysts have been developed for converting algae oil to diesel grade hydrocarbons in the presence/absence of a solvent. New $\text{SiO}_2\text{-Al}_2\text{O}_3$ based solid support materials have been prepared using a modified procedure. Also a low cost membrane from coconut shell was developed for microbial carbon capture cells (MCCs) for continuous algae cultivation and power generation.

b.5) Theme V: Biomass to biofuels - Acidogenic mixed consortia (dominated by Clostridium sp.) has been developed for hydrogen production by dark fermentation using algal biomass successfully. Structural model of a α -glucosidase (UnBGI1) from soil metagenome also successfully cloned and the crystal structure determined.

b.6) Theme VI: Bioreactor design - A black-box system of control (toolbox) for fermentors has been developed that are being validated with other processes and systems

b.7) Theme VII: Techno-economic and life cycle analysis of biomass-derived biofuels - Techno-economic analysis and Life Cycle Analysis (LCA) of biochemical refinery being studied to address optimal refinery locations.

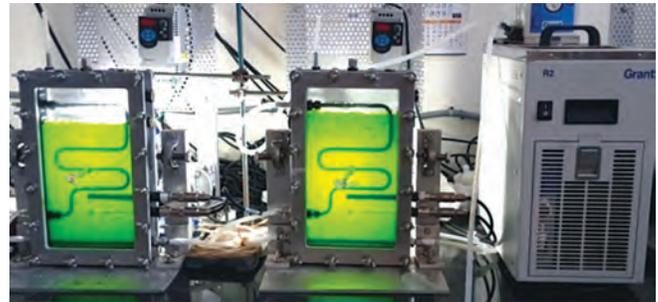


Figure 12. A. Microalgae production by flat panel rocking bioreactor; B. Hydrogen production using microalgae as a substrate in double jacketed reactor under Pan IIT Bioenergy Centre

c) Significant achievement of extramural Projects supported to various institutes:

c.1) Virtual Enzyme Center: This is a network project involving 6 partner institutes with complementary expertise of microbe engineering to product commercialization. The 6 work packages are divided among JNU, Delhi University South Campus, DBT-IOC Centre Faridabad, IIT Madras, Anna University, IIT Bombay. The purpose of establishing this network is to develop robust and cost effective indigenous enzyme for cellulosic ethanol production.

There are total 6 work packages complementary to each other. So far fungal strains isolated showing enhanced cellulase activity in SSF. Improved saccharification efficiency obtained in packed bed reactors in comparison to slurry reactors. Improved host platform designed for recombinant protein

production while Transformation protocol for *P. citrinum* and isolation of cellulase genes.

PEG-mediated protoplast method was established for the transformation of *P. citrinum*

Endoglucanase and β -glucosidase genes from *Thermoas cusaurantiacus* have been cloned

Developed an expression system for the *P. citrinum* and the IOCL strain

c.2) National Repository for Microalgae and Cyanobacteria (NRMC) at Bhartidasan University: A National Repository for Microalgae and Cyanobacteria (NRMC) has been established at Bhartidasan University, Trichirapalli. The aim of this proposal is to establish a functional repository for freshwater and microalgae and cynobacteria so as to provide these cultures to the researchers in university or institutions and to serve as a part of national network for phycologists. NRMC houses 1034 psychro- (150), meso- (814), thermo- philic (20) and hypersaline (50) microalgae in its germplasm and upgraded continuous survey and isolation.

A total of 21581 cultures (18822 Bacteria, 710 probable Actinomycetes, 1861 filamentous fungi and 188 yeast) had been accessioned, preserved and maintained in the repository. A total of 15000 cultures have been characterized by MALDI-TOF analysis. Many cultures have been supplied to various institutes and industries for research purpose.

c.3) Feedstock Development for various Biofuels: Commercialization of sweet sorghum as a complimentary feedstock for ethanol production in the sugar mills of Maharashtra, Tamil Nadu and Gujarat: Scientists at IIMR and ICRISAT Hyderabad are working on development of low lignin high biomass energy sorghums through introgression breeding

utilizing *bmr* 6 and 12 genes. Indian Institute of Millets Research (IIMR, formerly DSR) and ICRISAT at Hyderabad have developed 28 high biomass varieties of sorghum (without affecting grain production) and 20 brown midrib derivatives.

For the first time Network Team has successfully demonstrated that sweet sorghum can be grown in sugar mill areas and can be crushed in the sugar mills without changing the mill set up. A Pilot scale study is being conducted at Core green sugars and fuels private Ltd, Karnataka using RVICSH28 to generate more information on juice quality.



Figure 13. A) Sweet sorghum stalks ready to be crushed in the sugar mill; B) Sweet sorghum juice gushing out of the crusher in sugar mill industry without changing the nut and bolt of the machinery.

- Development of low-lignin high-biomass sorghums suitable for biofuel production was studied at IIMR Hyderabad: RSSV 138-1, SSV

20, IS 11861, [(N 592 x SPV 2071)-4]-1, [BN 111 x (SPV 462 x IS 21891)]-6-1-1 and SSV 84 x IS 21890 were promising for biomass yields under the multilocation trials. The identified region specific high biomass low lignin lines from the project will be grown on commercial scale to realize the targets of national bio fuel policy (20% blending ethanol by 2017).

- Feedstock for biodiesel: The Research & Development projects on improvement in Seed Yield of *Jatropha curcas* through Breeding and Silvicultural Practices, Phenotypic screening of oleaginous microalgae, Molecular studies of potential biodiesel producing strains of microalgae, Developing low water demanding cultivation system of algae for Rajasthan, On-site High Density Microalgae Cultivation, Photobioreactor Design and Harvest Technology for Algae Production have been supported. In the project on Computational Fluid Dynamic (CFD) Modeling of Algal Photobioreactors for CO₂ sequestration and Conversion to Value Added Products, a CFD model for 1000L pilot scale open raceway pond was successfully developed which predicts the hydrodynamics and aims at elimination of static zones in microalgal culture. CFD model for bench-top indigenously designed closed air-lift photobioreactor was developed which predicts water velocity, gas velocity, gas hold-up, mass transfer coefficient and light transfer for microalgal cultures. A semi-engineered 1000L open raceway pond with automation system for CO₂ sequestration and production of value added products was developed for *Spirulina* as model microalgae
- 2G Ethanol from Industry waste: Research projects on development of a cost-effective green technology for lignocellulosic biomass pretreatment using natural deep eutectic

solvents, development of microwave systems for pretreatment of lignocellulosic biomass for cellulolytic enzymes and ethanol production and consolidated bio-processing of lignocellulosic biomass by thermo tolerant yeast have been supported. Scientists at SPRERI have prepared 23 different natural deep eutectic solvents (NADES) for lignocellulosic biomass pretreatment. An integrated indigenous pilot-scale reactor successfully designed and developed at SPRERI for biomass pretreatment at elevated temperatures and pressures and subsequent solid-liquid separation process. Cloning, expression and analysis of the CBH1 and BGL1 genes under constitutive promoters with and without yeast mating factor α (89aa) secretary signal sequences has been done by Scientist at ICGEB, New Delhi.

d) Biorefinery: Research & Development projects have been supported on development of cost effective bioethanol production process from biodegradable municipal solid waste, Integrated biorefinery model-Process development for the concomitant production of Bioemulsifier, Lipid, Biodiesel, Glycerol and biomass as animal/fish feed using industrial waste in a renewable yeast feedstock, bioprospecting for novel lignocellulolytic glycosyl hydrolases and auxiliary enzymes from diverse thermophilic fungal strains using proteome based approaches and a project on pilot scale demonstration of Production of biofuel by carbondioxide concentrating bacterium. The work by Scientists at IIT Kharagpur on oleaginous yeast has progressed to the extent of lipid production and extraction using various low cost substrates. Consistently, the team is now able to produce about 35-40% lipid of the dry cell weight of the oleaginous yeast strain.

Development of an improved/intensified in-situ transesterification process also accomplished for oleaginous yeast biomass based biodiesel production

in terms of energy, time and low capital cost. The biodiesel product conformed to the ASTM D6751 and EN14214 standards and bioemulsifier after characterized found to be a glycolipopeptide complex with 56.8% carbohydrate, 12% protein and 2% lipid

e) Initiatives under Swachh Bharat Mission:

e.1) Demonstration of Bio-toilets in Schools of North East India: This programme is prepared based on integration of proven technologies and known knowledge customized in easily takeaway module for school children of North East region. So far 50 Units have been installed and operationalized (Assam- 35, Tripura-15, Mizoram=10, Manipur-10). TERI membrane reactor has been installed at DPS, Guwahati. All units are under evaluation for usage and data collection.

e.2) Waste to Energy: Through competitive process Waste to Energy proposals have been identified for demonstration of innovative and viable processes over traditional methods like land filling and saving the environment from adverse effects of global warming by minimizing the emissions of methane from landfill sites. One demonstration project and 5 R&D projects have been sanctioned during this year. Two demonstration projects are under consideration. It is expected that the successful technologies can then be transferred to Municipal Corporations for implementation to disposal of MSW more scientifically and environment friendly manner.

f) Capacity building in Bioenergy:

f.1) Energy Biosciences Overseas Fellowship: DBT “Energy Biosciences Overseas Fellowships” is a flagship scheme of DBT for bringing back the scientists of Indian origin who are working outside the country in the field of Energy Biosciences. Energy Biosciences Chairs are for

the senior scientists who are desirous of pursuing, complementing and enhancing quality of R&D in energy related biosciences in Indian institutions. Currently seven overseas fellows and two chairs have been working at various host institutions. Several processes in different areas of biofuels, enzymes, bioenergy at various Indian institutions are being developed by fellows enriching the R&D in the bioenergy field. Cumulatively around 20 papers have been published in international peer reviewed journals and two patents have been filed in the current year. This DBT scheme is managed by DBT-ICT Centre for Energy Bioscience, Mumbai.

f.2) Bioenergy-Awards for Cutting Edge Research (B- ACER): The Department of Biotechnology, Govt. of India and the Indo-US Science and Technology Forum (IUSSTF) have partnered for a dynamic visitation program called The Bioenergy-Awards for Cutting Edge Research (B- ACER) focusing on the capacity building in the frontier area of Biofuel and Bioenergy. The B-ACER Program has successfully completed one year and currently the second batch of 2017 B-ACER Awarded Interns and Fellows have commenced their Internships/ Fellowships at respective U.S. Universities. So far 11 Interns and 9 Fellows have been benefited from this Program including training for 6 Internships and 2 Fellowships during 2017.

g) International Collaboration in Clean Energy:

g.1) Indo-US Joint clean Energy: The project addresses the second generation biofuel R&D priority area of the US – India Joint Clean Energy Center emphasizing 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 feed stocks as well as biofuel.

Five year project successfully completed under bilateral program between DBT and Department of Energy US. High biomass sorghum varieties successfully tested under this project are being taken forward separately for Multi location trial and large scale implementation. Through this program both countries could connect relevant teams of scientists and engineers from both countries to promote clean energy.

g.2) The Indian Consortium for Advanced Biojet Fuel Technologies (Ic-ABFT): The Consortium has IIP Dehradun as lead institute and 4 partner institutes. Consortium has developed mechanical hydrothermal deconstruction to recover hemicellulosic sugars with 92% hydrolysis which gave 87% saccharification with commercial enzyme. Team has developed a proof of concept for hydro-processing of yeast SCO into renewable jet fuel.

g.3) US-India Advanced Bioenergy Consortium: Second Generation Biofuels: [Lead Institute - JNU] Partner Institutes- JNU, IISC-Bangalore, UDSC, ICGEB, IIT-Bombay, Bioseed Research India, NCBS, Bhartidasan University

Consortium is working together on two different tasks to obtain improved feedstocks i) mutant/engineered germplasm of rice and sugarcane with enhanced biomass and ii) engineered cyanobacterial strains with enhanced productivity for advanced biofuel generation.

g.4) DBT is also Coordinating Mission Innovation in Clean Energy and Biofuture Platform as a nodal agency to coordinate efforts for India

h) Indian Biological Engineering Competition (iBEC) PRE- iGEM Competition: National Competition Indian Biological Engineering Competition (iBEC) was launched in 2016 by Department in order select and support best Indian student teams to participate in this international contest iGEM (International Genetic

Engineered Machine) competition which is held every year in Boston, USA.

iBEC the Pre-iGEM competition encourages UG and PG students researchers to work in teams and solve real-world challenges by building genetically engineered biological systems. Each team manages their own projects, advocates for their research, and secures funding with a mentor. Teams are also challenged to actively consider and address the safety, security and environmental implication of their work. So far, Department has supported 7 students team from various institute like IITs, IISER, IISc., and Public/Private Colleges/Universities.

This year Pre-iGEM (iBEC) competition was announced by Department of Biotechnology in February 2017. In response, a total of 12 proposals were received and evaluated by an Expert Committee set up by Department. After a competitive application procedure, support provided to five best selected teams for consumable, registration and travel of INR 10 lakhs/ team to travel to Boston, USA to participate in iGEM 2017 held during November 9-13, 2017. 5 teams from various institutes were given support from DBT for research work and travel to US for iGEM 2017 contest. These teams presented interesting research projects and performed extremely well and 4 teams secured Gold and Bronze medals

ENVIRONMENTAL BIOTECHNOLOGY

The aim of the Environmental Biotechnology programme of the DBT is to support research and development programme in the areas relevant to waste management and environmental improvement. During the period, focus was on development of microbial technologies for environmental improvement, development of treatment process of industrial effluent, Bioremediation of xenobiotic compounds. Scanning of the microbial diversity of various environments

and deciphering their genetic information was also carried out with the aim of isolating microorganisms that could be used in the in bioremediation processes. With the objective to provide various possible wastewater clean-up options, Department has also identified priority research areas like in-situ detection, mapping and quantification of pollutants with innovative approaches, development & demonstration of wastewater specific effective bioremediation options like natural attenuation to bio-stimulation, bio-augmentation or a combination of filtration, phyto-remediation and microbial degradation etc.

Department took initiative on development of programme on remediation and reclamation of agricultural soils at Hexachlorocyclohexane (HCH) dumpsite. A brainstorming session has been organized in November 9-10, 2017 to identify priority areas for remediation to polycyclic aromatic hydrocarbons (PAH) in PAH polluted environment. A study has been undertaken on mapping of research outcome and development of compendium in the area of remediation of dye, dye intermediates and textile industrial waste. Site visits have been organized to understand issues relevant to textile industry wastewater management and explore the possibilities for development of industry-academia collaborative R&D projects to address challenges in textile industry wastewater management.

Department has initiated R&D projects on various aspects of wastewater treatment processes such as integrated eco-electrogenic system for efficient and sustainable treatment of textile wastewater, monitoring and assessment of emerging pollutants and phycoremediation, bioaugmentation of activated sludge for enhanced biodegradation of paper mill wastewater, field scale evaluation of bioreactor developed with indigenous microbial inocula for treatment of textile industrial effluents, assessment of the potential of Natural Genetic Biofilters for wastewater treatment in constructed wetland,

process development for tannery wastewater treatment involving membrane bioreactor (MBR) process integrated with microalgal bioremediation etc. Some of the salient achievements of the programme are highlighted as follows:

A project on biodegradation of chlorinated organics by extremophiles: Developing biocatalyst for effective remediation jointly carried out at IITD, New Delhi and Delhi University, Delhi. The investigators have optimized biodegradation of DDT using *Serratia marcescens* and the metabolites/ intermediates were characterized and possible pathway was deduced. It showed up to 60% of degradation under optimized conditions. In case of 4-CB, *Enterobacter sp.* and *Burkholderia xenovarous* showed about 84% and 75% degradation after 5th day, and complete degradation was observed after 15 days.

Under a pilot study for the bioconversion of hazardous DEHP plasticizer in plastics carried out at University of Calicut, a soil isolate *Achromobacter denitrificans SP1* was studied in detail for the degradation of DEHP plasticizer using in situ remediation. Also strain was further studied for the production and chemical characterization of alkaloid molecule 25-C Prodigiosin. The isolated alkaloid was further characterized by molecular modelling and docking studies so as to understand the interaction between the alkaloid and target receptors such as prostaglandin synthase-2, Icx2 and Jak3 kinase. This has helped to elucidate the metabolic steps involved in the degradation of DEHP.

In the project on bioremediation of polycyclic aromatic hydrocarbon contaminated soil using plant-microbe interaction in rhizosphere at Assam University, Silchar, five bacterium have been isolated from contaminated industrial sites. The bacterial consortium of five potential isolates was established as a result of positive interaction among them. The application of bacterial consortium increased the rate of degradation of Pyrene (60-80%). Microbial

community approach reveals that the proteobacteria, actinobacteria and firmicutes were highly abundance in presence of Pyrene treated soils, which have shown potential in degradation of Pyrene and also reduced the stress in the host plant.

Biosurfactant enhanced bioremediation of PAHs contaminated soil of oil field situated at upper Assam has been attempted at IASST, Guwahati. Investigators have isolated biosurfactant producing bacterial strains from crude oil leakage sites. Among 25 soil isolates, *P. aeruginosa* SR17 was found to produce high yield of biosurfactant (4.8 gm / litre), which was purified and further characterized for its chemical composition, CMC and surface tension properties. Further, this rhamnolipid biosurfactant was applied to the soil in order to study its effect on the removal of crude oil contamination. The results showed increased removal of PAHs.

Under a project on utilization of cassava bagasse (CB) as a substrate for the production of microbial exopolysaccharides: Xanthan and Curdlan at SASTRA University, Tanjavur, investigators have accomplished acid/alkali/enzymatic pre-treatments of CB to produce reducing sugars in the hydrolysate, isolation and taxonomic characterization of exopolysaccharide producing strains of *Xanthomonas*, *Agrobacterium* and *Alkaligenes*. They have obtained xanthan (best yields 0.32g/gCB), curdlan (0.003g/gCB and pullulan (0.02g/gCB ds) using the aforesaid isolates along with *Paenibacillus* and a fungus-like bacterium *Aeurobasidium pullulans*.

Under a project on improving biomethanation and bioremediation efficiency of cassava sago effluent by nitrogen amendments under HRAP system for safe recycling of cassava sago effluent, investigators have demonstrated that biomethanation efficiency of cassava sago effluent could be enhanced by addition of urea at C: N (40:1) ratio with cow dung and poultry droppings as inoculum source, and

anaerobically digested sago effluent can be further purified by *Spirulina* cultivation under HRAP system to achieve the twin objectives of improved bioremediation efficiency of sago effluent and *Spirulina* biomass production.

Project on design upgradation of vertical sub-surface constructed wetland unit for treatment of dairy wastewater carried out at GEU, Dehradun. Different designs of Vertical flow Sub-surface Constructed Wetland (CW) units were operated to assess the most appropriate design which can provide the maximum removal of pollutants such as BOD, TSS, Total Nitrogen, Total Phosphorous, ammoniacal Nitrogen, Total dissolved solids(TDS) from dairy wastewater. All the CW units showed good removal efficiency of pollutants from dairy wastewater. There was remarkable reduction in the average concentrations of all the pollutants (BOD, TN, NH₄-N, TP and TSS) in all the CW units. The present research findings may help in reducing the size of CW units yet providing higher removal of water pollutants from dairy wastewater coming out from dairy premises.

A phytoremediation treatment process for the degradation of dyes from textile industrial effluent has been developed at Shivaji University, Kolhapur. The developed lagoon could remove the dye and maintained the parameters like COD, BOD, TSS, TDS, pH and metals of real industry textile effluent to their acceptable value. After treatment of dye Rubine GFL, dye mixture and textile effluent showed nontoxic effects on agricultural seed of *Triticum aestivum* and *Phaseolus mungo*. Further research work of treating the textile effluent on actual dye disposal site is in progress. Further, on field application of macrophyte *Ipomea aquatica* in wastewater lagoon of capacity 60,000 L successfully carried out. Trials for onsite treatments are underway for finding the technological options from tertiary treatment of textile industry wastewater.

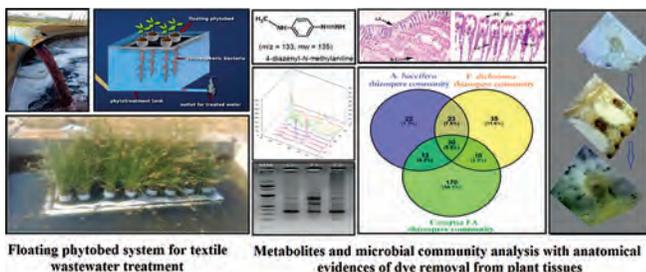


Figure 14.

In the project on bioremediation of degraded mangrove forest along the embankment of the river Ramganga being carried out at WBSU, Kolkata, investigators have made substantial progress not only in understanding the community composition of mangroves in degraded and non-degraded habitats but also identified the stress factor impacting the mangrove in degraded sites in terms of osmolytes. Stress in degraded site is expressed in higher Na⁺/K⁺ ratio and higher level. Considerable area in the site has been restored. On-site nursery is being regularly maintained following protocol standardized in the project.

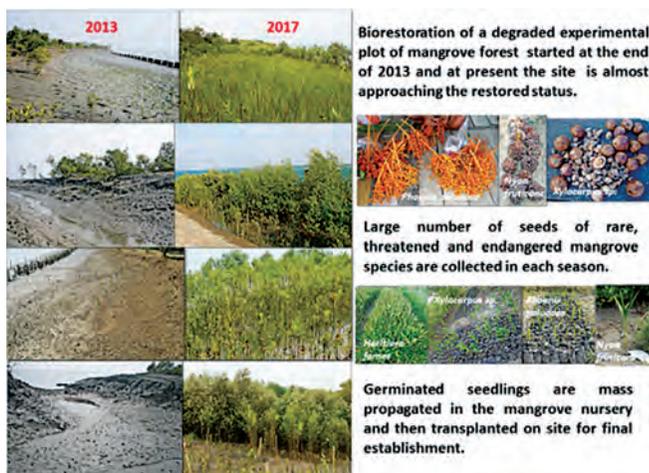


Figure 15.

Under a joint project between NCBS and CWS, Bangalore, genome-wide data has been used to prioritize the country's tiger conservation efforts in the Malenad-Mysore landscape of Karnataka. In a paper published in Nature Scientific Reports, investigators have chalked out ways to identify and conserve genetically connected populations, as well

as to maintain connectivity within them so as to carry out effective conservation efforts in the limited available protected area.

In the Pan India network project on preventing extinction and improving conservation status of threatened plants using biotechnological tool, field surveys during the last four years resulted in discovery of 906 new populations of 94 species. Ecological Niche Modelling for all the species was improved during the period and as on date the predictive modelling and field validation for 82 species have been completed. The models for 18 species, which have very few individuals/ populations are being improved. The molecular profiling of 17 species viz., *Aconitum spp.*, *Amentotaxus assamicus*, *Crepidium acuminatum*, *Cycas beddomei*, *Dipcadi concanense*, *Dipcadi goaense*, *Embelia floribunda*, *Embelia ribes*, *Embelia subcoriacea*, *Ilex embeloides*, *Ilex excelsa*, *Ilex khasiana*, *Ilex venulosa*, *Impatiens talbotii*, *Justicia beddomei*, *Madhuca insignis*, and *Rhododendron wattii* has been undertaken during the last one year. Standardization of macro-propagation methods was completed for 11 species. Micro-propagation protocols were developed for five species during the year. Out of 94 species studied in the project, 50 species were reported to have medicinal value. Further studies are in underway.

HUMAN DEVELOPMENT AND DISEASE BIOLOGY

Maternal and Child Health Programme:

Maternal and child health programme emphasizes 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 competitive grant support system.

Major New Initiatives Taken and progress in ongoing programmes are;

a) Healthy Life Trajectory Initiative: 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. The initiative is taking forward the knowledge that programming for many chronic diseases, including obesity, cardiovascular disease and metabolic syndrome occur early in life, starting from pre-pregnancy to pregnancy, infancy and childhood periods and that the effects can be inter-generational in nature. It is further recognized that early intervention through nutrition and life style changes may prevent these chronic diseases later in life. The study is a community-based, cluster randomized intervention with three arms (pre-conception, pregnancy and control), set in rural Mysore.

b) Human Placental Research: Placenta endures the beginning of a new life in pregnancy as the sole organ performing functions of multiple organ systems. This has excited scientists around the world to understand the detailed biology and pathophysiology of this organ.

This year several programmes have been supported chiefly promoting research on placental structure and function across pregnancy. The major area of support include isolating placenta derived nanovesicles and study various omics with a goal to develop biomarkers for placenta health and function across pregnancy giving important insights into future complications and outcome of a pregnancy. Effect of maternal fuel and nutrient supply on fetal growth and its impact on further development is another major area of support. Research on metabolic pathways for placental development and placental

regulatory preferences have also been supported.

The Centre of Excellence grant supported under this area investigates if intervention with vitamin B12, multi micronutrients and protein in adolescent girls before conception and through pregnancy will favorably influence ‘fetal programming’ of diabetes and obesity in the offspring. The trial is set in the preconceptional birth cohort ‘Pune Maternal Nutrition Study’ which has followed up parents (F0) and children (F1) over 20 years with over 90% follow up rate. The intervention is in the F1 generation. High quality biospecimens have been collected during screening, after starting intervention, during pregnancy, at delivery and upto 2 years after birth in the mothers (F1) and the babies (F2) for measurements of metabolic, nutritional, and endocrine phenotypes, as well as for DNA methylation, transcriptome, metabolome, and microbiome.

In the study blinded comparison showed that F1 generation daughters are taller, heavier and have higher circulating glucose and lipid levels during pregnancy compared to their mothers (F0). Moreover, the F2 generation daughters are heavier, longer and have lower fat measurements at birth compared to their mothers (F1). The success of the intervention in achieving the goals and the effect on molecular signatures will be known only after completion of the trial (Fig 16).



Figure 16. A participant family in the Pune Maternal Nutrition

Study (PMNS) and the Pune Rural Intervention in Young Adolescents study (PRIYA). The PMNS started in 1993 in married, non-pregnant women (F0 generation) who gave birth to F1 children who participated in the PRIYA trial of micronutrient supplementation and gave birth to F2 children. The picture shows F0 parents and F1 and F2 daughters in the front row and the great grandmother in the background on whom we have historical information.

c) Grand Challenge Research Programme on Preterm Birth:

A large network programme was initiated in 2013 to advance a comprehensive and cohesive research solution pathway to address multiple strategic priorities in preterm birth discovery and development, needed in our country and other low-middle income countries. A multi-disciplinary approach comprising methodologies of clinical, epidemiological, statistical, genetic, proteomic and imaging sciences is being used. The women are enrolled early in their pregnancy and are serially followed through their pregnancy till childbirth and 6 months post-partum. The cohort was initiated in August 2015. Till date, 3576 women have been enrolled and 2103 women have a documented end point of their pregnancy. The disturbingly high rates of PTB (15%), low birth weight (> 20%) and small for gestational age (13%) justifies the need for initiating this research program and for continuing to follow the large cohort to achieve the initial objectives. Preliminary data has shown some interesting clinical and biological risk factors that could aid in risk stratification.

A large bi-bank of longitudinally collected varied bio specimens with well characterized information on environmental, clinical, social, epidemiological determinants at different time points in pregnancy has been established at THSTI. The repository has an imaging bank that has currently over 1.3 lakhs ultrasound serial images on fetal morphology and biometry, blood flow of uterus, fetus, & placenta, >400,000 bio samples comprising of maternal plasma, sera, saliva, feces, high vaginal swabs, urine, cord blood, placenta, and there is development towards establishing an omics bank. With this

platform in place the plan is to expand the area of research for further innovative applications in PTB and other related adverse birth outcomes. The biorepository will be expanded to become a national resource for translational studies in maternal and child health. Governing processes will be put in place such that the clinical and epidemiological data, omics bank and the ultrasound images in the repository will be made available to stakeholders.

d) *Fetal and Neonatal Health Research*: An important effort is being made to generate high-quality, methodologically robust reference fetal growth charts for the Indian fetuses. Under this project, so far a total of about 140 women across different stages of pregnancy have been randomly assigned and examined to document the measurements of the fetal size parameters.

Sepsis remains one of the major killers of neonates across the world. One of the main reasons for this is inadequate means to diagnose sepsis early and accurately at the bedside. A study at AIIMS aims to address this issue by examining the role of procalcitonin- an upcoming promising biomarker in adults. In addition, a list of novel markers recently published as promising in developing countries is also being tested as proof-of-concept.

The clinical part of study was envisaged to complete enrolment by two years and thereafter complete the analysis in the next few months. An interim analysis shows that, the incidence of culture-positive sepsis was 14.9% (230/1546) and the pathogen profile shows *Staphylococcus aureus* (38.2%) as the most common isolate followed by *Acinetobacter baumannii* (31.7%). Further, very high rates of carbapenem resistance were detected in *A. baumannii* (90.5%) and *Klebsiella sp.* (60.0%). Over two-thirds of *S. aureus* and CoNS were methicillin resistant; vancomycin resistance was rare.

A programme support has been given to understand the immunological differences (Immunophenotyping

and function of monocytes, T cells and B cells) between small for gestational age (SGA) and appropriate for gestational age (AGA) infants and following up these infants for 6 weeks to determine reported neonatal infection-related morbidities. The aim is to identify immune differences, which can explain increased morbidity seen in SGA infants at the same time comparisons will also be made with adults. Adult and AGA monocyte subsets are compared and it was observed that overall the cord blood monocytes are not stimulated efficiently, especially the patrolling monocytes. The functional T cell assays on the CD4+ and naïve T cell subsets between the cord and adult blood populations reveal a two-fold difference in the activation status of the two groups upon stimulation. The study of functional characteristics of B cells derived from cord blood and adult blood display higher numbers of naïve B cells and immature B cell respectively and lower numbers of plasmablasts in neonates as compared to adults as expected. Functional assays for B cells have also been standardized.

Another important study aimed at identifying phenotypes of birth defects with limb malformations and to identify genetic etiologies for them has evaluated 100 patients with malformations of limbs and samples of the probands and family members are stored for DNA analysis. Detailed pedigrees and photographic documentation (with consent) have been collected. Sanger sequencing of candidate genes for cases with monogenic phenotypes identified pathogenic mutations in 11 of the 25 cases. Chromosomal microarray identified copy number variations in two cases out of 10 cases. Exome sequencing identified causative variants in 22 cases. In a case with distal arthrogryposis a mutation was identified in *LGI4* gene which has been identified as a cause of arthrogryposis in 2017; indicating a type of distal arthrogryposis is allelic to arthrogryposis multiplex congenital for which further functional studies are planned. Consanguinity is common in India and is of great help in identifying

mutations by exome sequencing. Exome data of 44 cases is yet to be analyzed / reanalyzed and compared with the data of the parents and search for novel genes is underway (Fig 17).



Figure 17. A child with distal arthrogryposis with a mutation in *LGI4* gene.

There is no data from India, on the prevalence of X-linked adrenoleukodystrophy (X-ALD) and other peroxisomal disorders, mainly because of inadequate availability of diagnostic facilities. Elevated blood C26:0-lysophosphatidylcholine (LPC) is considered to be a sensitive biomarker for X-ALD. A tandem mass spectrometry-based method is standardized for estimation of a panel of lysophosphatidylcholines (C26:0, C24:0, C22:0 and C20:0 LPCs) in 3.1 mm dried blood spots collected on filter paper, by heel or finger-prick. The results for proficiency testing were 100% satisfactory and the measurement of LPCs was found to be accurate and precise. Further studies are being conducted to validate the test in a cohort of symptomatic children with clinical features of leukodystrophy.

e) *DBT-ICMR Joint Working Group*: The Joint working Group with ICMR endeavors to identify invention and early-stage development of new medical technologies, early translation, development of innovative tools & technologies in the identified areas. A call for proposal under Maternal & Child health programme was made and now proposals on

pathophysiology of sepsis and also on rapid detection kits for sepsis are being processed for funding support.

f) Major Programmes on Kidney Diseases:

f.1) Pediatric Nephrotic Syndrome: Idiopathic nephrotic syndrome, the most common chronic kidney disease of childhood, is associated with significant morbidity related to disease relapses and immunosuppressive therapies. This *nationwide multicenter collaboration* proposes to help understand aspects of disease pathogenesis, disease course and impact of therapies. The project has enabled setting up of a *disease registry* for longitudinal cohorts of nephrotic syndrome, responsive and refractory to therapy with corticosteroids. The basis of steroid resistance is being examined through advanced sequencing techniques to develop algorithms for genetic testing in Indian patients. Studies examining additional aspects of the illness include: *(i)* disease pathogenesis, including studies on immune cells and microRNA & polymorphisms in genes involved in metabolism of immunosuppressive drugs; *(ii)* efficacy of therapy for the initial episode of nephrotic syndrome; *(iii)* long-term cardiovascular outcomes. The programme has been initiated at multiple centers.

f.2) Chronic Kidney Disease (CKD): 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 cardiovascular disease (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. Approximately 2500 patients have been

enrolled. Almost half of the subjects are reported to have occupational exposure to sand, dust, chemicals, animals etc. An equal proportion 52% subjects use drinking water from natural resource (well/hand pump/bore well/river). Large proportions (25%) of patients have used alternative drugs or medicines either before the onset of renal disease or for its treatment. It is significant as use of such drugs has been linked to various forms of AKI and CKD. Despite a diagnosis of CKD, the rates of recommended vaccination are poor. Whereas vaccination against HBV was completed in 29% of participants, only 1.6% participants had received vaccination against pneumococcus. About 16% of the participants have various forms of manifest cardiovascular disease at enrolment. It has been found that in contrast to African American population, polymorphisms in APOL1 gene are not found in Indian subjects with CKD. In an important finding from the GFR sub-study, it was discovered that the existing formulae used to calculate kidney function (glomerular filtration rate) using serum creatinine are inaccurate in Indian subjects which is likely related to poor muscle mass and vegetarian diet. Formulae based on cystatin C are more accurate. This has important bearing on how kidney function is measured in Indians.

f.3) International Network of Chronic Kidney Disease cohort studies (iNet-CKD): An important milestone for ICKD study is now inclusion in the iNet-CKD, a global consortium of CKD Cohort studies. The purpose of iNET-CKD understands CKD progression and its consequences around the world which can be enhanced through collaboration among study investigators implementing observational research studies in CKD. The PI is an elected a member of core group of iNET-CKD.

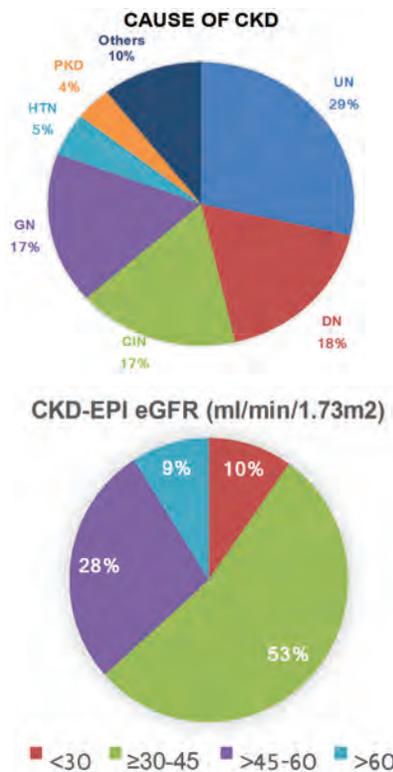


Figure 18. UN; Unknown, DN; Diabetic nephropathy, CIN; Chronic interstitial nephritis, GN; Glomerulonephritis, HTN; Hypertensive nephrosclerosis, PKD; Polycystic kidney disease

HUMAN GENETICS AND GENOME ANALYSIS

Under the initiative UMMID (Unique Methods and Management of Inherited Disorders) of Human Genetics and Genome Analysis program, during this year, some major steps have been taken by the Department towards better management of genetic disorders prevalent in our country in terms of facilitation of diagnosis and treatment facility. Considering the highest prevalence of genetic disorders, many consortia based R&D projects on Hemophilia, Hearing loss, Thalassemia, Cardiomyopathies, Maturity onset diabetes of the young (MODY) and many individual projects on other monogenic disorders have been initiated with the predefined deliverables. In order to support future research on inherited disorders, a major initiative in terms of establishment of disorder-based or

population-based Bio-banking facility has been taken during this period. With the aim to produce skilled clinicians and the establishment of diagnostic labs in the area of genetic disorders for adequate and effective genetic testing and counseling services in our country, a pertinent step has also been taken during this period.

India consists of ethnically, geographically and genetically diverse populations with several thousand endogamous groups. The load of genetic disorders is relatively high due to high birth rate and consanguineous marriage practiced in many communities.

By echoing lessons from a bench-to-community through translational genomics research, there is a need to foster the successful linking of large-scale genomics research projects with health care programs in our country. Considering these facts, as per the priority defined under UMMID (Unique Methods and Management of Inherited Disorders) initiative of this Human Genetics and Genome Analysis program, the following steps during this period have been taken by the Department to redefine the Human Genetics research in our country to harness the maximum benefit of this discipline in the line of developed countries:

In the beginning of the year, a Brainstorming meeting on Hemophilia was conducted with all pertinent stakeholders in this area viz: scientists, clinicians, industry people, representative of patient organization and Govt. Officials from ICMR, DHR and DBT considering the fact that India reports the second highest number of patients with Hemophilia A in the world. Subsequently, a call for proposal on Hemophilia was issued to invite proposals to find ways for implementation of viable, practical and sustainable hemophilia care strategies in our country.

In this line, a second call was issued on Monogenic Disorders under the priority 'Genomics to Health'. Many consortia-based proposals were designed and

formulated out of the concept notes received by the Department, in order to bring scientists working in the same area across the country together to address major problems on specific Monogenic Disorders.

To share limited resources and achieve optimal outcomes with the aim to assure common practices and quality standards and facilitate access to inherited disorder biomaterials for the scientific community, next Call was given to support the establishment of Bio-banking facility as a National Facility under the priority 'Genomics to Biology' of this program.

Considering the lack of sufficient trained manpower and diagnostic labs in the area of Human Genetics, later on another Call was issued to support training of clinicians cum creation of diagnostic labs across the country under the priority 'Genomics to Society' of this program.

The projects under the above Calls will be ready for funding in the next financial year.

Some of the significant achievements made during this period through the ongoing projects are given below:

Bio-registry [Asian Indian Donor Marrow Registry (AIDMR)]: Scientists from AIIMS, New Delhi are aiming to develop the state-of-art molecular immunology technologies for HLA typing for selection of histo-compatible donors for hematopoietic stem cell transplantation and for post-transplant monitoring. Significant efforts were made towards setting up and improving the requisite techniques like PCR-SSP (Sequence specific priming), SSOP (Sequence specific oligoprobing), Reverse SSO and sequencing based typing. The higher level of resolution obtained through these techniques are useful particularly in the unrelated hematopoietic stem cell transplantation and will be the basis of unrelated donor search through registry. Due to

these reasons, these techniques are being extensively used in the process of donor selection for bone marrow and renal transplantation, disease association studies as well as for teaching and training programs. Beside these, many short term training (1-15 days) and long term training (between 15 days to 2years) are also being offered to several students, doctors and scientists.

The study of scientists from SGPGI, Lucknow suggest that an element of genetic risk exists determining the pathogenesis of end stage renal disease (ESRD) involves deregulation of NK cells, their activity being inclined towards more activating state. This is the first report showing the association of the KIR cluster with ESRD. In an ancillary work they have also studied the genetic association of the KIR gene cluster among ESRD associated basic diseases like chronic glomerulo nephritis, diabetes mellitus, hypertension, chronic interstitial nephritis, polycystic kidney disease and autosomal dominant polycystic kidney disease. As per the study, differential behavior of KIR repertoire among these diseases may reflect the different immune mechanisms involved which may finally result into ESRD.

Chronic Obstructive Pulmonary Disease (COPD) Genetics Consortium in North Indian Population: Scientists from Public Health Foundation of India (PHFI), Gurgaon are aiming to create a bio-bank of COPD cases for future genetic studies. They have generated genotyping data by using the facilities available at Madras Diabetes Research Foundation, Chennai. They have used Sequenom Mass Array Technology for genotyping the genetic variants (GWAS hits) related to COPD and lung function. Finally, they developed bio-bank of serum, plasma and DNA samples related to COPD stored in required temperature in laboratory of PHFI, Gurgaon.

Gene Expression Profile of Human Retinoblastoma: To identify the differentially

expressed genes involved in the tumorigenesis and tumor progression in human retinoblastoma, a comparison of gene expression profiles of human retinoblastoma tissues and normal retinal tissues from cadaver eyes was carried out by scientists of AIIMS, New Delhi. Their gene expression data provide interesting insights into several genes and pathways that are dysregulated in retinoblastoma. Functional analysis of these genes leads to a better understanding of the development and/or progression of tumor. These genes belong to diverse cellular classes with functions in apoptosis, phosphorylation, cell cycle, DNA damage, transcription, oncogenesis, and tumor suppression. Their study has also shown for the first time that some of the key members of the MAPK/ERK pathway, Fas/Fas ligand pathway etc. are aberrantly expressed in retinoblastoma and can be used as therapeutic targets

Genetic mutations related to Maturity Onset

Diabetes of Young (MODY): Pregnant women with diabetes may have underlying beta cell dysfunction due to mutations/rare variants in genes associated with Maturity Onset Diabetes of the Young (MODY). MODY gene screening would reveal those women genetically predisposed and previously unrecognized with a monogenic form of diabetes for further clinical management, family screening and genetic counselling. In this study, undertaken at CMC, Vellore utilizing the Next generation sequencing (NGS) based protocol, fifty subjects were screened for variants in a panel of thirteen MODY genes. Of these subjects 18% (9/50) were positive for definite or likely pathogenic or uncertain MODY variants. The majority of these variants were identified and four with GDM. The identified variants included one patient with HNF1ASer3Cys, two PDX1 Glu224Lys, His94Gln, two NEUROD1 Glu59Gln, Phe318Ser, one INS Gly44Arg, one GCK, one ABCC8 Arg620Cys and one BLK Val418Met variants. In addition, three of the seven offspring screened were positive for the identified variant. Further NGS based comprehensive studies

with larger samples are required to confirm these finding.

Molecular diagnosis of Congenital Adrenal Hyperplasia (CAH):

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder due to deficiency of one of the enzymes involved in steroid biosynthesis. 21-hydroxylase (21-OH) enzyme is the most common among them that typically reduces cortisol and aldosterone secretion while simultaneously increasing androgen production. Irrespective of the genetic and gonadal status, androgen exposure in early fetal life leads to virilization of the external genitalia to varying degrees. Affected children present with genital ambiguity with or without salt wasting crises depending on the severity of enzymatic defect.

The genetic diagnosis of patients with CAH is complicated and very cumbersome. However, it is a useful adjunct to hormonal measurements in the genetic counselling of parents upon the birth of a CAH child and of adolescents during the transition to adult care.

AIIMS is one of the largest CAH cohorts in India consisting of 140 patients with various cultural, socio-economic backgrounds. Scientists of AIIMS have done gynecological evaluation in 32 patients as these patients desired to get married. Genetic counseling was given to the family members about the probability of risk transmission to the offspring. Many families have been restored from divorces, as their genetic diagnosis confirmed and convinced that both the life partners were equally at risk. Prenatal diagnosis (PND) was carried out in few couples who had a CAH child /had a history of previous CAH child's death and in fetuses.

Pharmacogenomics of Atorvastatin among Dyslipidemic Tamilian Population:

Hyperlipidemia is a major cause of atherosclerosis and atherosclerosis-induced conditions, such as coronary heart disease (CHD), ischemic

cerebrovascular disease, and peripheral vascular disease. Atorvastatin treatment among dyslipidemic Tamilian patients was associated with significant reduction in TC, TG, HDL-C and LDL-C levels. Scientists from JIPMER, Pondicherry reported that the studied genetic polymorphisms were significantly different for most parts from African Americans and Caucasians and also some genetic polymorphisms differed from that of North Indian population as well as between dyslipidemic patients and healthy controls. The study confirmed the unique genetic architecture of Tamilian population.

NON-COMMUNICABLE DISEASES

Cancer Biology: The mandate of the programme is new approaches for effective primary & secondary prevention; identify high-risk population based on exposure/genetic profile, biomarkers & non-invasive diagnostics suitable for field/homes, cancer vaccines; MAbs, small molecule inhibitors, targeted therapies, affordable & quality assured diagnostics; biosimilars. DBT is currently supporting 113 pilot projects for young investigators.

a) Major Initiatives: The Centre of Excellence was implemented to Rajiv Gandhi Centre for Biotechnology, Thiruvanthapuram and Regional Cancer Centre, Thiruvanthapuram. The aim is to establish a program involving fundamental researchers, clinicians, pathologists, bio-statisticians and computational biologists to understand the genomic landscape, pathogenesis, aggressiveness, metastasis of triple negative breast cancer and to develop innovative options for better diagnostics with prognostic value. The comprehensive understanding of genetics pattern of cancers will help us in identifying newer markers for cancer diagnostics, therapeutics, and help in designing of combination therapies.

b) Salient Achievement: Studies were carried to examine Immune responses to an onco-fetal antigen, hCG: A potential anti-cancer immunotherapy.

Exogenous hCG enhanced the viability of human colorectal and lung cancer cells and promoted the growth of syngeneic tumors in mice by inducing the synthesis of VEGF, IL-8, matrix metalloprotease (MMP)-2 and MMP-9, and increased invasiveness in an MMP-dependent manner. In addition, hCG consequently caused the TLR-2-mediated generation of the inflammatory, tumor-associated cytokines TNF- α and IL-6 from peripheral blood adherent cells. While anti-hCG antibodies restricted the growth of implanted tumor cells in nude mice, immunization of immune competent mice with a β hCG-TT conjugate supplemented with *Mycobacterium indicuspranii* provided synergistic survival benefit in animals implanted with syngeneic, hCG responsive tumor cells. These studies elucidate the pathways by which hCG can promote tumorigenesis, providing further rationale for anti-hCG vaccination in the treatment of gonadotropin-sensitive tumors.

In an attempt to study of the significance of DNA replication licensing proteins as markers of lung cancer and its precursors, the investigators have developed an innovative technique for sputum laboratory processing and documented the advantage of this technique over the conventional method. The malignant cells and metaplastic cells in sputum samples were characterized with DNA replication licensing proteins. The significance of these proteins as early detection markers of lung cancer is being evaluated.

Studies were supported to investigate Role of tumor derived glycosphingolipids in carcinogenesis. The results revealed a novel and critical role of the tumor derived glycolipid, GM2 in mediating metastasis and tumor progression. The role of ganglioside GM2 in mediating AIG, anoikis resistance and metastasis was confirmed using targeted genome editing tools.

Studies have been carried to explore the Myeloma Genome with reference to microRNA modulated gene expression. Microarray based comparative genomic

hybridization analysis of treatment naive *de novo* Multiple myeloma (MM) patients categorized 44% cases into hyperdiploid and 56% cases into non hyperdiploid subgroup. A comparison of miRNA expression profile of MM cases with healthy control samples suggested a differential expression profile of 98 miRNAs. The comparison of miRNA profile of hyperdiploid vs non-hyperdiploid myeloma cases suggested 67 miRNAs to be differentially expressed. An integrated analysis of miRNA and mRNA expression has revealed 241 differentially regulated genes as targets of differentially expressed miRNAs in MM as compared to controls. The correlation of miRNA and mRNA expression in hyperdiploid vs non-hyperdiploid MM suggested 25 differentially regulated genes as potential targets of differentially expressed miRNAs and are under further investigations.

Studies were undertaken for characterization of novel regulators of cell survival signaling in cancer cells. A siRNA-mediated knock down of HPIP, an estrogen receptor interacting protein reported to act as an upstream regulator of PI3K/AKT/mTOR signaling in cancer was shown to suppress Akt and MAPK activity and tumor growth. HPIP gene was upregulated under hypoxic as well as glucose limiting metabolic stress suggesting HPIP as a stress response gene in cancer cells. In addition, several missense mutations are identified in HPIP gene in human cancers. The functional significance of these mutations in relation to HPIP's oncogenic function is being investigated.

In a study to explore Global profiling and significance of alternative splicing events regulated by polypyrimidine tract binding protein 2 (PTBP2) in the advanced stages of chronic myeloid leukemia, it was observed that expression of PTB2 positively correlated with the progression of the disease and also increased with the increase in blast count. Imatinib treatment up-regulated miR223 in cultured bone marrow mononuclear cells isolated from CML patients and in 32Dc13-BCR-ABL cells with a

concomitant down-regulation of PTB2. Taken together, these results suggested that changes in the miR223/PTBP2 pathway may contribute to the abnormal splicing of several genes and shed light on the potential role played by miRNAs/RBPs in a subset of CML.

Studies were supported to examine Plakophilin3 (PKP3) role in tumor progression and metastasis in colon cancer. Preliminary results have indicated that PKP3 loss leads to an increase in resistance to drugs used to treat colon cancer such as 5-fluorouracil *in vitro* and *in vivo*. The resistance is dependent upon LCN2 expression and therefore identifies it as a possible target for therapeutic intervention.

Studies have been undertaken for development of genomics guided novel diagnostic and targeted therapeutic strategies for gastric cancer. A sub-classification scheme has been developed for 8 major sub-classes and upto 12 minor sub-classes of gastric tumors. The data have been verified in multiple available mRNA expression profiles of gastric tumors, comprising a total of 611 gastric tumor samples and is being evaluated for 60 gastric tumor samples. A genomics approach of "mRNA expression profile - to - gastric cancer sub-type identification" has been evolved and Biomarkers at the level of mRNA expression to define these subtypes have been identified. In addition, gene expression markers would also be investigated to understand their diagnostic potential at protein level and pathway focused drug screening system to identify suitable targeted drugs for the identified sub-classes of gastric tumors is under progress.

Studies were supported to examine the functional role of MAGEA3-cancer-testis antigen in pancreatic cancer. Preliminary investigation has provided evidences that demonstrate the role of MAGEA3 in the survival of pancreatic cancer cells under growth factor deprived condition. Ongoing and future studies will help in understanding the exact molecular

mechanism behind this pro-survival advantage conferred by MAGEA3 to cancer cells.

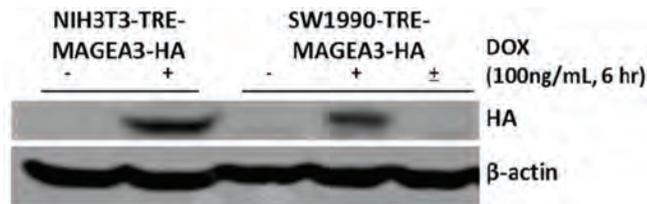


Figure 19. Western blot showing the expression of MAGEA3-HA protein in response to doxycycline in the generated stable cell lines.

In a study to identify and develop diagnostic, prognostic and minimal residual disease estimation markers for multiple myeloma (MM), a total of 298 new cases, 66 cases of progressive disease, 34 relapse cases and 36 patients of Monoclonal Gammopathy of undertermined significance (MGUS) have been recruited. All the MM cases showed large genomic heterogeneity with 47% cases being hyperdiploid with multiple trisomies of odd numbered chromosomes and 53% cases non-hyperdiploid. The most commonly observed genomic anomalies as detected by array CGH included monosomies 13, 14, X and segmental aberrations. The immunophenotypic characterization of 130 new cases suggested that CD19, CD56 along with cytoplasmic κ and cytoplasmic λ as most useful gating markers in delineating normal and malignant plasma cells. In addition, the frequency of MGUS patients (1.45%) in study is slightly lower in comparison to other Asian countries. The prevalence of MGUS was 2.5-fold higher in males than in females and with 60% cases having age more than 60 years.

In a study to investigate Inflammation regulated metabolic reprogramming and its implications in tumor progression, a histone deacetylase SIRT6 was observed to reconfigure HK2 promoter chromatin structure to favour a regulatory state conducive to diminished transcription. The role of protein arginine methyltransferase 1 in modulating chromatin landscape crucial for facilitating HLAB gene

expression was also identified. In addition, non-canonical role of TERT in metabolic reprogramming and DNA damage responses in GBM has been established. Further, it was observed that Warburg effect characterized by enhanced glycolysis and suppressed oxidative phosphorylation is associated with drug resistance in cancer cells.

Studies for assessment of the role of pterostilbene and its derivatives for prevention of bone loss in breast cancer induced bone metastasis revealed that pterostilbene-isothiocyanate has better anti-breast cancer activity than pterostilbene. Its effect was checked on osteoclastogenic cell line RAW 264.7 by adding RANKL, a chemical that induces osteoclastogenesis, it has been observed that the conjugate is also more efficient in preventing osteoclastogenesis as compared to only pterostilbene. Further studies are on-going to validate these preliminary observations and understanding the mechanism of action of this pterostilbene conjugates in inhibiting osteoclastogenesis and thereby augmenting osteoblastogenesis.

Studies were performed on exosome mediated regulation of angiogenesis in glioblastoma. *In vitro* characterization of recurrent glioblastoma stem cell line referred to as NSG70 derived from the surgical tumor specimen of the patient with recurrent glioblastoma was performed. A large number of novel long noncoding RNAs and proteins from exosomes were found and the investigators are validating these novel RNAs and proteins regarding their role in relation to radio-resistance in glioma.

Studies were carried to investigate differential expression pattern of autophagy and apoptosis related genes responsible for the deregulation of Imatinib induced cell death of chronic myeloid leukemia (CML) cell lines and subsequent development of Imatinib resistant cell line. The results demonstrated that imatinib resistant CML cells elevate expression of an array of autophagy related

genes, which could be used as a prognostic profiler of CML development. The results were established in K562 and experiments are ongoing in another CML line (KU812) along with patient's samples in order to validate the data.

Studies carried at *Center of Excellence on Evaluation of Biology and Mechanisms of Resistance in Leukemia* demonstrated for the first time a novel mechanism of resistance to arsenic trioxide in acute promyelocytic leukemia as well as a strategy to overcome it. Drug resistance AML was found to be modulated by inhibition of NF E2 related factor 2 (Nrf2), a master regulator of antioxidant response, suggesting the possibility of using Nrf2 inhibitors in combination with chemotherapeutic agents to modulate drug resistance in AML.

Metabolic Disorders & Autoimmune and other Non-communicable Diseases: The mandate of the program is to develop & support competitive R&D programmes and generate new programmes on detailed biology in 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.

Salient achievements: Several new projects related to cardiomyopathy, osteoarthritis and diabetes have been supported. Some of the significant findings are as below:

Nitric oxide (NO), being highly reactive in nature has pleiotropic functions ranging from intracellular signaling to anti-microbial effects and immunomodulatory functions. In a study to investigate the role of Nos2-derived NO in a mouse model of *Salmonella typhimurium* infection induced sepsis, it was observed that Nos2 is crucial for induction of pro-inflammatory cytokines and chemokines, neutrophil recruitment at the site of infection, increased resistance to the spread of infection,

reduced organ damage and increased survival of mice.

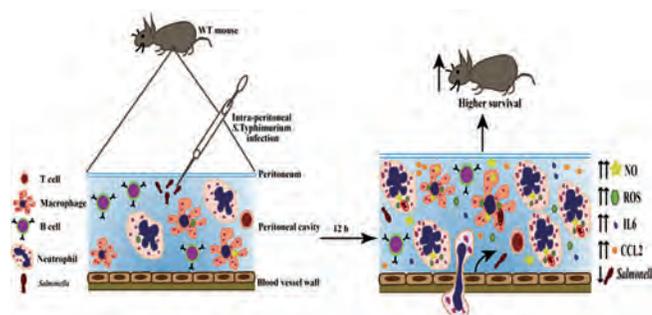


Figure 20. Proposed model for the role of Nos2 during sepsis-induced inflammatory responses. The induction of sepsis in C57BL/6 mice increases Nos2-derived NO, and other infection-induced factors which together result in a heightened inflammatory response and recruitment of neutrophils to the site of infection, i.e. the peritoneal cavity.

In a study to explore the etiology Biliary atresia (BA), a proteomic profiling was done on blood and tissue samples in children with BA. Two-dimension gel electrophoresis showed 10 different significantly expressed proteins which were found to play role in lipid metabolism, inflammation, immune response, and wound healing suggesting important role of immune inflammation in disease progression. The identified protein may be further evaluated as an early biomarker for the disease.

In a study aimed to investigate the factors involved in gastrointestinal motility in Type 2 Diabetic patients, it was observed that small intestinal bacterial overgrowth (SIBO) was more in type 2 diabetic patients as compared to controls and orocecal transit time (OCTT) delayed in patients. Lipid per-oxidation was increased along with catalase and superoxide dismutase (SOD) whereas reduced glutathione (GSH) was decreased. Furthermore, levels of substance-P were lower and serotonin higher in patients as compared to controls. In case of angiotensin converting enzyme (ACE) polymorphism, DD genotype was more pronounced in Type 2 diabetes patients and on correlation with gut motility, DD genotype individuals showed delayed OCTT. In case of SERT polymorphism, SS was pronounced in type 2 diabetes

patients and on correlation with gut motility, SS genotype subjects had fast OCTT.

Impact of vitamin D supplementation on vascular function and oxidative stress in patients with chronic kidney disease was verified in a study. It was found that cholecalciferol supplementation improves cardiovascular disease risk factor profile through positive impact on vascular function in subjects with early chronic kidney disease, and is effective in correcting the secondary hyperparathyroidism and bone health. This finding provides strong evidence for a new therapeutic modality for improving outcome in this common condition.

Hemolysis-associated anemia is characteristic of diseases such as atherosclerosis, lupus, malaria, and leishmaniasis. Studies were conducted to investigate immunological consequences of free hemoglobin (Hb), particularly in the context of pre-existing systemic autoimmune disease. Autoimmune anti-Hb antibody responses were detected in the sera of lupus patients. Lupus-prone mice exhibited heightened plasma Hb levels, and Hb triggered preferential release of lupus-associated cytokines from splenocytes derived from lupus-prone mice. Lupus-prone mice expressed increased titers of anti-Hb antibodies in serum and in kidney eluates. The results showed that Hb demonstrates both antigenicity and immunogenicity and triggers specific immuno-pathological effects only in mice prone to systemic autoimmunity.

Studies have been supported for culturing of primary cardiomyocytes as a tool in gaining insights into the physiology and pathology surrounding cardiac complications. Culture of murine cardiomyocytes was successfully standardized using keratin as a substrate which is easily available and cost effective. Using a battery of assays, the ability of these cardiomyocytes growth on keratin was demonstrated to respond to hypertrophic stimulus, thus validating the usefulness of this *in vitro* model to study hypertrophy.

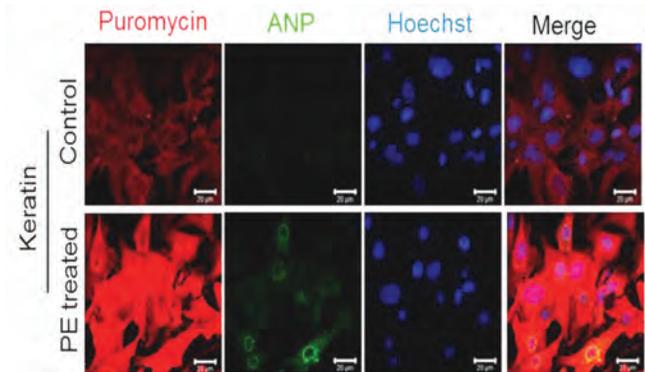


Figure 21. Induction of protein synthesis in PE treated cardiomyocytes grown on keratin, evaluated by puromycin incorporation assay

In a study to investigate role of thrombin in vascular anomalies, it was observed that thrombin induces endothelial inflammation by upregulating the expression of Angiotensin II (Ang-2) protein. It was shown that endogenous Ang-2 can modulate intercellular junctions, barrier property and inflammation of the endothelium. Elucidating the mechanisms of how thrombin increases the expression of Ang-2 will help to identify novel drug targets for management of coagulative vascular diseases.

Studies have been initiated to develop an assay for recognizing and analyzing epitope specific CD8+ T cells in the peripheral circulation of subjects with different types of autoimmune diabetes. The developed assay can further be used for monitoring disease progression and treatment/transplant approaches and screening immunodominant epitopes for vaccination/immunotherapeutic approaches.

In the present study to investigate the relation of Nox4, Insulin Receptor (IR) and PTP1B, it was found that Nox4 co-localized with both IR and PTP1B. FRET signal between Nox4 and PTP1B following insulin stimulation, suggest a dynamic regulation of the interaction between these proteins. The results provide further evidence that an interaction between Nox4 and PTP1B may be an important component of the link between the Nox4 ROS generating

apparatus and the regulation of cellular PTP1B catalytic activity and enhancement of insulin action.

In a study carried out to investigate immune cells migration across the BBB, it was shown that IFN- γ but no other cytokines perturbed the localization of tight-junction and cell adhesion molecules on endothelial cells. This study suggests that a strategy that controls the transendothelial migration of immune cells across the BBB will help in controlling the neuroinflammation and autoimmunity.

Studies undertaken to identify novel microRNA candidates regulating osteoblast functions led to the identification of miRNAs which negatively regulate osteoblast functions. These microRNAs were found to be down regulated in bones isolated from medicarpin treated BALB/c mice which has an osteoprotective effect. Thus, all these microRNAs may be potential therapeutic strategy for bone loss conditions.

Neuro Disease Biology: The Department has constituted a new Task force on Neuroscience with a mandate to have projects having disease centered approach.

Dementia is a devastating memory impairment condition. Considering that it is a chronic disabling condition that consumes resources at economic, social and psychological levels, longitudinal follow-up studies are vital for studying the impact of dementia at the level of family, community and the Nation, a comprehensive study was approved and implemented, which will provide reliable data regarding incidence, prevalence, biomarkers and risk and protective factors. The study will be multi-centric involving researchers and clinicians across the country. Long-term population-based and hospital-based cohorts of dementia patients will be set-up, and followed up. The Department has approved COE Epilepsy Phase II after successful completion of Phase I. Over 500 cases have been treated since

2011 and 1200 MEGs performed on patients from not only across the country but also from abroad. This COE has resulted in 56 publications in reputed journals. The Department has implemented 7 proposals in the area of Hypoxic ischemic brain injury (HIBI). National Initiative Phase II on Glial Cell Research was initiated to portray Disorders of Nutrition, Infections, Life style and degenerative disorders and CNS development, regeneration and reprogramming. 31 concept notes were received as an outcome of Brain Storming session on Glial cell research, out of which, 21 have been shortlisted for Inviting full proposals.

Salient achievements: The Department has been able to generate a considerable pool of neuroscientist by the tireless efforts since 2010; when a specific call for proposals was first advertised. Out of 208 projects implemented since 2010 covering - degenerative disorders, drug development, neuro inflammatory disease, neuro-infections, epilepsy, stroke etc, besides the multi-centric Glial project. Currently there are 50 projects in various stages of implementation and around 150 have been successfully completed. Some of the significant findings are as below;

An on-going study at NBRC, Manesar has shown that specific brain neuro chemicals alteration monitoring and quantization before the onset of neurodegenerative disorders is an important area of research. It was demonstrated that brain antioxidant, glutathione (GSH), is depleted significantly and clinically correlated with the clinical status (mild cognitive impairment (MCI) or Alzheimer's disease (AD)) of the patients. A comprehensive methodology was developed to bind together MRI derived information (brain volume etc.), neuropsychological outcome and MRS derived various neuro chemicals. The developed methodology has been submitted for National and International patent.

A translational stroke research facility (first of its kind in the country) has been established at AIIMS, New Delhi where translational human studies are being carried out in the field of discovery of novel genetics and protein biomarkers for stroke diagnosis and prognosis. An online platform for data capture and data analysis for multi-centric projects has been established. This collaboration enabled formation of multidisciplinary team of researchers from neurology, neuroimaging, neurobiochemistry, neurogenetics, biostatistics, epidemiology and others to utilize a wide range of technologies in stroke research.

In another study at NIMHANS, the findings has enabled in advance understanding of neuroimmunopathological abnormalities in Schizophrenia. In addition, state-of-the-art flow cytometry facility was established to train manpower in this cutting edge research technique.

INFECTIOUS DISEASE BIOLOGY

Infectious Diseases (ID) such as Malaria, Tuberculosis, HIV, Dengue, Chikungunya, Cholera, Leishmaniasis, Japanese Encephalitis, Filariasis etc. has caused serious epidemics in recent years and has started contributing to substantial disease burden. In order to address various issues and related concerns, DBT through Task Forces and Expert Groups is focusing in the area of infectious diseases specifically relevant to the country caused by various pathogenic agents like bacteria, viruses, parasites and fungi.

Salient achievements: The overall emphasis of the programs supported is to develop preventive, therapeutic and diagnostic tools for major infectious diseases. Some of the significant findings have been given below;

A study on ‘Development of Envelope based Tetravalent “All-in-one” Vaccine has led to the development of strategy that can be utilized to devise

a dengue vaccine candidate which is devoid of any viral interference, is non replicating, efficacious and safe to use. The present work has substantiated the ability of developing ‘Four-in-one’ Envelope-modified Tetravalent Dengue Virus-like Particles (E VLPs) as a potential Dengue vaccine candidate. The vaccine candidate is being evaluated for pre-clinical studies which upon successful completion will be further preceded to clinical trials.

Another study entitled ‘characterization of role of dengue virus and viral non-structural protein ns1 in affecting barrier and haemostatic function of vascular endothelial cells *in vitro* towards defining pathogenesis of dengue hemorrhage fever has resulted in two translatable components, a capillary motor biomarkers for dengue disease severity and a NS1 as novel therapeutic target.

A study on ‘Serum Proteome and Cytokine Profiling of Dengue Fever Patients to Decipher Disease Pathogenesis and Identification of Early Diagnostic and Prognostic Markers’ has revealed a few potential biomarkers like angiotensinogen, antithrombin-III among others which could be predictive markers for monitoring disease progression.

An investigation entitled ‘Microbiome of Human Lung in COPD Patients Attending Vallabhai Patel Chest Institute’ has helped to identify different bacterial phyla in COPD positive patients with 16s RNA gene sequencing employing illumine next generation technology. The study deciphered microbial markers associated with COPD cases, which could be used to develop non-invasive diagnostic method for COPD.

Efforts to understand the roles of critical protein translation machinery proteins in parasitic diseases like malaria have led towards structure-function studies that can probe these motors as new drug targets. The 3 D structures of pyrophosphatases, N-terminal GST-like domain and C-terminal EMAP II like tRNA binding of multi-synthetase complex (MSC) component protein p43 have been determined.

Structure based targeting of orthologous pathogen proteins has been proposed and has been validated through cell and enzyme assays. Co-crystal structure determination of parasitic prolyl-tRNA synthetases with quinazolinone based inhibitors and lysyl-tRNA synthetase with cladosporin derivatives have been achieved.

A comprehensive study on 'Molecular characterization of resistance mechanisms and epidemiological typing of clinical isolates of carbapenem resistant *Acinetobacter baumannii* (CRAB) in Septicemia and Meningitis patients' provided the mechanism of the existing carbapenem resistance determinants. The bla_{OXA-23} and bla_{NDM-1-23} are the major carbapenem resistance mechanisms observed among CRAB isolates. These isolates are representative of global diversity of the clinically important CRAB, maximum of the isolates are linked to the international linked clones. Whole genome sequencing of this collection of CRAB isolates will give major insights into the genetic diversity, resistome, mobile genetic elements and virulence determinates of CRAB in India.

DBT has sanctioned 'setting up the National Bio-bank Facility for clinical and basic research in HCV at ILBS'. This tissue bank facility envisages collection of high quality patient samples that will help in the biomarker discovery and validation as well as clinical trials and epidemiological study. In addition, the facility will serve as a service provider for bio-samples, education, training and capacity building, counselling and consultancy.

A study was supported on 'Diagnosis of neonatal bacterial Meningitis by 16 sRNA gene-based universal primer, PCR and procalcitonin assay for CSF'. The evaluation of three new methods for diagnosing neonatal meningitis, namely universal primer PCR for detecting 16 s RNA gene, CSF procalcitonin, CSF leucocyte esterase is underway. The findings may lead to better and accurate diagnosis of bacterial

meningitis on the basis of molecular techniques and novel inflammatory biomarkers.

RNA sequence analysis of HEV replicon transfected Huh 7 cells on Ion Proton Next Generation Sequencer at 24 h and 72 h time points post transfection to identify the temporal pattern of differentially expressed non coding and protein coding RNA pairs that play significant role in HEV life cycle was performed. In the sequencing data coordinated expression of a few long non coding RNA-mRNA and miRNA-mRNA pairs were observed that may play a significant role in HEV pathogenesis and life cycle. The screening of miRNA/long non coding RNA as potential prognostic/diagnostic biomarker for Hepatitis E is being evaluated.

a) HIV Vaccine Translational Research Laboratory:

The THSTI-IAVI HIV Vaccine Program is a unique public-private collaborative initiative that was set up to establish and build scientific capacity in India by engaging scientists with distinct disciplines towards complementing the global R&D efforts for discovery of AIDS vaccine, that would significantly bring down the disease incidence and burden in affected regions including India.

Rapid screening, identification, design and early development of HIV-1 envelope protein (Env) antigens based on circulating strains of HIV-1 in India that potentially would act as an immunogen towards eliciting broadly neutralizing antibodies following immunization. A screening, identification, isolation and characterization of broadly neutralizing antibodies (bnAbs) from donors of Indian origin.

HVTR laboratory focuses on developing Envimmunogens based on the virus strains circulating in India. By screening a number of HIV-1 primary Envs originated from Indian patients, HVTR laboratory has identified three HIV-1 Env antigen targets which have shown excellent antigenic and structural properties favourable to assess their immunogenicity in suitable animal models. The

immunogenicity of these antigens is currently being assessed in rabbit model. Selective modifications of these antigens are being done for their potential use in antigen-specific mAb isolation from single B cell cloning. In addition, by screening 200 antiretroviral therapy (ART) naïve slow progressing HIV-1 infected Indian patients, 11 patients who were able to elicit bnAbs in the natural disease course have been identified, 4 of them are found to make potent bnAbs showing >60-90% neutralization breadth across different HIV-1 strains of distinct geographical origins. These individuals are referred to as elite neutralizers. In active collaboration with the IAVI's Neutralizing Antibody Consortia (NAC), the HVTR laboratory is currently working towards isolation of broadly neutralizing monoclonal antibodies (bnmAbs) from these elite neutralizers which will immensely help in R&D endeavors in guiding rational next generation immunogen design and treating infected patients.



Figure 22. Structure guided approach being employed towards rational HIV-1 Indian Clade C Env (4-2.J41) protein based immunogen design.

b) DBT- ICMR Collaborative Research Efforts on HIV, AIDS and Microbicides: The mandate of this collaborative effort was to accelerate research efforts towards generation of knowledge for development of technologies to provide the basis for the development of HIV vaccines and novel therapies against HIV and Microbicides. Under this initiative, 14 projects were supported. In a study entitled 'Rapid Epitope Mapping of Neutralizing

Antibodies and other Entry Inhibitors of HIV-1, molecules with potential applications as HIV vaccines was successfully developed and tested in small animals and the challenge studies need to be carried out in non-human primates. Another study on 'Biosimilars of Antibodies with Multiple CD4s which will Irreversibly Neutralize Broad Spectrum of HIV-1 by Inducing Shedding of gp 120s' succeeded in engineering two CD4 fusion molecules that can strip gp 120s from pseudo HIV cells and block fusion by rendering the pseudo particles ineffective. The leads thus available will be taken into translational mode by identification of a commercial partner. A study on 'Microbicide for Prevention of HIV Transmission and other Sexually Transmitted Infections: In Vitro Efficacy and Pre-clinical Safety Evaluation' identified herbal formulations as microbicides for prevention of sexually transmitted HIV-1/HSV-2, which will be taken to the next level by HLL Lifecare Limited, Kerala. Discernable outcome of this collaborative effort has been 42 publications, 6 patents and training of manpower in the capacities of JRFs, SRFs and RAs.

In addition to the R & D projects, DBT has initiated inter-institutional HIV Research Program entitled 'Cohorts for HIV Resistance and Progression in Indian Children and Adults'. The networking program envisages on building specific HIV cohorts and a related national database and bio-repository to enable the conduct of studies that will provide a better understanding of the disease to aid in the design and development of novel tools for treatment and prevention of HIV/AIDs.

In a study at IIT Guwahati to investigate key enzymes and their respective inhibitors involved in the redox metabolism and associated pathways of the *Leishmania donovani* parasite, a potent antileishmanial compound which resulted in parasitic death via apoptosis and show synergistic effect with miltefosine has been identified. Further progress has enabled better understanding of the biology of the *Leishmania* parasite which will eventually lead to the

development of therapeutic interventions for the treatment of visceral leishmaniasis.

In another study aimed at studying the interaction between the flu virus matrix protein M1 and human nucleosomes, four individual human histone proteins namely were expressed in bacteria, purified to homogeneity and refolded into histone octamer *in vitro*. The octamer along with specific DNA sequence was reconstituted together to obtain nucleosome core particles. The M1 protein from Influenza virus was also expressed using bacterial system and purified to homogeneity. A complex of the M1 protein with the host nucleosome is currently being prepared for structural studies.

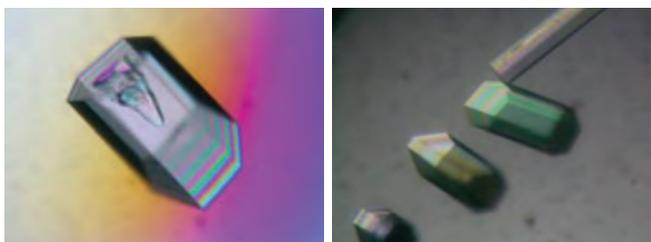


Figure 23. Images of nucleosome core particle crystals

A study was undertaken to characterize and establish IspE kinase gene as an antimalarial drug target and to identify novel compounds as antimalarials against *Plasmodium* IspE enzyme. IspE gene of *Plasmodium falciparum* (PflspE) and *Plasmodium vivax* (PvlspE), collected from seven topographically distinct malaria endemic regions of India showed that both PflspE gene and PvlspE gene is highly conserved. Further, the recombinant PvlspE protein/enzyme was expressed and characterized.

In a study carried to investigate gut microbiome in children with arthritis, it was found that children with juvenile arthritis had alteration in their gut microbial flora with increase in bacteria that can increase inflammation like bacteroides.

c) Tuberculosis (TB): India is the country with the highest burden of both TB and MDR TB. DBT has been funding 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 that involves various institutes for research activities that ranges from basic sciences to translational research.

In a CoE at IISc Bengaluru, Molecular dissection of *M. tuberculosis* integration host factor (IHF), revealed novel insights into the mode of DNA binding and nucleoid compaction. Similarly, molecular and functional characterization of *M. tuberculosis* RecD suggested that it is a novel member of the SF1 family of helicases and has role in the initiation of HR. Further, the studies on *M. tuberculosis* RecG and RuvA, RuvB disclosed the mechanism underlying Holliday junction resolution and multiple mechanisms of replication restart in bacteria. In a CoE at New Delhi, a Vitamin 'C' model was developed as a valuable system to probe host interactions with dormant *Mtb* that will provide an understanding of cellular events in host-directed therapeutics. In the CoE supported at University of Delhi 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.

Taking into account the fast spread of multidrug resistant and extensively drug resistant Tuberculosis in the country a focused RFA was issued by DBT and proposals for development of innovative, field-applicable and cost effective TB diagnostic biomarkers have been supported. Some of the significant findings have been highlighted below;

In a study at JALMA to study the induction of autophagy as a strategy for treatment of tuberculosis, particles to release the autophagy-inducing agent rapamycin in a rapid manner on deposition on the lung surface, or to target the majority of the drug to alveolar macrophages were prepared. Spray-drying and non-solvent addition

processes for the preparation on a laboratory scale were optimized. Powders comprised of these particles were assessed for amenability to deep lung delivery and *in vivo* lung deposition and macrophage uptake. It was concluded that spray-dried particles were suitable for use as a dry powder inhalation (DPI) formulation.

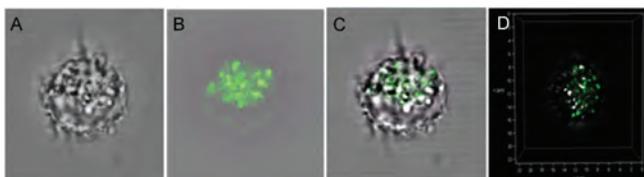


Figure 24. Different z-sections showed that the particles were internalized by cells, confirming that particles were able to reach in deep lungs and were taken up by alveolar macrophages. Confocal microscopy showing FITC-RAP-particle uptake by alveolar macrophages (A) Phase contrast micrograph (63 \times) of a lung macrophage recovered by BAL 5 min after inhalation of fluorescent-tagged particles. (B) FITC channel (C) Merged and (D) z-section of the same field.

In a study supported at JNU Delhi an approach to TB treatment was developed that reduces immune impairment, length of treatment and toxicity. Nano-formulated curcumin with 6- to 7-fold increased bioavailability than regular curcumin was developed and tested for efficacy in a murine TB model. The formulated nanoparticle drastically reduced the hepatotoxicity induced by the anti-tubercular drug INH. In addition, enhanced T cell-mediated immunity and prevented post-therapy susceptibility to re-infection and re-activation of the disease was observed. Further, it significantly reduced the length of treatment for attaining sterile infection and therefore reduced the risk for the generation of MDR and XDR variants of TB.

In a study carried at University of Hyderabad to analyze anti-mycobacterial role of sphingolipids against pulmonary infection with pathogenic Mycobacteria, it was demonstrated that S1P signaling promote IFN gamma mediated Th1 programming and bacterial defense and indeed represents a prospective drug candidate for controlling pathogenic mycobacteria. Further evaluation of receptors linked

to anti-microbial response is under progress.

In addition, DBT and ICMR have signed a MoU on Biomedical & Health Research wherein Tuberculosis was marked as critical area of partnership with prime focus on TB diagnostics. Validation of indigenously developed technologies for diagnosis of pulmonary tuberculosis and multi-drug resistant tuberculosis has been initiated by four major institutions and two Indian companies. 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.

VACCINE RESEARCH AND DEVELOPMENT

Department of Biotechnology (DBT) has made concerted efforts in strengthening vaccine research and development since its inception in 1986-87 through various endeavours. Currently major efforts are being implemented through the Vaccine Grand Challenge Programme (VGCP) and Indo-US Vaccine Action Programme (VAP).

VGCP aims 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 and major supports have been provided to R&D projects focusing on the development of candidate vaccines and vaccine related technologies.

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. The oversight to the program is provided by the VAP Joint Working Group (JWG) comprised of eminent scientists and policymakers from both the countries. The programme is under implementation since 1987. VAP-supported research projects have directly addressed critical health problems relevant to both countries.

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. The vaccine is manufactured in India by M/s Bharat Biotech International Limited, Hyderabad under cGMP conditions and is a more affordable alternative to the rotavirus vaccines already on the market. The vaccine is commercialized and based on the recommendations of NTAGI; ROTAVAC® has been introduced in the EPI programme of nine states.

Early implementation of Rollout of Rotavirus Vaccine in the Public Health System Under Monitoring: Subsequent to licensure, the competent body of the government of India, National Technical Advisory Group on Immunization (NTAGI) recommended the phased introduction of indigenous ROTAVAC® vaccine in the national program and advised that the early rollout be carefully monitored and observed by relevant government agencies with support from national academic institutes and the central government. The aim of this initiative is to gain experience on the following issues pertaining to the vaccine i.e.:

- Cold chain capacity at the sites
- Logistics for vaccine supply
- Preparation of tools and processes for

immunization

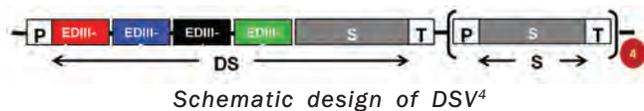
- Observation of practices at sites during immunization

The states identified for the pilot rollout were Vellore District, Tamil Nadu, Pune District, Maharashtra and Kangra District, Himachal Pradesh. The Central Unit based at CHRD-SAS coordinates the project; the Project Management Committee guides the Central Unit and conducts periodic reviews. The International Clinical Epidemiology Network (INCLEN) is assisting the public health system in the three states during the rollout. The limited roll out is coordinated by the Department of Biotechnology and an Inter-ministerial- Interagency Coordination Group Steering Committee co-chaired by Secretary, DBT and Secretary Department of Health Research & Director General, ICMR with the Secretariat at BIRAC of DBT.

Malaria Vaccines: International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi along with its translational research partner “Multi Vaccines Development Program” earlier known as “Malaria Vaccine Development Program”) has advanced the development of blood-stage vaccines for *P. falciparum* and *P. vivax* malaria over the last decade. Funding support through Vaccine Grand Challenge Program of Department of Biotechnology, Biotechnology Industry Research Assistance Council (BIRAC) and multiple international agencies including Malaria Vaccine Initiative (MVI), PATH and European Vaccine Initiative (EVI) has been received. These recombinant protein-based adjuvanted Malaria vaccines advanced through the translational development pathway of GMP production, pre-clinical immunogenicity testing, GLP compliant toxicity testing and Phase I trial after receiving all necessary regulatory approvals. All these translational development activities have been done with Indian partners or collaborators or through an out-sourced model. A brief of the vaccine candidates which have undergone development beyond lab bench are mentioned below:

JAIVAC-2 (Second Generation *P. falciparum* Vaccine Candidate): In its monovalent form JAIVAC-2 is an Alhydrogel formulation of Recombinant protein, MSP-Fu24 (a fusion chimera consisting of PfMSP-1₁₉ and an 11kd region of PfMSP3 (PfMSP-3₁₁). The fusion chimera contains both a T-helper (T_H) epitope as well as B epitopes that are the target of antibody dependent cellular inhibition (ADCI). In its bivalent form JAIVAC-2 is an Alhydrogel formulation of physical mixture of Pff2 and MSP-Fu24 protein. Presently both the formulations are undergoing Acute and Repeat Dose toxicity studies after approval from Review Committee on Genetic Manipulation (RCGM) and Animal Ethics Committee.

Dengue Vaccine: Department has been supporting the group at ICGEB, for the development of safe, efficacious and inexpensive tetravalent dengue vaccine. The dengue vaccine candidate is based on the host receptor-binding domain-III (EDIII) of DENV envelope protein. The four-in-one, tetravalent vaccine candidate, incorporates the EDIIIs of all four DENVs spliced together through flexible peptide-linkers in a single translational reading frame. Further, it is presented on the surface of Hepatitis-B surface antigen (HBsAg) virus-like- particles (VLPs).



These VLPs elicit serotype-specific antibodies capable of neutralizing various genotypes of each serotype and have been found to be immunogenic in mice and macaques. With the extensive evaluation of immunogenicity of DSV⁴ in mice and preliminary study in macaques, DSV⁴ can progress in parallel to the next stage of GMP production, toxicity studies and a dengue virus challenge study in non-human primates. The encouraging outcomes in the pre-clinical evaluation of DSV⁴ have enabled negotiation with a potential industrial partner to advance DSV⁴ to the next stage of GMP production and toxicity evaluation.

Major Initiatives implemented under Indo-US VAP: An Indo-US Candidate Vaccine Advisory Committee (CVAC) has been established to support VAP's mission to promote R&D efforts for important candidate vaccines, through their evaluation of candidates and subsequently provide recommendations to the VAP. So far two meetings of CVAC have been organized and 8 candidate vaccines have been reviewed and endorsed under VAP. Under CVAC, joint scientific consultations is being planned to explore opportunities for Chikungunya and Dengue vaccine trials in India.

a) Regional Prospective Observational Research for Tuberculosis (RePORT) India is a bi-lateral multi-organizational collaborative effort designed to advance regional basic and clinical tuberculosis (TB) science in India, strengthen TB research capacity and infrastructure and foster research collaboration within India and with other countries. The primary funding for Consortium research activities comes from the Indian Department of Biotechnology (DBT), 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 that is supported by a central biorepository, a central data management center and utilization of harmonized data elements and specimen collection standard operating procedures (SOPs). Each RePORT India Cohort Research Unit (CRU) site began implementing its individual "parent protocol" with distinct research objectives in 2014. In 2016, the Hinduja Hospital, in Mumbai has joined the RePORT India team and is now the sixth RePORT project/ site. The site is in the process of obtaining final approval and is poised to initiate enrollment shortly. The CRU sites and specimen biorepository received funding

so that they could set up activities for concurrent enrollments into the RePORT India Common Protocol. Center for Health Research and Development–Society for Applied Studies (CHRD-SAS) will support CRU site data management activities. Sites have been making preparations that will be needed for Common Protocol implementation. Biospecimens collected for the Common Protocol 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 (Cohort B). The National Institute for Research in Tuberculosis (NIRT) in Chennai, India will serve as the specimen biorepository. The primary objective is to provide specimens to Indian and other 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.

b) India-US collaborative research on Human Immunology: The goal of this funding program is to promote India-US collaborative research on human immune-phenotyping in the context of infectious disease and vaccine development, in collaboration with investigators of the HIPC (Human Immunology Project Consortium). During Phase-I, Five joint applicants have been supported. Each team includes one HIPC Project Leader and one Project Leader from India. Outcome from Phase-I has been assessed in Joint Working Group meeting of Indo-US VAP held in April, 2017. Planning to implement Phase-II of HIPC is under consideration.

c) Collaboration on AMR: On June 25, 2015, an LOI was signed between NIAID and ICMR/DBT to cooperate on AMR research. U.S. On Jan 20-21, 2016, a systems biology workshop was held in New Delhi, organized by ICMR and NIAID. Subsequently, the proposal on “AMR in *Acinetobacter* in neonates at Neonatal Intensive Care Units (NICUs)” developed through consultation between NIAID-AIIMS, have

been recommended for implementation under the aegis of Indo-US VAP.

d) A joint Indo-US Workshop on “Genomics and Bioinformatics to Explore Human Microbial Ecology in Health and Disease” was held at THSTI, Faridabad from 6th-8th September, 2017 to build analytical capacity amongst young scientists in THSTI and other research institutes across India. As an outcome of the workshop further collaborative efforts will focus on development of joint proposals for Microbiome Research.

The 29th Annual Meeting of the Joint Working Group (JWG) for the Indo-US Vaccine Action Program (VAP) was held in Rockville, MD, USA on April 11-12, 2017. The event commemorated 30 years of bilateral partnership between the National Institute of Allergies and Infectious Diseases (NIAID), National Institutes of Health (NIH), U.S. Department of Health and Human Services (HHS) and the Department of Biotechnology (DBT), Ministry of Science and Technology (MOST), Government of India (GOI). Another close partner to VAP is the Indian Council of Medical Research (ICMR) within the Department of Health Research (DHR), Ministry of Health and Family Welfare (MOHFW), GOI.

The VAP-JWG meeting was immediately preceded by the 2nd Meeting of the Candidate Vaccine Advisory Committee (CVAC) under VAP, on April 10, 2017. Deliberations and recommendations of CVAC were presented to the VAP JWG on April 12. A total of eight candidate vaccines were presented to CVAC for review: two dengue candidates, two TB candidates, and one candidate each for chikungunya, RSV, Zika and Inactivated Rotavirus. VAP JWG also approved of establishing a steering committee within CVAC to provide guidance on epidemiological studies for vaccines against flaviviral and other diseases. Lastly, VAP JWG encouraged NIAID/DBT engagement with CEPI on upcoming discussions pertaining to chikungunya and other vaccines.

On April 12, 2017, the bilateral Vaccine Action Program was renewed for another 5 years (till April 11, 2022) through formal signing of the VAP Joint Statement by DBT Secretary Prof. K. VijayRaghavan and NIAID Director Dr. Anthony Fauci.

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. Against a fresh grant announcement, 302 Lols were received. Based on the scientific merit and ethos of the glue grant scheme, the Lols were short-listed inviting full proposals from the short-listed PIs. The received proposals were further screened for technical and scientific merit and four proposals have been recommended for financial support.

STEM CELL RESEARCH & REGENERATIVE MEDICINE:

Stem cells and regenerative medicine is one of the thrust areas under the medical biotechnology programme of the Department. The mandate is to promote basic, early and late translational research and formulation of regulatory framework for stem cell research in India. The Department supports projects under Stem Cells & Regenerative Medicine programme with focus on: induced pluripotent stem cells; hematopoietic stem cells; mesenchymal stem cells and human embryonic stem cells. Scientific strategies includes basic biology of all adult stem cells, early and late translational research, developing gene editing technology for possible therapeutic applications, creation of animal models for various human diseases and training programmes on various component of stem cells and regenerative

medicine.

Major initiatives: Considering the need for an appropriate animal model to understand the disease biology and also to design good proposal for potential therapeutic applications of stem cells for various human diseases, a Strategy has been formulated for developing appropriate animal models to establish safety and toxicity of stem cells for human diseases.

The “National Guidelines for Stem Cell Research, 2017” was jointly formulated by Department of Biotechnology and the Indian Council of Medical Research to lay down standards for stem cell research and ensure that research with human stem cells is conducted in a responsible and ethically sensitive manner in the country. This document was released by the Hon’ble Minister for Health & Family Welfare on 11th October, 2017. *As per the Guidelines, all institutions carrying out research on human stem cells must constitute an Institutional Committee for Stem Cell Research (IC-SCR) and register with the National Apex Committee for Stem Cell Research and Therapy (NAC-SCRT). The registration of IC-SCR is mandatory and all the institutions working in the field are required to comply with the guidelines.* The guidelines states that any stem cell use in patient is investigational and it must only be done within the purview of an approved and monitored clinical trial and not offering it as therapy. The guideline is available on DBT website: http://www.dbtindia.nic.in/wp-content/uploads/National_Guidelines_StemCellResearch-2017.pdf.

Salient achievements: During the year number of projects has been supported on embryonic, mesenchymal and adult stem cells and also studies aiming to explore various factors involved in lineage commitment, role of cancer stem cells in chemoresistance and generation of iPSCs from various sources and its lineage specific differentiation. The supported projects have resulted in 30 publications in peer reviewed journals. Some

of the significant findings are as below;

Studies were carried to explore the role of an antioxidant enzyme Manganese Superoxide Dismutase (MnSOD) in lineage commitment during development using mESC model system. The results revealed that *MnSOD* is highly expressed in neurons differentiated from mESCs and its overexpression leads to rescue of neural differentiation even under non-permissive neural differentiation conditions. Further, it has been shown that *MnSOD* loss of function leads to abrogation of early neural differentiation. Thus, MnSOD may have a novel role in fate specification during development which might be highly significant when stem cell mediated lineage commitment is desired.

Studies at IISc., Bangalore provided an insight into the effectiveness of electroactive nanoparticles and

electric field (EF) stimulated culture methodologies as instructive cue for orchestrating lineage commitment of stem cells towards electrically excitable cells. Importantly, the study created a new paradigm in which a switch in the lineage commitment of hMSCs towards neural-like cells was achieved by exposing to direct current EF stimuli of physiological magnitude. Precisely, a combination of intracellular GNPs and extracellular conducting substrates largely influenced the transformation of hMSCs to neural-like cells. The results demonstrated that it is possible to recapitulate the electroactive environments of cardiac and nervous tissue, for directed stem cell differentiation in regenerative therapy by employing the nanoscale biomimetic properties.

In yet another study, it has been demonstrated that inhibition of BMP signaling by two independent methods resulted in the differentiation of mouse

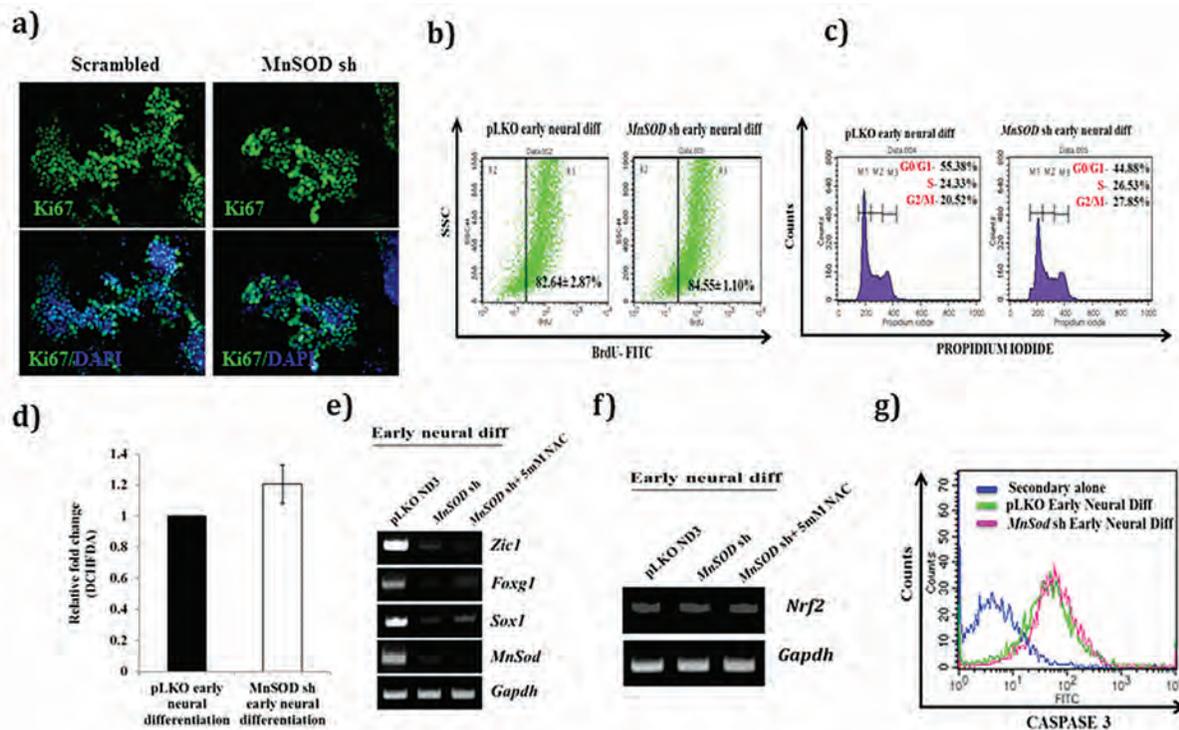


Figure 25. Effect of MnSOD on neural differentiation of mESCs is not mediated by proliferation, ROS and apoptosis: A) Immunofluorescence showing Ki67 staining in neural progenitors derived in presence and absence of MnSOD B) Flow cytometric analysis of BrdU incorporation in neural progenitors derived under MnSOD inhibition C) Cell cycle analysis of early neural progenitors generated under MnSOD knockdown D) ROS analysis in neural progenitors under MnSOD inhibition E) Gene expression analysis of neural differentiation performed under MnSOD inhibition and addition of NAC G) Immunophenotyping for CASPASE3 in neural progenitors harboring MnSODsh RNA.

BMSCs into neuron-like cells expressing both neuronal and glial markers up to day 15 in culture. However, on extended culture to day 30 these cells appear to no longer express any glial markers but retain the morphology of neurons as well as the expression of neuronal markers. This suggests that inhibition of Bmp signaling induces a plastic state in the BMSCs which last till 15 days when they may have the potential to differentiate into either neurons or glial. However, further culturing leads to loss of this plastic state and preferential differentiation into mature neurons. Further, this study also suggests the probability of a concerted influence of Bmp inhibition together with Wnt activation in directing the mouse BMSCs towards a neurogenic cell fate.

Human embryonic stem cell culture is difficult to manipulate due to their primed state of pluripotency which means these cells are in a state of differentiated rather than fully non-committed state. Therefore a study analyzing the expression of genes implicated in naïve vs primed pluripotency in mouse embryonic stem cells (mESCs) cultured in presence of absence of PKC signalling inhibitor was supported. The result suggests that in mouse inhibiting PKC signalling pathway could retain the cells in naïve state.

A preclinical study was supported with an aim to explore novel human stem cell-based therapy for augmentation in functional recovery following spinal cord injury (SCI) and to test if transient-modulation of PTEN gene in injured spinal cord may enhance functional recovery in spinal cord injury (SCI). The results revealed that localized *in vivo* PTEN modulation at the site of spinal cord injury creates a favorable regenerative microenvironment. In mice it was shown to reduce astrogliosis and reduce the events leading towards conversion to scar-forming astrocytes that further progresses the primary insult towards secondary injury and precipitate to functional loss in SCI. This qualitative data gives a strong evidence to further uncover detailed molecular mechanisms for correlation between astrogliosis and

PTEN knockdown in SCI subjects.

A study supported to understand cell-material interactions for cardiovascular regeneration and developing models to investigate cardiac diseases showed that for cardiac regeneration in stem cells the surface of the scaffolds could be coated with keratin and the scaffolds could be designed with directionally aligned topography. In addition, it was observed that stem cells and cardiomyocytes can be guided using topographical cues. These studies would enable the development of cardiac patches and lab bench models for studying cardiac diseases.

Relapse of cancer after chemo- or radio-therapy is the major caveat in treatment of cancer and the relapse has been implicated to presence of a population of relatively quiescent chemo-resistant cells termed cancer stem cells. Studies were carried to understand the properties and behavior of these cancer stem cells and to design treatment strategies to target these cells within a tumor so that total regression of the tumor may assure complete remission of the disease. In one such study, the differentiation potential of ovarian CSCs to endothelial cells was evaluated *in vitro* using the spheroid model followed by functional analysis. The flow cytometry analysis of the CSC derived endothelial cells showed that there exists a small proportion of endothelial cells (~10%) arising from cancer stem like cells in primary ovarian tumors showing functional attributes like uptake of acetylated low density lipoprotein and expression of endothelial nitric oxide synthase. Further, the reduction in expression of endothelial markers when treated with bevacizumab suggested that VEGF pathway is responsible for the endothelial differentiation of ovarian CSCs

Studies were undertaken to identify putative genes responsible for chemo-resistance in cancer stem cells, particularly of breast tumors, which may be targeted along with conventional anti-cancer drugs.

It was revealed that chemotherapy enriches the cancer stem cells. This finding was further endorsed by paclitaxel treatment of breast cancer cell lines which induces a G₂/M arrest in breast cancer cells but does not affect the cancer stem cells. Further, progressive work on SOX2, (a major pluripotent gene of chemotreated cancer stem cells) showed that it has a huge abundance in conferring and enhancing the stemness in breast cancer cells. Downstream studies with this highly abundant stem cell marker reflected SOX2/ABCG2/TWIST1 axis as the operational cascade behind chemo-resistance of breast cancer stem cells and can be a possible therapeutic target in future for remedial actions against breast cancer relapse.

In a study supported on retinoblastoma, induced pluripotent stem cells (iPSCs) were generated from orbital adipose mesenchymal stem cells (AMSCs) of RB patients carrying germline mutations. The RB-iPSCs thus generated from the orbital AMSCs retained the germline RB1 mutation and expressed pluripotency factors. Trilineage differentiation of the RB-iPSCs was confirmed by embryoid body formation and expression of ectodermal, endodermal and mesodermal transcripts.

Centre of Excellence on Stem Cell Research: DBT supported Centre of Excellence for Stem Cell Research at AIIMS, Delhi in 2008 has completed its Phase I in which construction of basic research lab, animal housing facility and cGMP Lab has been established. The Phase II has been supported this year with an objective to manufacture clinical (GMP) grade stem cells for clinical research; to explore various non-viral approaches for generation of iPSCs and to expand educational and training programmes at various levels. Workshop on '*In Vivo* Imaging for Preclinical Research' was conducted on 5th September, 2017, for generating manpower and skill development in preclinical research and enhancing knowledge in the area of preclinical research. This

Centre is also imparting training to graduate and postgraduate students. So far three PhD students, one DST inspire faculty and 2 postgraduate students have joined the lab for training in stem cell research. Up gradation of cGMP and procurement of equipments are under process.

Collaboration: 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; & Center for iPS Cell Research and Application (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)".

The ADBS programme aims to understand major psychiatric disorders in Indian population by harnessing the power of sophisticated clinical investigations, modern human genetics, and stem cell technology. The Department of Psychiatry at NIMHANS has been engaged in identifying families with a high incidence of mental illness and studying clinical aspects of these diseases. The families would be followed over a period of twenty years to observe the development of clinical disease and assessed using a range of clinical investigations including neuroimaging and neuro-psychological assessments at regular intervals. Pluripotent stem cells are being generated from identified families at inStem and NCBS to generate cellular models in which mechanistic aspects of cellular neurobiology relevant to mental illness will be studied, building on existing expertise in genetics and cell biology based research including the ability to generate neuronal cell models using state of the art stem cell technology.

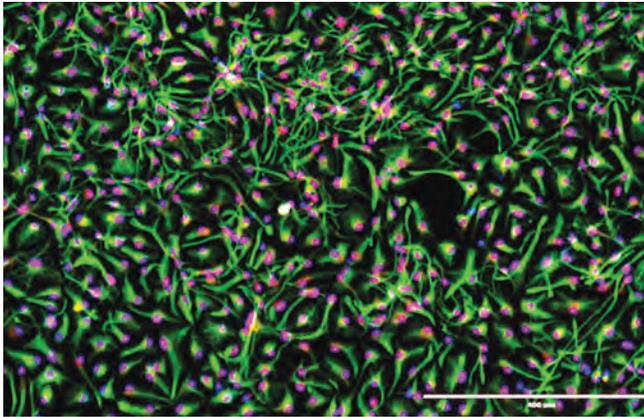


Figure 26. Cultured neural stem cells generated from a human subject in ADBS programme. NSC are stained to show the expression of markers of neural stem cells. Nestin (green) is a cytoplasmic protein. SOX2 (red) is a nuclear marker that colocalizes with DAPI (blue) that marks DNA.

The NAHD is an ambitious project which involves three major components – a gene therapy program capitalizing on the developments of vector-based gene therapy for haematological diseases in the world both as a clinical trial for haemophilia and preclinical research for other major haemoglobin disorders. Secondly, it aims at exploiting the iPSC technology to develop a bank of pluripotent cells lines from HLA homozygous individuals called a ‘haplobank’. A third major component is focused on a community based “Control program” for sickle cell anemia and beta thalassemia. To implement the control program in Odisha, collaboration has been established with the Department of Health and Family Welfare and the National Health Mission of the Govt. of Odisha.

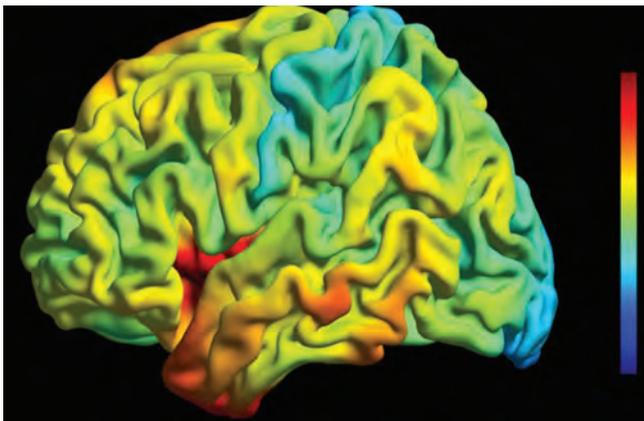


Figure 27. Structural MRI image (T1-weighted) of a

human brain (blue to red color gradient indicates increasing range of values in mm) generated in Indo-Japan ASHD programme: Structural MRI studies helps to measure various global and regional metrics (eg., volume, cortical thickness, surface area and gyrification index).

One of the key objectives of this Indo Japan collaborative ASHD programme is to build human resource capacity for the application of modern stem cell technology in the study of human disease. The first ADBS Human iPSC Workshop 2017 on “Reprogramming Human Somatic Cells to hiPSCs” was held in November 6-11, 2017 at inStem, Bangalore. The workshop included lectures by leading experts in the field and also the practical sessions on cell culture techniques involved in generation, characterization, propagation and differentiation of hiPSCs. Further the training program in iPSC technology at the Center for iPS Cell Research and Application (CiRA of Kyoto University) was implemented for the second year in November-December 2017. Eight Indian researchers from various Indian institutes were selected and trained at CiRA, Japan. Under the aegis of this program, a process for distribution of iPSC lines has been implemented. Requests for ADBS bio repository resources are routed through a web-portal (<https://www.ncbs.res.in/adbs/bio-repository>). Distribution of control iPSC cell lines has begun and cell lines have been distributed to 8 labs in Mumbai, Delhi and Bangalore.

GENOME ENGINEERING TECHNOLOGIES

Genome engineering/editing technologies has ability to rapidly and economically introduce sequence-specific modifications into the genomes of a broad spectrum of cell types and organisms and has immense potential to accelerate scientific breakthroughs and discoveries in disciplines as diverse as synthetic biology, human gene therapy, disease modelling, drug discovery, neuroscience, and the agricultural sciences. The priority areas include

applications in the study of emerging diseases, to manipulate/engineer genomes, develop transgenic systems and develop genome-based diagnostics. Some of the highlights of research activities carried out are mentioned below:

Studies were undertaken at NABI, Mohali to develop and apply genome editing tools in allohexaploid wheat. To improve the nutritional quality of wheat IRO3, a bHLH transcription factor that negatively regulates iron transporters and IPK1 which is involved in the phytic acid biosynthesis were identified. These two genes were selected to be knocked out in order to achieve high iron and low phytate content in wheat crop. To choose a target site SS finder tool was utilized and unique target site of 19 nucleotides followed by PAM-NGG (protospacer adjacent motif) was taken from exon carefully. To check the possibility of potential off targets, multiple BLAST analyses were performed against different wheat databases and NCBI-SRS. *Agrobacterium* mediated wheat transformation with the developed CRISPR constructs is underway.

Studies were initiated at IVRI, Izatnagar to develop chimeric recombinase by fusing catalytic domain of 'hyperactivated' site-specific recombinase mutant evolved to target multiple genomic locations with nuclease-null Cas9 (dCas9) protein which would be supported by guide RNAs for genomic targeting at the desired genomic loci in human (HEK-293 cell) as well as bovine (MDBK cell) genome. The RGR architecture was designed and sequences for synthetic genes coding Gin, \hat{a} and Sin 'hyperactivated' recombinase mutants were obtained. The resulting chimeric recombinase platform would have immense potential for safer targeted DNA integration in the mammalian genome such as generation of stable cell lines, generation of iPSCs, gene therapy and production of transgenic animals.

Studies were initiated at Visva-Bharti, Shantiniketan, West Bengal to develop Genome engineering

platform for modification of nisin gene of *Lactococcus lactis* W8 to generate novel therapeutic using recT mediated oligonucleotides. Lactic acid bacteria was screened from fermented dairy foods for the presence of *recT* by PCR technology using primers designed from the information of genome sequence in the database. Colonies positive for *recT* genes were identified by 16S rRNA gene sequence analysis and the identity of the isolates were confirmed by BLAST search at NCBI. The *recT* sequences of isolated *L. fermentum* strains showed 99% identity with those of sequenced genomes of reported *L. fermentum*. The investigation on expression of recombinant proteins in *E. coli* and *L. lactis* W8 is currently in progress.

Studies have been undertaken by NCBS, Bangalore on Genome Engineering using CRISPR to enable discovery in lipid signalling to generate genetic tools to understand the specific functions of phosphoinositide signaling using *Drosophila melanogaster* as a model system. An optimized workflow for designing and optimizing guide RNA's (gRNA) for CRISPR/Cas9 mediated genome engineering in *Drosophila* cells was established. Transgenic *Drosophila* strains expressing optimized gRNA constructs for genome engineering of genes involved in phosphoinositide signalling were generated. 100 gRNAs and 45 gRNA pairs were identified with a potential to generate gRNA transgenic lines which would be used to develop complete knockouts and tissue specific deletion mutants.

A small zebra fish culture facility with an infrastructure for embryo micro manipulation has been set up at L.V. Prasad Eye Institute, Hyderabad. Several gRNA constructs were designed to target zebra fish *abca4b* and *rd3* genes.

At National Brain Research Centre, Manesar studies were initiated on CRISPRi system to investigate novel regulatory mechanisms of synapse formation by long non-coding RNA. A genome wide sequencing

approach was used to identify lncRNAs expressed in the hippocampus through an unbiased screen using the next generation sequencing technique. Enrichment of these newly identified long non-coding RNAs at the hippocampal synapses was further verified by quantitative PCR. Furthermore, a set of lncRNAs that are activity regulated during the window of synapse formation and can potentially modulate the activity-dependent process of synaptic maturation were identified. Experiments are in progress to perform the loss of lncRNA function by CRISPRi-mediated knockdown and subsequent assessment of the functional synapse development by the whole-cell patch clamp recording.

Human Resource Development: Department has also initiated fellowship program to provide best and brightest Indian students and scientists to gain exposure and access to world class research facilities in leading U.S. institutions as well as to promote research and capacity building in the frontline area of Genome Engineering and Editing technologies. Through IUSSTF program for overseas fellowships with the following two modules: (i) *Genome Engineering/Editing Technologies Initiative (GETin) – (a) Overseas Fellowship* for Indian citizens (b) Student Internship and, (ii) *Genome Engineering/Editing Technologies Initiative (GETin)-Visiting Fellowships* are attracting 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. In the current year, 5 students and 5 young scientists were selected under the Student Internship program and Overseas Fellowship program module, respectively to acquire training and conduct research work in different U.S. institutions.

BIOENGINEERING

Bioengineering is a highly interdisciplinary area of research involving cross-disciplinary knowledge from

engineering and other quantitative sciences for unravelling the complexities of biological systems and provide cost-effective solutions for improved quality of life. Some of the significant achievements made during this period are:

Point-of-care bio-photonics device for rapid detection of oral cancer: Early diagnosis of cancer and its proper therapeutic management is the key factor in determining survival and morbidity of oral cancer patients. Scientists at Amrita Centre for Nanosciences & Molecular Medicine, Kochi are intending to develop a point of care device based on Surface Enhanced Raman Spectroscopy (SERS) technique for the rapid detection of oral pre malignant and malignant lesions. The device will benefit from its ability to differentiate and classify the oral lesions, particularly in scenario like mass screening of populations at rural areas. Under this project, a SERS catheter device for oral cancer diagnosis has been developed and a portable direct read-out Raman spectrometer for SERS based oral cancer diagnosis has been customized. In addition to instrument design, they have also developed a SERS enabled optical fiber probe and Ag-TiO₂ SERS substrates. Development of oral cancer xenograft animal models and testing the Raman system *in vivo* is under progress.

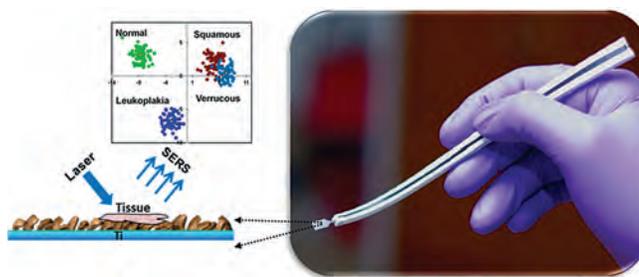


Figure 28. SERS Catheter device for oral cancer diagnosis

Photoacoustic spectroscopy based objective assessment of breast tumor progression: The breast cancer incidences in India varies from 5-30 per 100,000 women with an annual incidence of approximately 1,44,000 new cases making it the

most common female cancer in urban India. Early diagnosis of tumor detection is the need of the hour. To address this, scientists at Biophysics Department, Manipal University, Manipal, Karnataka are utilizing the technique of photoacoustic spectroscopy to record the molecular alterations subject to disease initiation at much earlier stage without affecting the individual. The technique is very promising in terms of sensitivity, accuracy and safety. It is based on detection of acoustic or sound signal in a sample induced upon pulsed/modulated excitation at suitable wavelengths. In this project, breast tumor was induced in experimental animals (nude mice). The tumor growth was assessed at different time points *in vitro*. The tumor mass was extracted and the corresponding photoacoustic signatures were recorded at 281nm excitations and compared with the similar information obtained from control samples. In order to find correlation of tumor development with clinical breast cancer samples, a photoacoustic spectroscopy study involving clinical samples were also undertaken obtaining Institutional ethical approval and collecting samples with prior informed consents. Preliminary results obtained from the corresponding malignant and normal breast tissue samples showed clear differences between them indicating the usefulness of the photoacoustic technique in capturing minor variations subject to disease initiation within the tissue samples under study.

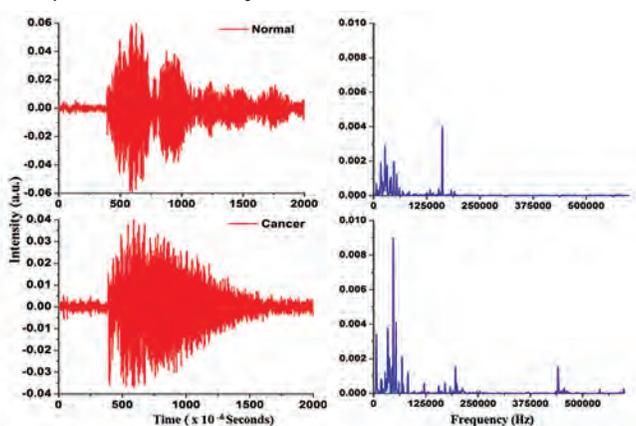


Figure 29. Typical photoacoustic pattern in time domain (left) and the corresponding FFT patterns in frequency domain (right) of clinical breast tissue samples recorded at 281nm pulsed laser excitations

Robot design for 3D Bio Printing of tissue embedded cellular vascular constructs: One of the major limitations of current tissue engineering strategies is the incorporation of vasculature within the constructs. Recent studies on developing cellular vascular constructs with 3D printing opens up possibilities for bioprinting full-fledged viable tissues. However for bioprinting vasculature, an important challenge is bioprinting multiple cellinks simultaneously to mimic the multicellular structure of blood vessel. To address this, scientists at Amrita Centre for Nanosciences and Molecular Medicine, Kochi are trying to design a high-fidelity bio-robot for 3D bioprinting of tissue embedded vascular construct. Next, to build the multi layered bio printed vascular construct, they are in process for identification of suitable gel matrix for endothelial and smooth muscle cells necessary for cell inks and also for optimization of cell seeding, cell growth and self-assembly of endothelial cells in defined gel matrices *in vitro*. HUVECs encapsulated Carrageenan gel was printed and the cells were seen to be viable in over 24 hours post printing, optimization of similar printing with Human Smooth Muscle cells (hSMCs) is ongoing.

Process optimization and development of ceramic composites for total hip arthroplasty:

In order to minimize the revision surgery procedures in total hip arthroplasty or total knee arthroplasty due to loosening of implants, research efforts are being made to improve materials and surfaces of load bearing implants. A project has been sanctioned in IIT Kharagpur to develop improved materials for the implants which are hard and have high fracture toughness, wear resistance, good lubrication and cytocompatibility. Under this project, the composition for synthesis of Al_2O_3 matrix composites were optimized and prepared by conventional sintering at different temperatures. Microstructural, mechanical, wear and wettability of Al_2O_3 ceramics composites were carried out. Preliminary evaluation of Ti alloy composites in terms of hardness, corrosion and wear

has been completed. *In vitro* tribological and wettability evaluation of Al_2O_3 composites has been performed on conventionally sintered samples. The microstructural non-uniformity and the presence of porosity in the composite coatings appeared to reduce the corrosion resistance of the coatings.

Peptide nanofiber matrix as drug delivery system for fungal keratitis: Human corneal epithelium consists of heterogeneous population of cells residing on the stroma. The corneal epithelium is one of the major barriers for delivering drug across its different layers. In this project, scientists at Vision Research Foundation, Sankara Netralaya are trying to develop peptide nanofibrous polymer matrix as drug delivery vehicle for treatment of fungal keratitis. They have designed, modelled and simulated 6 self-assembling peptide sequence *insilico* and proceeded further with one of the potential peptides. They have custom synthesized the peptide and have shown its internalization to primary corneal epithelial cells. They have also synthesized nanofiber with bovine serum albumin, Gelatin and Polycaprolactone polymer. The Gelatin-PCL composite was able to maintain the transparency required for visual acuity. The cells were plated on nanofibers and showed good attachment. PCL-Peptide composite was also made and its release study is in progress.

Surface Modified Hybrid Bioimplant to Enhance Implant Durability: The importance of implants has been drastically increased for the past few decades. Titanium (Ti) is better suggested implant material, but the biocompatibility and bioactivity are essential requirement to improve the properties of an artificial implant (Ti) to reduce the allergic reactions (joint pain and inflammations) and also exhibit chemical bonding to living tissues and formation of bone-like apatite layer on its surface. Zirconia (ZrO_2), when reinforced in HAp, improves the mechanical property comparable to natural bone and is considered as a good load-bearing material. In addition, incorporation of Silver (Ag) into HAp and

metal oxide (ZrO_2) is appropriate to elevate the antimicrobial property, particularly from implant-associated infectious microorganisms. Under the project supported in Sathyabama University, Chennai, titanium toe model was designed by 3D printing system and pure HAp was prepared from goat femur bone. HAp- ZrO_2 -Ag composites were pelletized and the composite pellets were characterized by XRD and FESEM-EDS analysis. The parameters for the composite coating have also been optimized.

Nanoenabled Biosensor for Detection of *Neisseria gonorrhoeae*: Under a collaborative effort between Delhi Technological University (DTU) and AIIMS, New Delhi, a bi-analyte sensor is being developed against the *opa* gene and *porA* pseudo gene of *Neisseria gonorrhoeae* with development and standardization of a duplex PCR for *N. gonorrhoeae*. At AIIMS, PCR was standardized for *porA* pseudo gene and for *opa* and *porA* pseudo gene duplex. The primers of *porA* pseudo gene were found to be specific only for gonococcal DNA and did not show any cross-reactivity with DNA from other bacterial species. Moreover, the PCR was found to detect DNA in spiked pus samples. The specificity of the duplex PCR however showed cross reactivity to *Neisseria meningitides* and *Neisseria lactamica* and studies are underway on resolving this peculiar case of duplex cross reactivity. The duplex PCR is being validated with clinical samples. In DTU, synthesis and structural characterization of polyaniline (PANI) and gold-PANI (Au-PANI) nanocomposites were carried out for electrode fabrication. The synthesized PANI and Au-PANI nanocomposite were deposited onto pre-hydrolyzed indium tin oxide (ITO)-coated glass substrates. Cyclic voltammetric studies were conducted to characterize the fabricated electrodes. The best current response was obtained for PANI2/ITO due to formation of a uniform thin layer. Further, the peak current for Au-PANI/ITO was found to be higher than that of PANI2/ITO which indicated the

synergistic effect of the excellent electrochemical properties of gold nanoparticles incorporated with the PANI fibers.

Conducting Cryogel for Peripheral Nerve Regeneration:

A project was funded at IIT Kanpur on developing conducting cryogel scaffold for enhanced peripheral nerve regeneration. For this, the effect of electrical field stimulation on neuronal cell viability, proliferation and differentiation, was evaluated by synthesizing CGPpy conducting cryogels through cryogelation technique. Schwann cells when electrically stimulated showed 47% and 35% increase in schwann cell proliferation at day 3 and 5 respectively, as compared to their control. Further, the effect of EF stimulation on the neurite lengths of neuro2a cells was also evaluated under uniform electrical field. The results showed immediate neurite like extensions in most of the cells as compared to their control. For the enhanced peripheral nerve regeneration CG cryogels were synthesized with aligned porous architecture as filler in the hollow conduits for developing a nerve guidance channel (NGC). The aligned nerve guidance channels (aNGCs) were characterized for their mechanical, physicochemical and biological properties. For aNGCs, the neuro2a cells were cultured for a period of 7 days and found to be compatible with increased proliferation with time. Further, the *in-vitro* regeneration experiment was done to examine the ability of aligned longitudinal channels in providing guidance cues to the migrating and proliferating cells. The nuclear shape index value and degree of alignment of the migrated cells from the dorsal root ganglion (DRG) explants were analyzed. The calculated degree of alignment for the cells migrated from DRG's was more than 57% reflecting that the developed NGCs are providing guidance cues and governing cellular alignment.

A Centre of Excellence Project has been supported on "Translational Research on Biomaterials for Orthopedic and Dental applications" implemented

in 8 Institutes across the country. This has 3 main components. The first component deals with development of lab scale component of polymer-ceramic hybrid composites as acetabular cup for total hip replacement. To address this, High Density Polyethylene (HDPE) based composites reinforced with graphene oxide (GO) were prepared and polyethylene (PE) was immobilized onto GO sheets to improve the interfacial adhesion. A good combination of yield strength, elastic modulus and elongation at failure were recorded for their composites. Cytocompatibility assessment using osteoblast and mesenchymal stem cells corroborated good cell attachment in culture and modulation of protein adsorption and cell proliferation was demonstrated together with better elastic modulus and yield strength. The aim of 2nd component is to design and fabricate truncated femoral head from commercially available high purity Nano powders and optimize various manufacturing steps to obtain dimensionally stable femoral head. So far, a rapid and robust process was optimized to develop highly dense oxide bioceramics, which consist of finer microstructure and optimum mechanical response. *In-vitro* cell culture with a murine myoblast cell line exhibited an increase in the number of mitochondrially-active cells and good cellular attachment confirming excellent cytocompatibility. The aim of 3rd component is to design CAD based model of two piece dental implant manufacturing via conventional and 3D printing technology; efficacy of dual ceramic coating on specific parts and investigate the cytocompatibility. During the period multiple novel CAD based 3D models of a complete 3 piece-dental implant system are designed. An acrylic based ink was formulated for 3D inkjet printing of Titanium and ceramics. The novel implant system was fabricated using advanced CNC and EDM with high dimensional tolerance. The novel implant prototypes were coated with hydroxyapatite with uniform coating thickness and good surface roughness combination.

BIODESIGN PROGRAMME

The Department has implemented Biodesign programme with the aim to develop innovative indigenous and affordable medical technologies and devices as per unmet clinical needs of India and train researchers, innovators, entrepreneurs to create an ecosystem for medtech innovations and entrepreneurship in the country. This Program is established in four centres: School of International Biodesign implemented 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. Few highlights of the programme during the year are given below:

School of International Biodesign Program (SIB): This programme is a frugal medical device innovation program implemented by the Department as a joint programme between a medical school (AIIMS) and an engineering institution (IIT-Delhi) in collaboration with international partners. The Department has authorized Biotech Consortium India Limited (BCIL) for management of its Intellectual Property and other techno-legal activities. SIB focuses on training young innovators. During this year, 12 medical technology innovators (doctors, engineers, designers, entrepreneurs) have been trained in the Biodesign process. Two medical device technologies have been developed: a) Apparatus and Methods for Extracting Body Fluid for Sampling or Testing; b) Apparatus and Methods for Non-Invasive Monitoring of Analytes for a Biological Subject and three technologies have been validated. During this year two technologies were transferred to medical device companies: a) *brünacousta-A* Novel Switchable Doppler Stethoscope was licensed to M/s. Brun Health Pvt. Ltd, Telangana; and b) *Inochicare- Advance Wound Care Dressing* was licensed to M/s. Inochi Care Pvt. Ltd., Assam. A new

medical technology start-up company has been set-up by the Fellows trained under this programme in sync with the 'Start-Up' India programme. Two products developed under this programme have been commercially launched during this year:- a) *Sohum-Auditory Impairment Screening Device* developed by SIB start-up M/s *Sohum Innovation Labs India Pvt. Ltd* and b) *Noxeno-Nasal Foreign Body Removal Device* developed by SIB Start-up *InnAccel Technologies Pvt. Ltd.* During this year six trademarks and one Industrial design have been granted by Indian Trademark Registry and an European Patent has been granted for "A cardio pulmonary resuscitation device and an integrated resuscitation system thereof". In addition, twelve patent applications (National, International and National phase filing) have been filed to protect the medical technologies developed by the Fellows under this programme. The 11th Annual Medtech Summit has been successfully organized on December 2nd, 2017 under the aegis of this programme to provide a platform for interaction among national and international participants and leaders in medtech innovation.

Centre for Biodesign and *in-vitro* Diagnostics, THSTI: The Center for Biodesign was established as a niche centre at THSTI with focus on diagnostics and extends support services from strategic bench work to commercialization. The Centre has evolved core expertise around Products and Platform Technologies for diagnostics. During the year, Center has developed a functional prototype of a highly specific, finger-prick whole blood compatible point-of-care strip-test, '*Ezy-Typ*' and the test is under clinical validation at *Kalawati Saran Children Hospital, New Delhi*. In addition, three kits ('*TB-Detect*', *TB Concentration and Transport*; *TB-Extraction kit*) have been developed for TB and Drug resistant TB diagnosis. The '*TB-Detect*' kit provides a mechanism for improving the current TB smear microscopy test by equipment-free bio-safe sputum concentration. The '*TB Concentration and Transport*' kit provides a mechanism for convenient, dry, bio-safe sputum

collection, processing and subsequent transportation for molecular DST tests. The 'TB DNA extraction kit provides inhibitor free M.tb DNA purification suitable for DNA sequencing and other Molecular DST testing. These kits are ready for multi-centric validation through ICMR. Two patents were filed during the year with four articles published. Three products are in final stage of development: i) High affinity DNA aptamers against *Mycobacterium tuberculosis* ii) Multiplexed Point-of-Care test for tropical febrile illness TB and iii) High sensitivity multiplex point-of-care assay system for the detection of blood borne infections.

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. During the year, studies were carried out to delineate mechanism of physiological flows through arterial vessels. In this study, they used flow visualization and computational fluid dynamics to study unsteady flows in a highly curved tube. They have also developed a micro-mechanical device for providing a mechanical stimulus to cells cultured on it and observed the change in the deformation of the nucleus of the cell. Under another initiative of mechanobiology of breast cancer project, with a combination of ridge and array micro machined pillars, they were able to quantify the directional preference of collective cell migration. In another related study, engineered gel systems were used to characterize the forces exerted by the cells, known as cellular traction force-microscopy technique. Experimental and computational aspects of this study were conducted and reported. The computational technique improved the accuracy of estimated forces applied by the cells on the soft substrate.

Healthcare Technology Innovation Centre (HTIC), IITM: Healthcare Technology Innovation Centre (HTIC) is an R&D centre which has been

established by DBT in IIT Madras to bring together technologists, engineers, doctors and healthcare professionals, industry and government to develop healthcare technologies for the country. HTIC is delivering innovations and technologies that are reaching the field through government and industry partnerships, bringing benefits to society. HTIC's Mobile Eye Surgical Unit, MESU™, a first-of-its-kind technology in the country has conducted around 8000 surgeries in over 40 rural locations and is continuing operations in states of Tamil Nadu, Andhra Pradesh and Jharkhand. Eye PAC™, an ophthalmic image computing technology, developed by HTIC is creating global impact and has reached 1500+ installations in 26 countries so far with around 2 million eye examinations. A new product for newborn eye screening, "3nethra neo" has been recently introduced into the market under this programme which is the first indigenous technology available in market for screening retinopathy of prematurity, a critical premature condition. The Center's first indigenous point of care technology and product for quantitative immunodiagnosics developed in collaboration with J Mitra Pvt. Ltd. has completed pilot manufacturing and is expected to reach over 1000 labs by end of 2017 addressing a market of around 50,000 tier-2 labs in the country and is expected to benefit around 2 million people annually in coming years. HTIC is expanding its R&D and engineering capabilities to develop more complex and high end technologies and systems currently lacking in the country, such as high end diagnostic systems, minimally invasive robotic surgical systems, endoscopic imaging systems, non-contact physiological monitoring, intelligent medical image computing, and trauma care solutions.

NANOBIOTECHNOLOGY

Nano biotechnology provides a new frontier for scientific and technological advances to exploit biomolecules and materials at nanoscale to address challenges related to health, agriculture, energy and

environment. DBT has been engaged in promoting interdisciplinary research, fostering innovation and promoting translational research in various cutting edge areas of Nano Biotechnology. The efforts have led to promising knowledge outcomes with translational potential and being supported for early translational research. Some of the highlights of research work are mentioned below:

Dysregulated proto-oncogene c-Myb has been implicated in leukemogenic and pathogenesis of AML. Studies were undertaken at INST, Mohali for identification and characterization of the epigenetic mediator, polycomb protein Bmi-1 as c-Myb targets for mediating suppression of differentiation and promoting proliferation resulting leukemic transformation. A Bmi-1 inhibitor PRT4165 loaded HSA Nano formulation to achieve targeted drug delivery was synthesized and characterized to overcome current treatment limitations. PRT4165 loaded HSA Nano formulation resulted in decrease in cell viability of AML cell line U937 better than its free bulk drug crystalline state. The current study shows, PRT4165 encapsulated (HSA-NPs) Nano formulation may overcome limitations of placebo drug and showing therapeutic efficacy compare to bare drug and hold promise for future translational potential against AML therapy.

Studies have been carried out at NIPER, Mohali to develop nanocrystalline solid dispersion (NSD) of hesperetin (HRN) with enhanced oral bioavailability for cancer treatment. A NSD system was developed for enhancing the oral bioavailability of HRN using mannitol (MAN) which was found to be the 'best' performer in generating NSD powder of desired quality attributes. The two-component NSD system was further improved by adding sodium lauryl sulphate (SLS) and dioctyl sodium sulphosuccinate (DOSS) using quality-by-design (QbD) approach. The multi-component HRN-MAN-SLS-DOSS NSD system was found to show improved crystallite size (558.2 ± 49.1 nm) and better *in vitro* dissolution

behaviour (2.9-fold higher dissolution efficiency) than its physical mixture.

In a translation study pursued at ACNSMM, Amrita Vishwa Vidyapeetham, Kochi for treatment of infectious wounds using antimicrobial Nanocomposite Chitosan Bandages, chitosan composite bandages were developed and characterized. It was found that the composite bandages were highly porous, flexible and capable of absorbing fluid. Cell viability studies on human dermal fibroblast cells proved the non-toxic nature of the bandages. The *in vitro* antimicrobial study showed the activity of the bandages against microbes. In addition, the long term antibacterial study confirmed that the nano-composite bandage significantly improved antimicrobial property compared to the commercial available bandages. *In vivo* experiments carried out in Sprague-Dawley rats showed better infection reduction than commercially available bandage. These antimicrobial composite chitosan bandages has huge potential in infection control and wound healing.

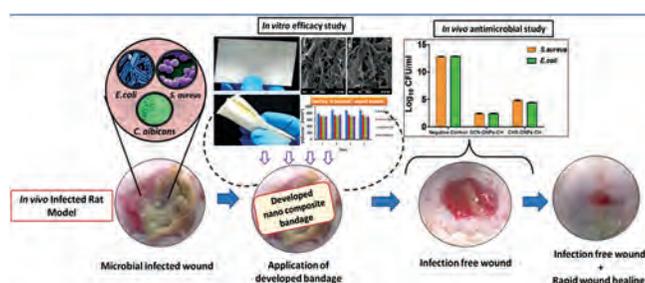


Figure 30. Study on antimicrobial nanocomposite chitosan bandage

Breast cancer is one of the major causes of cancer related deaths in females worldwide and the conventional nanotherapeutic delivery system available in the market lacks the targeting and imaging modality. Studies have been carried out at IIT, Mandi to engineer multimodal 'third generation' nanotherapeutic delivery system, targeted specifically to breast cancer cells for cancer therapy. Au Nano rattles and plasmonic nanocapsules having

a rod-shaped rattle structure were synthesized and thermodynamic and kinetic parameters were determined. Au Nano rattles also showed excellent catalytic performance towards the degradation of environmental pollutants like p-NP and organic dyes and hence their application would also be deployed as an agent of environmental remediation.

At Regional Centre for Biotechnology, Faridabad, a synthetic scheme for bile acid-phospholipids and bile acid-Drug-phospholipid conjugate technology was developed. A gastric pH stable bile acid derived amphiphile where Tamoxifen is conjugated to lithocholic acid derived phospholipid (LCA-Tam-PC) was designed and synthesized. To track and quantify the intracellular and intra tumor drug concentration nitrobenzoxadiazole (NBD) fluorophore conjugate, LCA-Tam-NBD-PC was synthesized. *In vitro* studies revealed increased IC_{50} values of LCA-Tam-PC due to stable conjugate of the drug. Pharmacokinetic and bio-distribution studies using LCA-Tam-NBD-PC validated the enhanced gut absorption, blood circulation, and tumor site accumulation of phospholipid conjugate that led to improved antitumor activity of LCA-Tam-PC. The study could be used to design the repertoire of bile acid phospholipid-drug conjugates as a new platform technology for oral delivery of chemotherapeutic drugs.

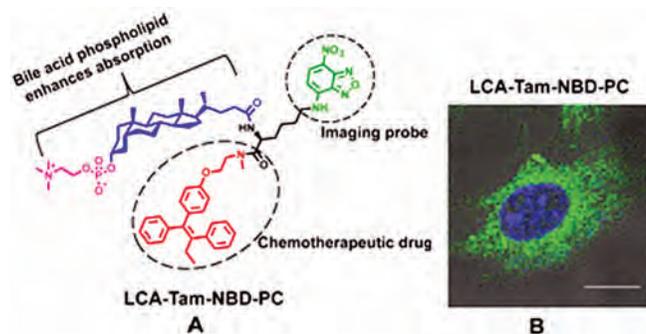


Figure 31. Molecular structures of LCA-Tam-NBD-PC (A) Confocal micrographs of MCF-7 cells LCA-Tam-NBD-PC.

Studies were carried out at Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore for controlled release dispensers for delivery of

semiochemicals. Mesoporous silica and carbon were used as nanomatrix for delivery of semiochemicals of coconut rhinoceros beetle, red palm weevil and tomato pin worm, *Tuta absoluta*. Pheromone loaded into the nanomatrix had a controlled release over a spatio temporal scale. The nanomatrix required lower load of pheromone as compared to commercial lure and had also had extended release rate to trap insects.

Major challenge in the treatment of neurodegenerative diseases is that the presence of polarized endothelial layer composed blood brain barrier (BBB) that restricts the entry of therapeutics into the brain. Studies have been carried out at Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum to develop Blood brain barrier targeted Nanoconstructs for the diagnosis of brain diseases and the delivery of therapeutics into the brain. A nanomaterial system based on atomic sized gold cluster conjugated with a brain targeting molecule, L-dopa was successfully developed for brain targeting, imaging and delivery of therapeutics. Carrier efficacy of the system was tested by physically conjugating a model drug, pilocarpine which showed slow and sustained release of the drug both *in vitro* and *in vivo*. The study will open new horizons in the area of diagnosis and treatment of neurodegenerative diseases.

At IIT Delhi, translational research work is being pursued to develop stimuli responsive biocompatible polymeric particles for targeted drug delivery in breast cancer. An efficient, scalable stimuli sensitive (redox sensitive) polymer was synthesized with optimization using three step synthesis procedures. The polymer is composed of biocompatible components, polycaprolactone or (poly lactide can also be used), polyethylene glycol, linked through disulfide linkage. The polymer was characterized using proton NMR (1H -NMR) and gel permeation chromatography (GPC) and performed *in vitro* and *in vivo* evaluations for assessing its drug delivery

efficacy. Tumor regression study in animals has shown that drug delivery efficiency of the developed nanosystem is comparable to that of the marketed formulation, DOXIL. The developed nanosystem has added advantages such as stimuli sensitive nature, which could achieve more specific tumor targeting, ease of manufacturing, scalability and cost effectiveness.

Studies were carried out VIT, Vellore to develop a better therapeutic approach for the treatment of rheumatoid arthritis (RA). Withaferin-A, a steroidal lactone incorporated with mannosylated liposomes (ML-WA) was administered to adjuvant induced arthritic rats in intent to target the synovial macrophages. The result showed a successful internalization of ML-WA, reduced oxidative stress and a progressive gain in the body weight. ML-WA treatment upregulated the production of osteoprotegerin (OPG) and downregulated the release of receptor activator of nuclear factor-B ligand (RANKL), favouring osteoclastogenesis negatively. Correspondingly, the ankle joints were found intact with no bone erosion and cartilage degradation in ML-WA treated AIA rats as evidenced by histopathological analysis. Concentration and the gene amplification of M1 macrophage mediated pro-inflammatory mediators were curtailed and anti-inflammatory cytokine was found abundantly released in ML-WA treated AIA rats. The results signified that targeted delivery of ML-WA ameliorated the severity of inflammation and bone resorption in AIA rats via M1 to M2 macrophage repolarization.

Photothermal therapy (PTT) is a promising therapy for cancer treatment where plasmonic nanoparticles convert NIR light to heat leading to hyperthermia induced cell death. At CSIR-NIIST, Kerala, spatio-temporal synchronization of PTT and chemotherapy was adopted as an insightful approach to enhance the therapeutic efficacy. Localized photothermal-chemotherapy was initiated by gold nanorod (GNR) conjugated to (i) Raman signature molecule (RSM)

i.e. squaraine dye (SQ) attached target specific peptide substrate susceptible to matrix metalloproteinases (MMP2 & MMP9), over-expressed in extracellular matrix of cancer cells and, (ii) lipoic acid appended doxorubicin, conjugated through acid labile hydrazone linkage (LAH-DOX). The fabricated targeted theranostic nanoconstruct exhibited the potential for pre-clinical and further clinical studies towards efficient cancer treatment and future scope to be evolved as a promising nano medicine.

05

**Biotechnology Based
Programmes for
Societal Development**

Department continue to support projects under its 'Biotechnology based Programme for Societal Development' with an aim to promote use of biotechnological processes and tools for the benefit of the society including rural population, SC/STs and women community. 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 broad focused areas are fish farming, poultry farming, vegetable seed production, integrated farming, entrepreneurship development, vermicomposting, spirulina and pulses cultivation, popularization of biofertilizer and bio-pesticides, horticultural crops, bio-resource utilization, value added products, sericulture, women and child health, hygiene and nutrition. Large number of rural, SC/ST and women population including youth have been benefited through the implementation of these projects. Some of the major achievements of the programmes supported are highlighted below:

BIOTECHNOLOGY BASED PROGRAMME FOR RURAL DEVELOPMENT

Fish Farming: A project on propagation of culture-based-capture fisheries in selected reservoirs of Konkan and Western Ghat regions of Maharashtra was supported at College of Fisheries, Ratnagiri for the benefit of tribal communities mainly *Katkari*, *Bhoi*, *Koli* involved in inland fishing. Considering the dearth of fish-seedlings to stock the inland water bodies of the region, a comprehensive carp fish hatchery production unit was established with an annual capacity of 50 million of fish spawn. The hatchery is providing quality fish fingerlings of Catla, Rohu, Mrigal and common carp to the tribal inland fishing cooperatives. Several training and demonstration programmes have been conducted on various aspects for the tribal fishermen on reservoir fisheries management, production of fish fingerlings in the

ponds and cages and ornamental fish production, preparation of value added fish products, water analysis and development of fish brooders. The average fish production from the reservoirs has been increased from 25 kg/ha to 285 kg/ha with an increased average additional income per family of tribal fishermen Rs. 42,415/- per annum. Due to the implementation of these activities migration has been reduced and 56% of household have stopped migration.

In another project on productivity and production enhancement, freshwater pond water bodies were utilized for livelihood generation of the Aila Affected SC/ST Communities of Islands of the Sundarban, West Bengal. Various training programmes were conducted and nearly 200 farmers were trained on various aspects of fish culture and quality seed production of *C. catla*, *C. mrigala*, *L. bata* and improved variety of *L. rohita* (Jayanti-Rohu). Vanaraja-chicks were also distributed to promote integrated farming along with fish culture.

Another project on integrated farming for sustainable livelihood generation was implemented at Gauhati University, Guwahati. The beneficiaries were selected from Village *Kulsi* and *Dimali* of rural Kamrup district of Assam. Several training programmes have been conducted on integrated fish cum duck farming. To facilitate composite and integrated fish farming, all the selected ponds were renovated by dewatering, bottom scrapping, dyke trimming followed by manuring with cow dung, lime and super phosphate in recommended dose. After pre stocking management of the selected ponds, 3000 yearlings in average (40g to 50 g in weight) of *Catla*, *Rohu*, *Mrigal*, *Grass carp* and *Silver carp* were stocked in all the ponds. When the yearlings attained average weight of 80 to 100 g, after two months, 100 ducklings (Campbell strain) (ratio of male : female : 1:4) at the age group from 2 to 3 months and average weights of 0.81 kg to 0.95 kg were introduced equally in five ponds and were reared in

the duckery constructed for the purpose. After one year of rearing, average growth of *Catla* was recorded maximum (1.0 kg) followed by *Silver Carp*, *Rohu*, *Mrigal* and grass carp with maximum weight of 0.8kg, 0.6 kg, 0.5kg and 0.4 kg respectively along with production of average 500 number of eggs and 50 ducklings from each duckery. Adoption of Integrated duck cum fish farming has increased the additional income of the farmers.

Cultivation of Spirulina: A project on small scale backyard cultivation of *Spirulina* for selected NGOs from various districts of Tamil Nadu as an income generation activity and as a health supplement was implemented by Shri AMM MurugappaChettiar Research Centre, Chennai, Tamil Nadu. A total of 27 beneficiaries were selected for setting up *Spirulina* cultivation facilities at their locations and 75 beneficiaries were trained on *Spirulina* cultivation techniques and 27 *Spirulina* tanks were constructed with dimensions (6m x 3m x 0.45m) having capacity of 8000 L. All beneficiaries have started *Spirulina* cultivation, harvesting the algae in their own backyard tank and sold around 1550 kg of *Spirulina* in the local market @ Rs.800/kg. Some beneficiaries have been using *Spirulina* powder as an animal feed for their cattle (50g/day) and also have been selling *Spirulina*-maize powder mix to local poultry farmers and earning additional income of Rs. 8000/ month with a minimum of 10 kgs of *Spirulina* production.

Cultivation of Pulses: A project on development of pulses based sustainable bio-village models through action research for livelihood security under different agro-ecosystems in Uttar Pradesh was implemented by Indian Institute of Pulses Research, Kanpur. Eight quintal quality seed of pulses as chickpea (Var. JG 14 and JG 16) and lentil (IPL 316) was distributed to 55 farmers in village Benipur, Nagla in Shahjhanpur and Kucharam in Chitrakoot, UP for demonstrations cum seed production. Two farmers societies namely Maa Durga Krishik Seva Samiti, Kucharam, Chitrakoot and Benipur Swami

Vivekanada Seva Samiti, Shahjhanpur were registered under Act 21, 1860 for group mobilization under the project. One IIPR Mini Dal Mill has been given to the beneficiaries of Shahjhanpur for processing and value addition of pulses. To generate awareness and promote organic pulses production 10 Vermi-compost units using earthworm (*Eiseniafetida*) have been established at village Kucharam in Chitrakoot district. To maintain pulse crop cafeteria at KVK, 26 promising cultivars have been supplied for demonstration cum evaluation of suitable varieties for the region.

Agripreneurship Development: A project on community based mass production of bio-control agents in J&K, popularization of low cost technology for Agri entrepreneurship through farm based bio-control units was implemented at SKUAST-Jammu. Farmers were trained to rear the host insect on which the bio-control agent was to be reared e.g. *Corcyra*, *Spodoptera litura* and *Helicoverpa armigera* and subsequently mass production of *Trichogramma* and NPV bio-control agents. Around 350 farmers were exposed and 60 farmers were successfully demonstrated low cost production system in the farmer field. Sufficient quantity of *Trichogramma* (>950 Tricho cards) has been released over 50 ha area. The intervention popularized were trap cropping; pheromone trap system to monitor and mating disruption; and promotion of bio-control agents like *Bacillus thuringiensis* and *Trichogramma* and botanicals like neem oil and neem cake. These techniques have given very good results in Sudhamahadev in Udhampur district and adjoining villages like Basht, Gaurikund and Mantalai. As part of public private collaboration, the technological intervention under the project got integrated with a local company operating under Actech Agro Private Limited. A young local farmer was motivated for farm enterprise as a KisanUtpadak Company in the project implementation area. The company is engaged in

promotion and popularization of interventions and bio-control agents.

Rural Bio-Resources: A network project on establishment of rural bio-resource complex for ecologically sustainable utilization for the economic empowerment of Himalayan region community implemented at HESCO, Dehradun in collaboration with GBPUAT and GBPIHED. Two rural Bio-Resources Complexes have been established at Garhwal and Kumaon (Chokhutiya) of districts Almora and Dehradun, respectively. A total of 26 villages from Almora and 22 villages from Dehradun have been selected to implement the project activities. Farmers have been imparted training on backyard vegetable cultivation, polyhouse vegetable cultivation technologies, organic farming, mushroom cultivation, processing and preservation techniques of fruits, bio briquetting, poultry farming, vermin composting. More than 800 beneficiaries from 48 selected villages have been benefited through adoption of this practice for their livelihood generation.

BIOTECHNOLOGY BASED PROGRAMME FOR SC/ST POPULATION:

Fish Farming: A project on carp seed production in FRP hatchery and development of integrated rearing system for livelihood development of SC/ST communities in Khordha District of Odisha was implemented at ICAR-CIFA, Bhubaneswar. A total of 192 beneficiaries having 9.19 ha pond area were selected from Balipatana, Baliana, Banapur & Begunia blocks. Several training programmes on scientific aquaculture management have been conducted for the tribal farmers. Induced carp breeding operations were conducted in all 3 hatchery units i.e. Puranapadhan, Kantabada and Aranga. At Puranapadhan Village, 17.25 million carp spawn (*Catlacatla*- 2.5 million; *Labeorohita*- 9.25 million; *Cirrhinus mrigala*- 3.5 million; *Cyprinus carpio*- 1.5 million and *Ctenopharyngodonidella*- 0.5 million) were harvested (Fig.1). More than 400 farmers have

been benefitted through adoption of fish farming for their livelihood generation.

Poultry Farming: A project on Giriraja poultry rearing and propagation for socio-economic upliftment of scheduled caste community in Imphal East District, Manipur was implemented at Central Agricultural University, Imphal, Manipur. The project was implemented in Andro-villages which are socio-economically backward and schedule caste dominated village in KeiraoBitra sub-Division of Imphal. A total of 200 scheduled caste beneficiaries were selected for training and demonstration on scientific Giriraja management, marketing, and formation of SHG. One week old Giriraja chicks along with feeds, medicines were distributed to the beneficiaries for rearing.



Figure 1. Harvesting of fish by the farmers

Popularization of Bio-fertilizer and Bio-pesticide: A project on popularization of biofertilizer and bio-pesticide for enhancing the rice and wheat production of SC/ST farmers of Jaunpur and Azamgarh district, U.P. was implemented by Institute of Environment and Sustainable Development, Banaras Hindu University, Varanasi. Training programmes were conducted for awareness creation on bio-fertilizers and their use led to 25-30% increase in yields and 40-50% in income with respect to wheat, maize and vegetable crops. Farmers also saved 25-40% chemical fertilizers by biofertilizers application. Adoption of bio-fertilizer and bio-pesticides helped

the farmers for livelihood generation.

Agri- biotechnologies: A project on socio-economic upliftment of the rural and peri urban SC/ST population of Srikakulam district through agri-biotechnologies was implemented by Agri Biotech Foundation, Hyderabad. Training programmes were conducted on rising vegetable seedling using pro tray technology and use of vermicompost. Resource mobilization was done for construction of vegetable seedling nurseries and vermicompost followed by distribution of nursery implements. Adoption of this technology benefitted 187 farmers for livelihood generation.

Horticultural crops: A total of 120 tribal farmers have been benefitted through a project on perennial horticultural crops under rainfed cultivation, implemented at Horticultural College and Research Institute, Tamil Nadu Agricultural University Coimbatore. Three villages viz., Monthanthotti, Neergundypudur and Kaunakakai were selected at Western Ghats of Tamil Nadu and six beneficiaries were identified to establish orchards with nutrient rich perennial horticultural crops for their better livelihood. Training and demonstration programmes were conducted on cultivation of perennial horticultural crops, preparation of processed foods at home, bee keeping and developing kitchen gardens. Training manuals on cultivation and processing of perennial horticultural crops and profitable horticultural crop cultivation were also distributed to the beneficiaries. Farmers were also provided spade, crowbar, hand hoe, digging fork, shovel, secateurs, sickle sprayer and ladder; planting materials and farm inputs like fertilizers, vermicompost and bio-nutrients for establishing orchards.

Vegetable Seed Production: A project on quality seeds production of some important high value vegetable crops (tomatoes, brinjal and okra) was implemented by KVK, Manipur in the villages which are predominantly engaged in vegetable growing areas. Ten self-help groups were constituted from

the project villages and they have been given training on vegetable seed production particularly for tomato, brinjal and okra. A total of 20 training programmes were conducted on different aspects of quality vegetable seed production for the farmers.

BIOTECHNOLOGY BASED PROGRAMME FOR WOMEN

Ornamental Fish Culture: A project on ornamental fish culture was implemented for the empowerment of rural women and youth in Kozhikode district of Kerala through KVK, ICAR- Indian Institute of Spices Research, Kozhikode, Kerala. Training on various aspects of ornamental fishes covering marketing, fish feed preparation, aquarium have been conducted and twenty five fish culture demonstration units have been established at the field of beneficiaries. Training and demonstration programmes conducted helped the rural women to adopt ornamental fish culture as a livelihood option. The marketing of fishes are being done by KVK. Two self-help groups namely Angel JLG in Perambra block panchayath and Jaya activity group in Koorachundugrampanchayath of Kozhikode district, Kerala were formed. Regular monitoring of health status of the fish and water quality of culture tanks are being done. A training manual and a leaflet in local language (Malayalam) have been published and distributed to the beneficiaries.

Poultry Farming: A project on sustainable livelihood generation for rural women through improved backyard poultry farming was implemented at College of Veterinary Science and Animal Husbandry, Central Agricultural University, Mizoram. A total of 541 parent Vanaraja chicks (80 male birds and 461 female birds) were supplied by Project Directorate of Poultry, Hyderabad. Ten women from ten selected villages were imparted training to enhance their skill to serve others as local service providers in their respective villages and establishment of rural poultry resource centre. The project was implemented in two districts

of Mizoram, viz., Aizawl and Mamit covering 5 villages in each district. More than 2000 chicks have been distributed to 89 beneficiaries. The average egg production is about 600 eggs per family per month and farmers are earning about Rs. 6000-8000/- per month. The rearing of Vanaraja birds helped the beneficiaries to utilize the income derived from the selling of eggs and birds in meeting day to day expenditure activities like education fee of children, food items, small savings etc. The additional income of the enterprise helped them in reducing the hard work done by these women like going to jungle in search of vegetables for selling, fire woods or doing labourers job in others house to meet the expenditure of their families. People from the nearby area have also shown interest in poultry farming and the project beneficiaries are selling their chicks to them.

Health and Hygiene: A project on immunological, genetic and behavioural profile of women with urinary tract infections was implemented at King George's Medical University, Lucknow. 869 women were screened with complains suggestive of UTI and their urine and blood samples were taken for analysis. Out of these, 103 women had *E. coli* infection and 60 had some other bacteria. These 103 women were followed for next 12 months, fortnightly and asked for symptoms experienced during previous episode as a guide for self-diagnosis of any recurrence. Only 22 women reported recurrence of symptoms. 1500 healthy women were also recruited from family planning clinic for screening and urine samples of 22 women showed presence of 10^5 CFU/ml of bacteria (15 *E. coli*, 7 other bacteria) in the absence of symptoms. Cytokine detection for all women was done and 78 cystitis and 11 recurrent cases were reported and IL-8 was found to be higher at the time of index episode than in infection free period. A demonstration cum talk programme was also conducted at *Navyug Kanya Mahavidyalaya, Lucknow* and brochures were distributed to the 600 women faculty and senior students. Awareness was created among women with low socio-economic

status educating them about simple lifestyle changes related to their sanitation and sexual habits or personal hygiene which may reduce the infection rate, thus improve quality of life and avoid loss of work. A demo-cum-talk session was also conducted at *Masala Mathri Kendra* and distributed brochures to 120 poor women and girls. A health education program was also organized at an organization of Self-Employed Women Association (SEWA-Lucknow), and 80 women participate in the programme. Besides this, regular health awareness program on daily basis is being done at Obstetrics and Gynaecology outpatient department of the college. Around 40,000 to 50,000 women have benefitted through implementation of this project.

A Network Programme on Breast cancer screening was continued in four districts of North-East India namely Manipur, Meghalaya, Mizoram and Tripura through coordinating agency Cancer Foundation of India, Kolkata. A total of 7919 women have been sensitized on breast health in Agartala Govt. Medical College, Tripura and 2009 in Civil Hospital, Aizawl, Mizoram. 6319 women have been sensitized on breast health in Manipur and 2023 in Meghalaya. A dedicated Breast Clinic was established in the host institutions for community screening. The breast health education plan was focused on breast self-examination (BSE) to identify the early signs of breast changes and reach out to the designated Breast Clinic for clinical follow up. A 3-day Training on Data entry and Analysis was also organized in Shillong, Meghalaya for Data Managers and Social Workers working in the Project from participating centres.

A project on Genetic awareness, diagnostic & counselling programme on maternal and neonatal health was implemented at Department of Molecular & Human Genetics, Banaras Hindu University, Varanasi, U.P. In this project, emphasis was given on the need of pregnancy care, genetic awareness and to inculcate healthy lifestyle into routine practice with the help of gynaecologists, medical superintendent

and health education officers of the local area. Training programmes have been organized for genetic counselling, awareness campaigns for ASHA, Anganwadi workers in the villages focusing mainly on pregnant females, reproductive age group women as well as adolescent girls. These programs are determined to develop local population's insight into female reproductive health right from the adolescent age. Families were motivated towards pregnancy care, nutritional interventions for anaemic pregnant females as well as adolescent girls, management of pregnancy related complications and other sensitive social issues such as gender determination. Seven-day workshop was also organized for medical professionals and research scholars to provide a common platform for clinicians and researchers for the better understanding and use of modern age technologies for effective management of maternal and neonatal health issues.

Value Added Products: A project on socio-economic upliftment of rural women through development of value added meat products was implemented at Faculty of Veterinary science and Animal Husbandry, Sher-e-Kashmir University of Agricultural Sciences and Technology, Jammu. Five hands-on training programmes were conducted at division of Livestock Products Technology and nearly hundred women participated from different villages of R. S. Pura, Jammu were trained on various technological aspects in the development of various value added meat and egg products and their packaging, preservation and marketing. Special emphasis was also given regarding the development of shelf stable meat products. A few trained women have also introduced different value added products in their already established shops.

Ericulture: Eri silk is the product of the domesticated silkworm, *Philosamiaricini* that feeds mainly on castor leaves. The 'Ericulture' is a household activity practiced mainly by tribal of north-eastern part of the country. A project on ericulture for upliftment of socio

economic condition of rural tribal women in Assam was implemented by The Energy and Resources Institute (TERI-NE), Guwahati. Ten villages of Kamrup and Udalguri districts of Assam covering 120 women beneficiaries have been selected for production of disease free laying (DFL) rearing and spinning of Eri Silkworm. Several awareness generation and capacity building programmes have been conducted. Under this project separate rearing houses for the beneficiaries have been developed and 60 improved Eri spinning machines have been provided to the beneficiaries. Trainings programmes on different aspects of Eri silkworm rearing, spinning, pest and diseases management and issues related to post cocoon management were conducted, which benefitted 110 women.

06

**Biotech Product
& Process
Development**

BIOSYSTEMS AND BIOPROCESS ENGINEERING

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, *in-silico* modelling and process systems engineering are being encouraged. Some of the achievements of the projects supported are as follows:

Engineering *Bacillus subtilis* to develop an efficient platform for enzyme secretion: This project is being implemented at IIT Bombay with the aim of efficient manipulation leading to design of secretion systems in bacteria. Towards this aim, scientists have developed a computational model to address the issue of design of nucleotide sequences in *B. subtilis* which maximize the protein secretion from the organism. The approach, adopted is independent of the target protein, and is based on the thermodynamics of protein secretion and expression. Efforts have also been made on making general modifications in the organism which target effective secretion and stabilization of secreted proteins. They have so far, successfully built constructs which house upto three modifications.

Valorisation of waste to carboxylic acid by integrated acidogenic fermentation process using bio-refinery approach: This study is being carried out at IICT Hyderabad with the aim to develop integrated bioprocess that provides a novel solution for waste valorization towards resource recovery with carboxyl platform as a focal point in the framework of biorefinery. Among all redox condition studied (pH 5 to pH 12), pH 10 operation (6.3 g/l) exhibited higher volatile fatty acid (VFA) productivity of 6.3 g/l using

food waste as feedstock. Application of pre-aeration to waste prior to feeding at semi-pilot scale biosystem assisted the suppression of methanogenic activity and exhibited 10% higher VFA production than the control. Acid pretreatment strategy helped in enhancing the VFA production (PT; 11.1 g/l) when compared with untreated parent biocatalyst (UT; 6.1 g/l). Taguchi methodology served as a systematic mathematical approach to understand the acidogenic process. Pretreated biocatalyst along with higher COD load and bicarbonates presence led to enhanced cumulative hydrogen production, whereas pH in combination with sulphate, nitrate, and bicarbonates increased the degree of acidification.

Process development for the enzymatic conversion of grease into long chain fatty acid: Grease is widely used as a lubricating agent in almost every machine to reduce the friction generated between the two moving parts. Disposal of grease waste poses a serious problem and becomes a threat to the ecosystem as it is non-biodegradable. In most of the countries, waste grease has been dumped in the litter site or in the sewages without any pre-treatment leading to severe environmental issues. Utilization of grease as a substrate opens up new strategy for product development vis-a-vis its remediation.

In this study metabolic pathway used by *Penicillium chrysogenum* to convert grease into long chain fatty acid was studied and a process has been developed to convert grease waste into Fatty acids, which has huge market globally.

Bioprocess development and application of laccase from *Basidiomycota* sp.: The laccases are the enzymes that have proved to be an effective tool in many industrial processes like waste water treatment especially in dye degradation and toxic waste treatment. It can also act upon plant litter and degrade the most recalcitrant complex natural polymer such as lignin. Being the most important

ligninolytic oxidative enzymes, they have large market potential in biotechnological processes. Therefore, novel laccase producing microbes having wider and different substrate specificities, with improved stability carries high importance.

Studies carried out under this project at Moolji Jaitha College, Jalgaon, Maharashtra led to optimization and the scaling up of the laccase production, which has resulted in the reduction of the production cost from Rs. 49/L to Rs. 2.28/L. The crude laccase produced was found effective in bioremediation of textile as well as non-textile dyes (~80-90 %); suitable for its applications in textile and pulp industry. The detoxification of dyes by laccase was found to be very efficient which was evaluated by microbial and phytotoxicity assay.

Metabolic engineering of *Zymomonas mobilis* for production of Malic acid: The enzyme pyruvate decarboxylase converts pyruvate into ethanol. The major flux goes from pyruvate to acetaldehyde which is further converted to ethanol, to lactate, and to acetyl CoA which enters TCA cycle. For diverting the metabolic flux towards malic acid, the study involved the deletion of pyruvate decarboxylase and lactate dehydrogenase genes in *Zymomonas mobilis* ZM4.

The deletion in the present study done at IIT Delhi was performed using electroporation of linear PCR product. This is the first report of deletion of a gene in *Z. mobilis* using this approach. This will make genome engineering in this bacterium easy and rapid.

Whole cell catalysed biotransformation for synthesis of fructo-oligosaccharides (FOS): The feasibility of using whole cells of *Microbacterium paraoxydans* for synthesis of FOS has been demonstrated using cell bound enzymes at IIT Delhi. In order to use invertase/inulinase activity for FOS synthesis, cells were induced with sucrose, inulin or left un-induced. Maximum FOS yield of 40 g/L was

obtained using sucrose-induced cells indicating role of invertase activity in trans-fructosylation activity. Using these cells, pH, temperature, substrate concentration, whole cells concentrations were altered to investigate their effect on FOS yield and important parameters were identified. These parameters will be optimized with an objective to obtain maximum conversions. Selective separation of the sugars from synthesized FOS using various resins was also evaluated. Results are likely to find applications in industry as these molecules are prepared currently using purified enzymes.

Bioprocess development for caffeine degradation using whole cells and enzymes:

Industrial applications: This study is being done at IIT Madras, Chennai. Sequence of the genomic DNA fragment of *Pseudomonas* sp. revealed the presence of ndm genes similar to that present in *Pseudomonas putida* CBB5. Five ndm genes namely, *ndmA*, *ndmB*, *ndmC*, *ndmD* and *ndmE* were cloned, over-expressed and purified to homogeneity. Biochemical characterization of NdmD was done. NdmD, the reductase component of caffeine demethylation system found in *Pseudomonas* sp. has an extra Rieske domain in its N-terminal when compared to other RO reductases. Investigators made two deletion constructs $\Delta 114$ NdmD and $\Delta 250$ NdmD where N-terminal Rieske domains were deleted from full length NdmD. Far UV CD spectral profile shows that the deletion constructs folds into native structure even when the Rieske domain was deleted from NdmD. Functional assays proved that the N-terminal Rieske domain is not required for the catalytic activity of NdmD.

Centre of excellence in vaccine delivery using biodegradable polymer particles: This centre was supported for creating a facility for large scale manufacturing of polymeric nanoparticle using spray drying for vaccine delivery and to develop nanoparticle based pneumococcal vaccine consisting

of carbohydrates of 4 Pneumococcal serotypes of predominant Indian origin (without using conjugation of carrier peptide).

A large scale nanoparticle formulation laboratory has been established at NII, New Delhi for delivery of biologicals. Investigator has shown that polymeric nanoparticles entrapping capsular polysaccharide induced neutralizing antibody titer from single dose immunization. A process of conjugation of polysaccharide to recombinant protein has been standardized. Preparation of nanoparticle entrapping carbohydrates of other serotypes has been established and are being evaluating for immunogenicity. Serotype 1,5, 14, 6B and 19F have been procured and being used for immunization studies. Novel proteins from *S. pneumoniae* have also been expressed in *E. coli*. Purification and immunogenicity tests are underway. Work on development of cell wall polysaccharide based pneumococcal vaccine has also been initiated.

Centre of excellence for biopharmaceutical technology: This COE is being implemented at IIT-Delhi, New Delhi. Some of the achievements are:

a) Cloning and expression of Lucentis: Lucentis is a 48 kDa humanized monoclonal antibody fragment, which is mostly produced as inclusion bodies in *E. coli* expression system. It has been approved to treat the “wet” type of age-related macular degeneration (wetAMD), a common form of age-related vision loss. Lucentis gene was amplified, cloned and over-expressed in *E. coli*. The expression conditions were optimized, wherein optimum results were achieved in S.O.C. medium, at induction time of 12 hrs at 16 °C with IPTG (Isopropyl β -D-1-thiogalactopyranoside) concentration of 0.4 mM.

b) Fabrication of microchip: A disposable PMMA chip was fabricated by using laser, thermal and UV bonding technique for preparation of water in oil emulsions. PMMA sheet was cut and micro channels were engraved using laser ablation technique. UV and

thermal bonding methods were used to bond lower and upper PMMA sheet.

PUBLIC HEALTH, FOOD AND NUTRITION BIOLOGY

The mandate of Public Health Food and Nutrition programme is addressal of micronutrient deficiencies, severe acute malnutrition, food fortification, probiotics for human health and well-being, food safety, molecular detection of GM traits in foods, development of low cost foods/supplements and utilization of agricultural residues for value added products and capacity building in Food Science and Nutrition Biology.

Biology of childhood undernutrition and healthy growth with an emphasis on linear growth retardation: A centre of excellence on the mutations in GUCY2C and human disease, the gut and beyond was implemented in IISc, Bangalore in the current year. The effects of the most severe mutations in GC-C on gut physiology would be studied. Mouse would be humanised using the mutant human GC-C and organoids developed from this mouse would be monitored for functions related to GMP accumulation. The transgenic model being generated would be used to study the mechanisms of secretory diarrhoea.

Effect of maternal protein and vitamin B₁₂ supplementation on placental vasculature : Low maternal vitamin B₁₂ status during pregnancy has been reported to be associated with higher risks of intrauterine growth retardation. With an aim to dissect out the mechanism for this association 74 human placental samples were collected and were categorized as low (n = 37) and high (n = 37) vitamin B₁₂ groups respectively. The expression level of endoglin (ENG) using real-time PCR with respect to maternal, placental and neonatal parameters was observed to be significantly higher in the low vitamin B₁₂ group. Further studies are ongoing for estimation

of placental expression of angiogenesis associated genes in low and high maternal B₁₂ groups to delineate the placental signalling pathway through which ENG is likely mediating the effect of maternal vitamin B₁₂ status on fetoplacental growth.

Assessment of dietary advanced glycation end products (dAGEs) and mechanistic studies to evaluate the effect of dAGEs on inflammatory markers in subjects at risk for type 2 diabetes:

dAGEs are the main source of AGEs in body and may increase oxidative stress and inflammation which may lead to risk of cardiovascular diseases and diabetes. dAGEs of Indian foods were determined and efficacy of low AGE vs high AGEs diet on biomarkers of inflammation and among obese individuals in Chennai was evaluated in randomized cross-over intervention trial. The change in blood glucose and insulin were assessed and found to be significantly higher in low dAGEs diet. Carboxymethyl-lysine (CML) which is a blood biomarker of AGE was significantly lower in participants of low dAGEs diet compared to high dAGE diet.

Effect of zinc supplementation prior to iron on iron absorption, and iron status in deficient rats:

It was demonstrated that zinc induces the intestinal iron absorption via induction of DMT1 (apical transporter) expression and its membrane localization. The inhibition of zinc induced iron absorption due to DMT1 silencing suggested that zinc induced iron absorption is indeed mediated by upregulation of DMT1 expression. It was also demonstrated that zinc induces the activation of PI3K and its downstream targets AKT, mTOR and 70S6K. Inhibition of zinc induced PI3K activation by LY294002, abrogates the effect of zinc on iron absorption and DMT1 expression. Moreover, it was also demonstrated that zinc induces the expression and activity of IRP2, but not IRP1 in caco-2 cells. These results suggested that zinc induced iron absorption in intestinal cells is mediated by induction of DMT1 expression via PI3K/Akt/mTOR signalling

pathway. The specific role of IRP2 is being probed further.

Development of aptamer based detection system for Aflatoxin M1 in milk:

Aflatoxin M1 (AFM1) is present in milk of lactating animals fed on aflatoxin B1 contaminated feeds and is a class 2B carcinogen. Untruncated (72 nts long) and truncated (18 to 42 nts long) aptamers were evaluated for AFM1 recognition which was detected by colour-change in aptamer-conjugated-gold nanoparticles in presence of AFM1. Untruncated and truncated aptamers recognised AFM1. An electrochemical aptasensor for detection of trace amounts of AFM1 has been developed. This required immobilization of aptamer on screen printed gold electrode comprising of working electrode, counter electrode and reference electrode and was achieved by sequentially layering dithiodipropionic acid, streptavidin and biotinylated-tetraethylene glycol-aptamer. Immobilization of aptamer was monitored by cyclic voltammetry (Figure 1). Further work is in progress to validate the identified aptamer for development of sensing system in milk.

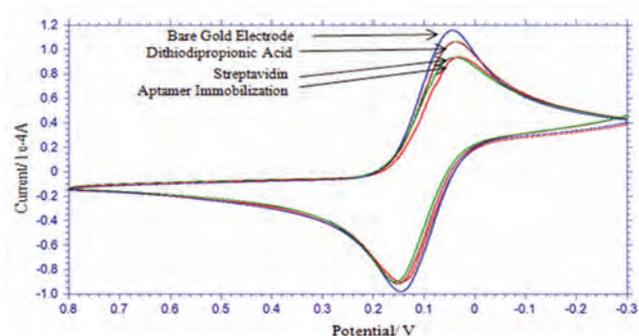


Figure 1. Voltammetry study of the immobilised aptamer

Development of high-throughput nanobiosensor for the detection of Salmonella sp. in food:

A DNA aptamer pool, specific to six strains of the common food pathogen, *Salmonella typhimurium*, has been obtained after 11 iterative rounds of cell-SELEX (systematic evolution of ligands by exponential enrichment). This

is to be used to fabricate a simple, specific, rapid diagnostic tool for detection of *Salmonella typhimurium* at point-of-care.

Development of cost effective diagnostic tools for the determination of food adulterants and contaminants using metal nanoparticles: A chemosensor has been developed for the detection of highly toxic pesticide, quinalphos (Qp) using 2-amino-4-thiazoleacetic acid capped gold nanoparticles (ATA-AuNPs) by both naked eye and spectrophotometry. Determination of methyl parathion (MP) by colorimetry, spectrophotometry and spectrofluorimetry methods using N-CDs as a fluorophore was also demonstrated. A chemosensor has been developed for the determination of an artificial sweetener saccharin using 3, 5-diamino-1, 2, 4-triazole capped gold nanoparticles (DAT-AuNPs) by both naked eye and spectrophotometry.

Molecular detection and quantification of shiga-like toxin producing *Escherichia coli* in fresh vegetables: The persistence of Shiga-like toxin producing *Escherichia coli* (STEC) strains in the agricultural soil creates serious threat to human health; however, the survival of STEC strains is not yet understood thoroughly. The results of the survey conducted at different time course indicate that the occurrence of STEC in vegetables like carrot, coriander, cabbage, lettuce, radish like raw vegetables. The survival pattern of STEC strain (O157-TNAU) was compared with non-pathogenic (MTCC433) and genetically modified (DH5 α) strains on different tropical agricultural soils and on a vegetable growing medium, cocopeat under controlled condition using EGFP-tagged strains. A simple realtime PCR protocol has been standardized to assess the pathogenic population directly from the vegetable and soil.

Development of domestic defluoridation filter using synthesized nano gamma alumina particles as adsorbent material: Activated

alumina that is present in gamma phases is known to be one of the efficient adsorbent fluoride among inorganic contaminants of water. Efforts are being made to synthesise nanoparticles of gamma alumina using sol-gel and precipitation processes. Nanoparticles synthesized by sol-gel aqueous and non-aqueous based processes were found to possess better adsorption capacity of 15000-25000mg/kg but were expensive. Alternate attempts are being made to synthesise nanoparticles of gamma alumina by precipitation process with equally good adsorption capacity of around 12000-15000 mg/kg at low cost. Further efforts are being made to simplify the synthesis process and make more energy efficient. On the other hand, efforts are being made to incorporate synthesised nanoparticles in conventional sediment removal filter using nanocoating methodology. The filtered water maintained drinking water standard as per BIS for drinking water but neither aluminium nor any toxic secondary contaminants were found.

Role of probiotic lactobacilli in modulation of intestinal epithelium mediated barrier functions and immune signals: *In vitro* effects on epithelial barrier functions of two indigenous probiotic strains *Lactobacillus rhamnosus* and *Lactobacillus fermentum* against *E. coli* and LPS of pathogenic *E. coli* (O26:B6), Caco-2 cells were studied. Cells treated with probiotic strains demonstrated appreciably lower flux of phenol red. The probiotic treatment significantly increased the mRNA expression of ZO-1, Claudin-1, Occludin and Cingulin compared to significant suppressed expression by *E. coli*/LPS treatments than control. Both probiotic strains either increased the mRNA expression of tight junction genes or maintained equal expression to untreated control cells under exclusion and competition assays with live *E. coli*/LPS. The maintenance and restitution of cytoskeleton actin architecture, tight junction structures (ZO-1 and Claudin-1) or polygonal cell morphology on probiotic

treatments during *E. coli*/LPS infection were clearly visible by immuno-fluorescence and transmission electron micrographs compared to their diffused and fragmented appearance when cells were infected with *E. coli*/LPS alone. In conclusion, both probiotic strains effectively attenuated *E. coli* or LPS induced leaky epithelial barrier function.

Innovation and demonstration of technologies for improved production and enhanced shelf life of Tomato: To improve the tomatoes shelf life, a process based on atmospheric cold plasma (ACP) has been developed along with a special ready to drink beverage based on tomato fruit juice, coconut water and other additives. The processes for utilization of tomato and tomato processing by-products in the development of fibre, mineral and antioxidant rich novel nutritional bakery products has been standardized.

Preparation, characterization and application of vitamin A and D loaded milk protein nano-complexes: Vitamin A and D deficiency diseases are the consequence of lower dietary level and their low bioavailability which necessitates fortification in food. FSSAI approved the fortification of toned/double toned /skimmed milk. Incorporation of fat soluble vitamins in low fat foods requires stabilization in an aqueous medium and protection against deteriorating factors. Hence, solubility of milk proteins was improved by succinylation through modification of some physicochemical characters. Evaluation of milk fortified with these milk protein-Vit A nano-complexes suggested that these nano-complexes could be added to food products with minimal effect on sensory acceptability, physicochemical characteristics and product shelf life. Vitamin A content was lowest in sterilized milk followed by boiled and pasteurized milk. Milk protein-Vit A nano-complexes fortified milk showed higher *in-vitro* bioavailability of vitamin A as compared to free vitamin A fortified milk.

Development of Molecular Diagnostics and Immunotherapeutic Vaccines for Prawn and Brinjal Allergy: Prawn and brinjal are proved as two major sensitizers for an atopic population of India and other countries as well. The investigators have collected food allergy patients sera (n=57 for brinjal and n=65 for prawn) and 20 healthy sera as a negative control. These patients were tested by the Immuno-cap method. Serological detection of allergens was done by probing the muscle proteome of prawn and fruit proteome of brinjal. As on date, cloning, purification and characterization of two novel allergens viz. a 14 kDa profilin from brinjal and a 32.8 kDa tropomyosin from fresh water prawn is done. Both the allergens displayed frequent IgE-reactivity as confronted with patient sera. Further studies are ongoing for characterization of the antigenic determinants of these allergens using various computational as well as peptide-based approaches.

Aptamer probes for detection of celiac disease epitopes of gluten in commercial varieties of Indian Wheat, Rye and Barley: Synthesis, screening and characterization of six immunogenic peptides from alpha-gliadin, gamma-gliadin and HMV glutenin fraction of wheat was completed. Aptamer candidate with good binding candidates in micro molar range were obtained against two peptides. Currently the investigators are screening gliadin and glutenin from different wheat varieties with the developed aptamers.

Center of excellence on “the effect of amino acids, vitamin A and their metabolites and oxidative stress on low birth weight”: To test the hypothesis that supplementation of protein and vitamin B12 during pregnancy could improve biochemical fluxes, placental epigenetics and birth outcomes, an intervention trial with a daily supplement of 500 ml of skimmed milk during pregnancy was performed in low BMI pregnant Indian women. The novelty of this study is the use of stable

isotope tracers that measures fluxes of amino acids, since the investigators had earlier shown that arginine and methionine are deficient during pregnancy. In consequence, this study has led to the creation of an Indian human placental archive from the St. John's mother-baby cohort, a unique resource that is being utilized to understand the placental molecular mechanisms mediating the role of maternal nutrition on fetoplacental growth and adverse birth outcomes such as intrauterine growth restriction. The findings from this study suggest that women with high Hb tend to have higher oxidative stress in early pregnancy, and are therefore likely to bear the brunt of possible harmful effects of iron supplementation. On the other hand, women who were even mildly anaemic appear to have benefited by the supplementation. The ongoing study is evaluating the effect of an indigenous traditional food preparation using curry, mint or coriander leaves, which are high in beta-carotene. More importantly, this study has set up a new way to measure vitamin A status, by measuring its stores, rather than using serum retinol values, which are tightly regulated and unlikely to show toxicity. This has been done using stable isotope technique and stores will be correlated with intrauterine foetal growth in healthy pregnant women.

Capacity Building in Food Science: The Department has initiated an Integrated M.Sc-Ph.D programme at Gauhati University, Guwahati in Food Science for imparting teaching during two years of M.Sc followed by research in Food Science to enhance research capacity in "Food Sciences" by carrying out focussed R&D in (a) Fermented Foods (Solid) b) Functional and Flavoured Tea products including tea based health drink and c) Exploration of exotic fruits and vegetables of North Eastern region for bioactive components. As on date the first batch of 5 MSc students have joined the course. The Department has also constituted an Expert Committee for a periodic review of this programme.

BIOSAFETY RESEARCH

The programme aims at implementation of the Rules, 1989 of Environment (Protection) Act, 1986 for the manufacture, use, import, export and storage of hazardous microorganisms, GE organisms or cells and products thereof for research and development. The Rules, 1989 delegated the Department of Biotechnology to administer functioning of i) Institutional Biosafety Committees (IBSCs) which operate directly from the premises of the institutions and ensures on-site assessment and monitoring of adherence to the biosafety guidelines with overall oversight of the regulatory process, at the institutional level and ii) Review Committee on Genetic Manipulation (RCGM) that monitors & reviews all ongoing research projects involving high risk category and confined field experiments and ensure the compliance of biosafety rules & regulations, as well as framing and implementation of safety measures and guidelines, while conducting research on high risk group microorganisms and GE organisms.

During the year, the RCGM evaluated about 349 applications in 5 meetings in the areas of agriculture, healthcare and industry. The applications were for: import/exchange of high risk group microorganisms and recombinant research related materials including seeds, gene constructs, plasmids, and vectors, living modified organisms (LMOs); conduct of pre-clinical toxicity studies and evaluation of pre-clinical study data; conduct of event selection trials (ESTs)/ Biosafety Research Level 1 (BRL1) trials in confined conditions for transgenic crops under development viz. cotton, corn, rice, chickpea and pigeon pea from universities/public & private organizations for biosafety clearance.

Eleven Central Compliance Committee (CCC) teams with more than 25 experts from plant breeding, physiology, plant biotechnology, entomology, pathology, silkworm biology etc., along with experts

from the states and members of state agricultural university (SAU) were constituted and visited containment facilities of genetically engineered silkworm & mosquito and biosafety research trial sites and interacted with the in-charges of the trials and the Directors of Research of the respective SAUs and institutes for monitoring the compliance of biosafety rules & regulations while conducting the trials as stipulated in Biosafety Guidelines.

In the pharmaceutical sector, 11 rDNA products were permitted for conducting pre-clinical toxicity studies by 10 private/public institutions & companies. Based on the evaluation of pre-clinical study reports, 6 rDNA products developed by 5 private/public institutions & companies were recommended by RCGM to Drug Controller General of India [DCG (I)] for appropriate phase of clinical trials.

To assess the veracity of spread of unapproved herbicide tolerant (HT) cotton in the country and to confirm the presence of gene(s) and, strategies and measures to contain any illegal activity a 'Field Inspection & Scientific Evaluation Committee' (FISEC) was constituted with subject experts, and nominees from concerned ministries and states as advised by Prime Minister's Office. The committee interacted with technology developers, seed producers, farmer's groups and non-government organizations in three separate meetings, to assess the illegitimate spread of HT cotton in various states and its report will be submitted shortly.

Continuing the reform initiatives for Biosafety regulation, the department has revised the Recombinant DNA Safety Guidelines, 1990 with significant enhancement in scope as per the Rules, 1989; harmonized provisions, containment facilities and operating procedures with international best practices; and revision of risk group agents and regulatory overview. After public consultation, "Regulations and guidelines on biosafety of recombinant DNA research & biocontainment, 2017"

was released on 5th December, 2017 during the Meeting of States Parties of the Biological Weapons Convention (BWC) held at Geneva, Switzerland. The Indian Biosafety Knowledge Portal (IBKP) is in the final stage of development. The portal would ensure biosafety compliance at the organizational level in addition to online submission-tracking-review-processing, monitoring and authorization of the applications submitted by various applicants to RCGM.

The Biosafety Support Unit (BSU) established in partnership with Regional Centre for Biotechnology (RCB) evaluated applications submitted to RCGM for approval, and also developed Risk Assessment and Risk Management Plan (RARMP) documents on applications submitted for biosafety clearance; prepared comprehensive documents on the GM food labelling policy; and on notified/certified GM food testing laboratories in India, and also played a major role in updating and revising "Recombinant DNA Safety Guidelines, 1990. BSU has supported Genetic Engineering Appraisal Committee (GEAC) in preparing a comprehensive safety assessment document titled "Assessment of Food and Environmental Safety (AFES) for GE mustard" and analyzing the comments received on AFES document of GE mustard. BSU was also involved in 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 biosafety regulation of GMOs among various stakeholders as well as for in-house capacity building.

As a measure to ensure strict compliance of biosafety guidelines for rDNA activities by universities, public & private institutions, laboratories, and industry through their Institutional Biosafety Committees (IBSCs), 36 new IBSCs have been constituted, while 63 old IBSCs have been 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 06 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, relevance&

essentiality of the projects, resources & manpower established, intellectual property (IP) generated; the Department had recommended 13 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. Following patents have been granted during 2017-2018:

Sr. No.	Country & Patent No.	Name of the Inventor(s) /Applicants	Patent Title
1	US Application No. 14/323,687 (Patent No. 9,556,437 B2)	KUNZANG CHOSDOL BHAWANA DIKSHIT SUBRATA SINHA 1. ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI 2. NATIONAL BRAIN RESEARCH CENTRE, MANESAR 3. DEPARTMENT OF BIOTECHNOLOGY, NEW DELHI	FAT1 GENE IN CANCER AND INFLAMMATION
2	Us Divisional Application NO. 15/458,040 BASED ON PCT/IN2013/000534 PARENT APPLICATION US 14/424,037	SYED SHAMS YAZDANI NEHA MUNJA ANU JOSE MATTAM 1. INTERNATIONAL CENTRE FOR GENETIC ENGINEERING AND BIOTECHNOLOGY, NEW DELHI 2. DEPARTMENT OF BIOTECHNOLOGY, NEW DELHI	MODIFIED BACTERIA FOR THE PRODUCTION OF BIOALCOHOL

3	139/Del/2007(282490)	NEESHMA JAISWAL SUNIL KUMAR SANDEEP K. MALHOTRA ANSHU MALHOTRA 1. UNIVERSITY OF ALLAHABAD, ALLAHABAD 2. DEPARTMENT OF BIOTECHNOLOGY, NEW DELHI	AN IMPROVED APPARATUS FOR COLLECTION OF HONEY BEE TOXIN
4	889/DEL/2010(288480)	ARVIND SAHU ARCHANA P. KADAM 1. NATIONAL CENTRE FOR CELL SCIENCES, PUNE 2. DEPARTMENT OF BIOTECHNOLOGY, NEW DELHI	PETIDES THAT INHIBIT FACTOR B, C2 AND COMPLEMENT ACTIVATION, AND THEIR USES
5	741/DEL/2010(286667)	KISHORE KUMAR KRISHNANI 1. CENTRAL INSTITUTE OF BRACKISHWATER AQUACULTURE 2. DEPARTMENT OF BIOTECHNOLOGY	QUANTITATIVE METHOD FOR DETECTING A MICROBIAL POLLUTANT
6	433/DEL/2009(289249)	ANIL KUMAR TRIPATHY SIMARJOT KAUR 1. BANARAS HINDU UNIVERSITY, VARANASI 2. DEPARTMENT OF BIOTECHNOLOGY, NEW DELHI	A METHOD FOR PRODUCING CALCIUM CARBONATE NANOPARTICLES USING RECOMBINANT CARBONIC ANHYDRASE FROM AZOSPIRILLUM BRASILENSE

07

**Biotechnology
Information System
Network**

The Biotechnology Information System Network (BTISnet), established in the year 1986, is now spread across the country with around 170 centres. These centres are closely networked as BTISnet and classified into various categories based on the centre's expertise, infrastructure, capabilities and number of students and researchers. The BTISnet includes – 6 Centres of Excellence (CoEs), 12 Distributed Information Centres (DICs), 49 Distributed Information Sub-Centres (DISCs) and 103 Bioinformatics Infrastructure Facilities. The network also consists of one supercomputing facility for Bioinformatics and six interactive graphics facilities. A large number of bioinformatics R&D projects are being supported through this programme. The network supports 6 teaching programs in M.Sc., M.Tech. and Ph.D. in Bioinformatics and Computational Biology to generate skilled manpower. Further, the BTISnet centres conduct short term trainings and workshops for the benefit of research community including experimental biologists. The centres also provide Bioinformatics and Computational Biology services to the scientific community.

CENTRES OF EXCELLENCE (COEs) IN BIOINFORMATICS

The COEs act as research and training activity hubs for regional and neighbouring academic and research institutes, with a focus on quality research, education and services.

The COE at IIT-Delhi, New Delhi has developed a whole genome analysis methodology and software based on DNA energetics (ChemGenome) available at <http://www.scfbio-iitd.res.in/bioinformatics/genefinding.htm>; an all atom energy based computational protocol for protein tertiary structure prediction (Bhageerath-H) available at http://www.scfbio-iitd.res.in/bhageerath/bhageerath_h.jsp and a binding free energy based methodology for protein/DNA targeted lead molecule design

(Sanjeevini) available at <http://www.scfbio-iitd.res.in/sanjeevini/sanjeevini.jsp>. The centre has provided extensive hands-on training to 131 youngsters, divided into five batches, over 10 days workshops.

The COE at Bose Institute, Kolkata, has developed several useful tools like: PluriPred, a web server for prediction of the proteins which have important role in pluripotency (<http://bicresources.jcbose.ac.in/ssaha4/pluripred/>); PPIMpred, a prediction server of small molecules that inhibit Protein-Protein Interactions of MDM2/p53; c-MYC/MAX and BCL2/BAK available at <http://bicresources.jcbose.ac.in/ssaha4/PPIMpred/>; LMDIPred, a prediction server, which allows predicting linear peptide sequences from a protein interacting with SH3, WW and PDZ domains, available at <http://bicresources.jcbose.ac.in/ssaha4/lmdipred/>; EnPPIpred, a prediction server that predicts Protein-Protein Interactions (PPIs) in enteropathogens including *E. coli*, *Vibrio cholerae*, *Salmonella typhi*, *Shigella* & *Yersinia*, available at <http://bicresources.jcbose.ac.in/ssaha4/EnPPIpred/>.

The School of Computational and Integrative Sciences (SCIS) at JNU, New Delhi is involved in research and teaching programs in areas which are highly interdisciplinary in nature. The centre runs several academic programmes like MSc-PhD degrees in computational and integrative sciences. Teaching and research programs are supported by good computational and communication infrastructure consisting of computer clusters with multiprocessor nodes, large-memory nodes and graphics processing units (GPUs) to facilitate specialized research in the new building of SCIS. The COE at Savitribai Phule Pune University, Pune, has developed several tools and databases like RTD Phylogeny. Other server developed for typing of viruses & bacteria are updated and maintained. They have also developed AllerBase – an exhaustive database of allergens.

DISTRIBUTED INFORMATION CENTRES (DICs)

The focus of DICs is on quality research, education and services. The DIC at Anna University, Chennai has developed a database of tripeptides (http://www.annauniv.edu/biotech/tphome/tpdist_hm.html) and a server for protein local structure deformation prediction (<http://www.annauniv.edu/biotech/tphome/mutserv.html>).

The Assam Agricultural University, Jorhat DIC has thrust activity area of application of bioinformatics in agricultural biotechnology research as well as imparting trainings to the students and scientists across the North Eastern states of India.

The DIC at CSIR-IMTECH, Chandigarh has developed databases and software both for in-house use and for scientists world over and has published more than 250 research articles in reputed international journals. Recently, the DIC has developed the following databases: PEPlife: a repository of the half-life of peptides; ProCarDB: a database of bacterial carotenoids; CPPsite 2.0: a repository of experimentally validated cell-penetrating peptides; ZikaVR: an integrated Zika virus resource for genomics, proteomics, phylogenetic and therapeutic analysis, and SATPdb: a database of structurally annotated therapeutic peptides.

The DIC at Indian Agricultural Research Institute (IARI), New Delhi specializes in Agri-Informatics and Bio-Statistics and has developed SNP Prediction tool “SNPredictor” using PERL scripts. This software is able to predict all potential Single Nucleotide Polymorphs (SNP's) for a given EST data. They have also developed miRule (Rule based micro RNA prediction Tool) that predicts the presence and position of the mature miRNA in the input precursor sequence. The centre has expertise in bigdata analytics in agri-bioinformatics and uses advanced supercomputing hub for OMICS knowledge in

agriculture with ‘Advanced Super Computing Hub for Omics Knowledge in Agriculture’ (ASHOKA) for data analysis work in collaboration with Indian Agricultural Statistical Research Institute.

The DIC at National Brain Research Centre, Manesar specialises in Neuroinformatics. The centre is involved in understanding the pathways for neurodegeneration that may lead to brain disorders. The centre has developed Dyslexia Assessment for Languages of India (DALI) tool for identifying, assessing and ameliorating reading difficulties in children. It has also developed a platform for metabolite signal quantization for magnetic resonance spectroscopic data (Kalpana): technique for estimating biochemical signatures from the brain using MRI-MRS of patients for clinical/diagnostic applications.

The DIC at National Institute of Immunology (NII), Delhi has developed several database and prediction methods including databases of cleavage & cross-links in RiPPs, substrates of human PDZ domains, analysis of PTM catalyzing enzymes, and tools for analysis of miRNA-mRNA base-pairing, construction of phospho-networks, substrates for MHCs & kinases, solvent accessibility of phosphosites and others.

The DIC at Pondicherry University, Puducherry has developed several software like: FuzzyApp - Fuzzy logic based allergen protein predictor, DualPred - Dual targeted protein predictor, APSLAP - an adaptive boosting technique for predicting sub-cellular localization of apoptosis protein, E-Learning modules in bioinformatics and immune epitope prediction database & tools, amongst others. The centre has also developed several databases like: Clostridium-DT(DB): a comprehensive database for potential drug targets of *Clostridium difficile*, the Arabidopsis stress responsive gene database, (SEDB) structural epitope database, VPDB: viral protein structural database, membrane proteins database and many others.

DISTRIBUTED INFORMATION SUB CENTRES (DISCs)

These DISC were mainly established with the aim to provide service to the research community. However, the centres are now also imparting training in bioinformatics through workshops. The DISC at ACTREC, Mumbai, has developed several databases like Oral Cancer Gene Database 'HlStome': The Histone Info base and PDZome. The DISC at Bharathidasan University, Tiruchirappalli has developed software Syn-R-io (www.nfmc.res.in/synrio) and Cyanopatt (www.nfmc.res.in/bca/patm/ps.html). The major objective of the DISC at Biotech Park, Lucknow, is to showcase the R&D and academic strength of Lucknow in the area of Biotechnology and to serve as the nodal point for industry-academia interactions. The centre has developed several tools like IC50 Convertor Tool (JAVA-based standalone program, which is highly applicable in QSAR modelling) and a siRNA prediction tool. Databases developed by the centre include a database of Antidiabetic plants based on clinical/experimental trial, HDVDB: a data warehouse for hepatitis delta virus and fruits in Uttar Pradesh. The DISC at Birla Institute of Scientific Research, Jaipur has developed PIASP2, GNufa and BISR-PRIMER tools. Databases developed by them includes Database of Medicinal and Aromatic Plants (DOMAP), Database of Interaction Specificity in Protein-Ligand Complex (Disprolic) and Database of Food Borne Human Pathogens (FOODPATH). Central Sericultural Research and Training Institute, Mysore has developed Mulberry Genome Database, which consists of extensive molecular marker data on DNA polymorphism, DNA fingerprints, binary scores, similarity and dissimilarity index matrices, phylogenetic relationship in terms of dendrogram and marker segregation pattern. They have also developed other databases relevant to sericulture like SilkTF (Silk worm Transcription factors), MulsatDB (mulberry specific SSR markers, design primers and locate markers on strawberry

chromosomes) and SilkPPI (protein-protein interaction in Silkworm, *Bombyx mori*). Indian Institute of Advanced Research (IIAR), Ahmedabad, has developed databases for adhesins, plant pathology, plant lectins and tritryps protein classification. Indian Institute of Spices Research (IISR), Kerala has developed databases like Radobase - a database on burrowing nematodes, IPVdb - a database on plant viruses reported from India and PiperPep - a database of experimentally generated peptides from black pepper. Indian Institute of Technology (IIT), New Delhi has developed several tools like Zif-Predict-a webserver for predicting zinc fingers and their target sites, Zif-NN-a tool for designing zinc fingers for any target DNA synergistically, Zif-Predict IHBE- a tool for designing zinc finger proteins for any target DNA using either modular or synergistic approaches and CRISPCut- a webserver for designing optimal sg RNAs for CRISPR-Cas9 based experiments in human cells. Mahatma Gandhi Institute of Medical Sciences (MGIMS), Wardha has developed MTB-PCDB: *Mycobacterium tuberculosis* proteome comparison database, MycoProtease-DB: a database of MTB and NTM proteases and hpvPDB: human papillomavirus proteome database. At National Botanical Research Institute, Lucknow, DISC has developed Indian Legumes Database Management (ILDm), Herbarium of Indian Legume Database Management (HILDm), and databases for Indian legumes.

BIOINFORMATICS INFRASTRUCTURE FACILITIES (BIFs)

The aim of these centres is to promote biology and biotechnology teaching through bioinformatics. The scheme is designed to expose teachers, scientists and students to the use of bioinformatics in helping biotechnology. Andhra University, Vishakapatnam BIF has developed AqualInfoBase-Sequence relationship between the aqua living system and human diseases based on nucleotide/protein sequences and marine secondary metabolites database (MSMDB). CCS Haryana Agricultural University, Hisar has developed

databases of crop plant diseases and plant mites. The BIF at Institute of Himalayan Bio Resource Technology, Palampur has developed several software-TAREF: a tool to refine microRNAs target prediction in animal, *filterR*:parallely coded tool for fast next generation sequencing read filtering and cleaning; *p-TAREF*: a concurrent application for fast and accurate plant miRNA target identifications; *miR-BAG*: an Avant-garde parallely coded tool, based on machine learning for accurate miRNA identification that works universely on genomic and NGS (Next Generation Sequencing) data; *miReader*: a highly accurate cutting edge algorithm to identify mature miRNAs from NGS read data; *pPromotif*: a novel and accurate algorithm to identify transcription factor binding sites on plant genomic sequences; *Assembly Validator*: a tool to detect mis-assembly in *de novo* assembled contigs and others. ICGEB, New Delhi developed altered pathway analyser (APA) and Anti-Hepatitis peptide resource. Maharani's Science College for Women, Bangalore had developed databases for *Phytophthora*, bamboo and *Ectomycorrhizals*. Maharshi Dayanand University (MDU), Rohtak has developed databases-*MalVec*: a database of Indian Malaria Vectors and Mosquito Borne Disease Database (MBDD): an integrative database of 4 major Indian mosquito borne diseases – Malaria, Kala-azar, Dengue, Chikungunya.

University of Hyderabad, Hyderabad has developed *Orfin* and database- *MycorrdB* (intergenic regulatory regions to all mycobacterial Genes/ORFs), *CyanoPhyChe* (A database for Physico-chemical properties of cyanobacterial proteins), *ClostrIndb* (database for the analysis of *Clostridium* species), *MycoindB* (Mycobacterium information database) and *NeMedplant* (database of medicinal plants from Northeast India).

NORTH EASTERN BIOINFORMATICS NETWORK (NEBINET)

Under the special drive to strengthen the North Eastern States of the Country a Bioinformatics

network 'NEBINet' consisting of 31 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 26 BIFs (at various universities, colleges and institutions). In order to monitor the progress of these centres the interactive meeting of NEBINet was organised in Meghalaya at St. Edmond's College, Shillong on 16th& 17th November, 2017.

The DIC at North Eastern Hill University, Shillong is identified as one of the seven Bio-Resource Information Centre (BRICs) and portal development under the first phase of Indian Biodiversity Information Network (IBIN), DBT. It is also the Nodal Centre of North East Bioinformatics Network (NEBINet) in NER. The centre is currently working on *Helminth* parasite database. 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 BIF at Mizoram University, Mizoram has developed databases of snakes, beetles and butterflies of Mizoram. Assam Agricultural University, Khanapara, Guwahati has developed a database of Biotechnology and Bioinformatics Resources of North East India (BABRONE) and Indigenous Livestock and Poultry Resources of North East India (ILRONE). They have also developed a globally accessible online server "Serotyping of common clinical isolates of Salmonella by Multiplex PCR" in collaboration with the Vaccine Research Institute of San Diego, USA. The Assam University, Silchar has developed a database on anti-diabetic phytochemicals and is named as *DiaBank*. The BIF at Central Agricultural University, Tripura has developed database on Fisheries Resources of Tripura. The College of Veterinary Science & Animal Husbandry (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 DM College, Imphal has done morphometrics and molecular phylogenetic analysis of 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*, *Silurana tropicalis*, Silk Worm, Turtles, Fish & HIV-2 polypolyprotein. Manipur University, Imphal centre is actively engaged in development of a comprehensive database for pollen grains found in Manipur state. The centre at Nagaland University, Kohima has done nucleotide compositional analysis and statistical clustering of 90 species of *Paphiopedilum* species. The BIF at IBSD, Imphal is creating an 'Application Database' for the anti-tuberculosis properties of plants available in Sikkim Himalayan region.

OTHER ACTIVITIES

Bioinformatics R&D Activities: The first R&D proposal in bioinformatics was received by the department in 1999. Since then the department has supported about 130 projects, out of which 111 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. IISc, Bangalore has developed a method for antitubercular drug discovery which identifies activity related substructures from a series of acid alkyl ester derivative compounds, and predicts its anti-TB activity. IIT-Madras, Chennai has made interesting discovery about the conformational changes of monomeric FtsZ in GTP-bound, GDP-bound, and nucleotide-free states. ICGEB, New Delhi has conducted proteomic analysis of lysine and arginine methylome of the malaria parasite, *Plasmodium falciparum* and developed a new machine learning based tool for prediction of arginine methylation.

Annual Incentive Awards-2016 for the BTISnet Centres: In order to ensure continuous up scaling of research activity, enhancement in quality of publication and to encourage the centres that perform better, a series of incentive awards for publications have been constituted. Centre(s) receiving the best prizes in their respective categories are provided with extra research grant along with certificate. In the year 2016 the best COE award was given to JNU, New Delhi, the best DIC award to CSIR-IMTECH, Chandigarh, the best sub-DIC award to CSIR-CDRI, Lucknow and the best BIF awards to CCS University, Meerut; ICGEB, New Delhi and Sri Venkateswara College, New Delhi. The 28th BTISnet Annual Coordinators meeting is being organised on 3rd and 4th March, 2018 in Tirunelveli, by Manonmanium Sundarnar University, Tirunelveli. The focal theme for this meeting is "Translational Bioinformatics". The 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 2017 will be announced in this meeting.

DeLCON Consortium: The DBT's Electronic Library Consortium (DeLCON) 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. The total members of DeLCON Consortium is 33 Institutions. Besides the DBT Institutions, an emphasis has been given to institutions and universities across the states in North Eastern India. DeLCON provides current as well as archival access to more than 1000+ core peer-reviewed biology and biotechnology journals and a bibliographic database (SCOPUS) in different disciplines from 22 overseas publishers and aggregators. Presently there are 28 members and 20 publishers in this consortium.

08

**Biotechnology Parks &
Incubators**

The Department of Biotechnology promotes Biotech research and helps to translate research into products and services. The Biotechnology Parks, offer facilities to Scientists, and Small and Medium sized Enterprises (SMEs) for technology incubation, technology demonstration and pilot plant studies 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.

BIOTECH PARK, LUCKNOW, UTTAR PRADESH

Biotech Park, Lucknow primarily a technology incubator, has been set up jointly with the Government of Uttar Pradesh. Biotech Park is based upon a society framework, with the scientific community and endeavoring in knowledge creation and dissemination, in promoting / incubating at the same time creating an ecosystem towards Bio-Entrepreneurship. Over the years, Park has attracted 29 companies out of which 18 graduated out and presently Park is home of 11 companies. The focus of the Park is to assist knowledge creation and promote biotech entrepreneurs through a service driven framework.

The Biotech Park is continuously striving to achieve its mission to develop knowledge based economy in biotechnology, assure benefits of biotechnology to all sections of the society. The Park holds conferences, workshops, seminars and participates in relevant events like Kisan melas and goshthis regularly to create awareness in the emerging fields of biotechnology.

Biotech Park is an active partner with UP Skill Development Mission, Govt. of Uttar Pradesh and

providing training in the areas of Flavor, Fragrances & Perfume and Agriculture. Six Trainees of Biotech Park were sent to Grasse, France by U.P. Govt. for further exposure. During the year Biotech Park signed 5 MoUs and Agreements.

BIOTECHNOLOGY INCUBATION CENTRE, HYDERABAD, TELANGANA

The Genome Valley of Hyderabad has now emerged as the largest biotechnology hub of the country and close to about 150 national and multinational companies have started their operations. Several of these are start-up companies. The Valley provides employment to about 8000 technical and scientific work force. Buoyed by the success, APIIC has initiated phase-III of the Genome valley for biotech industries.

Envisaging the growth of Biotechnology sector, the Indian Institute of Chemical Technology Hyderabad (CSIR-IICT), Government of Andhra Pradesh and Department of Biotechnology, Gol, in the year 2004, decided to establish the BTIC with the following basic objectives:

- Accelerate the commercialization of new technologies
- Nurture and mentor emerging ventures
- Assist new enterprises to forge appropriate linkages with other biotech companies, academia and government

With its state-of-the-art R&D infrastructure, furnished laboratories & office space, utilities, support services and amenities, the BTIC has emerged as the best Incubation Center not only in genome valley but also in India, in two years of its operation. The Centre, which is the first publicly owned and privately operated R&D venture in the country, has now become a role model for other such enterprises. The existing infrastructure has successfully attracted more than 10 new companies in the cluster; most

of them being startup/early stage companies. To provide analytical services to the biotech and allied industries, The Advanced Analytical and Characterization Resource (AACR) facility is established as a joint initiative of BIRAC, SBTIC and CSIR-IICT.

TIDCO CENTRE FOR LIFE SCIENCES (TICEL) BIOTECH PARK, CHENNAI, TAMIL NADU

The Park was established by Tamil Nadu Industrial Development Corporation Ltd. (TIDCO), an undertaking of the TN State Government with support from DBT. DBT sanctioned grant for purchasing equipment towards establishing a Biotechnology Core Instrumentation Facility (BTCIF). Laboratory facilities at BTCIF include Microbiology, Molecular Biology, Fermentation, Downstream Processing, Purification, Analytical Support, Animal Cell Culture Facilities and Utilities. The sources of income include sample analysis services, hands on training for students/ trainers, lease rentals from equipped laboratories. This Park has created infrastructure for Biotech R&D on 5 acres of land in Chennai. 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.

THE GOLDEN JUBILEE BIOTECH PARK FOR WOMEN, CHENNAI, TAMIL NADU

Golden Jubilee Biotech Park for Women is a successful first of its kind women centric life sciences ecosystem. The Golden Jubilee Biotech Park for Women Society is a 'not for profit' institution with a Mission of providing opportunities for professionally

qualified women to take to a career of remunerative self-employment through the organization of environment friendly biotechnological enterprises. The first phase of the park became operational in May 2001 with a seed funding Rs. 4 Cr from the Department of Biotechnology.

The Park has 20,000 sq ft of built up area as modules of 1,000 sq. ft. each, while land modules have been given on long-term lease. Since its inception the Park has turned over 500 skilled women entrepreneurs, technocrats and workers; presently the park has close to 200 women entrepreneurs & technocrats and workers with 40% of them being skilled. The Women workforce is at 60%. Presently it houses 13 companies inclusive of 5 start-ups and three incubatees. Over the last few years the Park has had more than 500 interns who have benefitted from the Park and there is an increasing interest among faculty and students who desire refresher programmes and internships.

The new addition to the Park is the establishment of a 5,000 sq ft Incubation centre with the support from BIRAC under its BIONEST programme. Dr Harsh Vardhan the Hon'ble Union Minister launched this new Incubation Facility at the recently held International India Science Festival in Chennai.

BIOTECH PARK TECHNOLOGY INCUBATION CENTRE, GUWAHATI, ASSAM

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. Assam Govt. has extended budgetary support for procurement of land and for construction of perimeter fencing and land development cost for the permanent campus of Guwahati Biotech Park. The Incubation Centre in the interim facility will be shifted to this permanent location.

BIOTECHNOLOGY PARK, BANGALORE, KARNATAKA

The project was sanctioned at a total Project Cost of Rs 32.26 Cr; with contribution from Karnataka Biotechnology & Information Technology Services (KBITS), Department of IT, BT and S&T, Government of Karnataka and Department of Biotechnology, Government of India. Bangalore Bioinnovation Centre (BBC) is envisioned to be a state of the art Bioinnovation Centre catering to the needs of start ups in the broad areas of Life Sciences and facilitate Innovation driven Research.

Located within Bangalore Helix Biotechnology Park at Electronic, BBC is located in 10 Acre campus with total built up area of above 50,000 sq ft. It houses a state of art Central Equipment Facility as well. The Centre is nestled between thriving Academic Institutions like Institute of Biotechnology and Applied Biotechnology (IBAB), Centre for Human Genetics and the upcoming area for anchoring Big Companies/MNC's. The Centre caters to the broad areas of Life Sciences i.e. Healthcare (MedTech/Pharma/Bio-Pharma), Agriculture, Food/ Nutrition, Industrial Biotechnology and Environmental Biotechnology.

The Centre is registered as a Section 8 not-for-profit Company and is managed by Independent Board of Directors and professional staff. Services include plug-and-play, infrastructure lab space and common equipment, high-end equipment and facilities, mentorship, funding, networking, branding, legal, finance and accounting. The Centre is currently nurturing 23 start-ups and 4 companies have already graduated.

BIOTECHNOLOGY INCUBATION CENTRE, COCHIN, KERALA

The Department of Biotechnology has set up a Biotechnology Incubator Center (BTIC) at Kerala Biotechnology Park in 4 acres of land with a total built up area of 50,000 sq.ft. It has been established for accelerating and supporting the research process of entrepreneurs. A common facility lab in an area of 8000Sq.ft is also set up for the entrepreneurs as well as incubates in the biotechnology park. Rajeev Gandhi centre for Biotechnology is the Institutional Partner of Kerala Industrial Infrastructure Development Corporation (*KINFRA*) for operating the Lab. At present, Kerala Start Up Mission (KUSUM) and RGCB are managing the facility.

The BTIC was made operational in the year 2009 and there are 16 start-ups currently housed in the centre, five companies have graduated in the Business Enterprise Zone (BEZ). A common facility lab is being used by entrepreneurs as well as incubates.

09

**International
Cooperation**

Global collaborative research is imperative for science to have impact on scale. Partnering with the best in the world will catapult Indian science to the next level of innovation and transformation. It is vital that collaborating countries envisage science programme which will have footprint for generations to come, and with this in mind the government of India is increasingly trying to promote collaborative research, which holds the promise of applying the best academic methods in solving the myriad economic, social and environmental challenges. By linking experts from around the world and involving stakeholders from wider society, research networks can more easily identify problems, adopt a multi-disciplinary approach to solving them and monitor the impact of solutions. Department of Biotechnology, implementing many such joint programmes.

BILATERAL R&D PROGRAMMES:

Australia: Department is partnering with Department of Innovation, Industry and Science (DIIS), Govt. of Australia to support joint research in cutting edge areas of science and technology. In the last 10 years of this collaboration, 55 projects and 10 workshops have been supported in the areas of Healthcare, Agriculture and Bioenergy. 132 papers have been published in various journals, 7 patents have been filed. 15 Technologies and 13 products/process have been developed.

Significant Achievements from some of the projects are as follows:

The Indian Investigators at Indian Institute of Science, Bangalore have developed some novel strategies to generate effective, high levels of humoral and cell mediated immunity against HCV by immunizing animals with 'HCV like particles' and DNA construct expressing HCV non-structural proteins, respectively. These have been shown to trigger immune response in mice and pigs.

Investigators at Indian Institute of Chemical

Technology, Mumbai have successfully scaled up the lab scale extraction and purification process of kafirin to pilot scale with 1 kg/day kafirin production. This kafirin has been successfully used to cast packaging films, edible coating for fruits (e.g. strawberries), beadlets as carrier for nutraceuticals (e.g. antioxidants) and medicines (e.g. doxorubicin). Further, kafirin has also been evaluated for coating of gelatin capsules making them useful for sustained/delayed release applications in pharmaceuticals.

The cereal cyst nematode (CCN), *Heterodera avenae*, is one of the major biotic constraints in wheat production around the world. Scientists at IARI, New Delhi have identified, cloned and functionally validated 40 key genes involved in various parasitic functions using the RNAi approach. It was found that RNAi silencing of different genes reduced nematode multiplication by 53-93.8 % over control in terms of infection, development and reproduction.

In the studies at Punjab Agricultural University, Ludhiana trigenome Brassica hybrids (Allohexaploids) were successfully produced. These hybrids showed very high biomass accumulation and were tall and late to mature.

Brazil: Under Indo-Brazil cooperation, six joint projects were recommended against the second Joint call for Proposals (2016-19). Among these, three projects were focused on bio-medical research including developing novel microparticles based formulation strategies for cancer immunotherapy; deciphering the cellular and molecular mechanisms of amyotrophic lateral sclerosis using human iPSCs, and studies on secreted proteases of host-*Mycobacterium tuberculosis* interaction for novel drug discovery and vaccine development. Remaining three were supported towards integrated biorefinery for production of fuel and chemicals from Algal Biobased systems; production of bioethanol and Wastewater to Bioenergy: value-added products from sugarcane bagasse and microalgae biorefinery approach in Indian and Brazilian scenario.

Canada: Department collaborates with IC-IMPACTS (the Indian Canada Centre for Innovative Multidisciplinary Partnerships to Accelerate Transformation and Sustainability), Canada International Science and Technology Partnerships, Canada (ISTP, Canada), Grand Challenges, Canada and NRC: PBI, Canada in all areas of Biotechnology. Till date 20 projects have been supported under the joint calls. In the project executed by Indian Institute of Technology Ropar, bignelli based organic receptors were characterized. The CuS quantum dot were synthesized and functionalized with bignelli based organic receptor. The bignelli decorated hybrid CuS quantum dot was further characterized and used for antibacterial activity studies against *Escherichia coli*, *Staphylococcus* spp. and *Salmonella* spp. The Antibacterial activity of these hybrid material exhibit very good result in laboratory condition.

Denmark: Department collaborates with Innovation Fund, Denmark in the area of Health Science Biotechnology and till date 12 projects have been supported. The study by KEM Hospital, Pune, Deep Nursing Home & Children Hospital, Ludhiana and CCMB, Hyderabad investigates epigenetic signatures (DNA methylation) in the children born in gestational diabetes pregnancies in India and Denmark. Over 500 pregnancies have been studied in Pune and Ludhiana and comparisons made with the European cohort with the aim to establish standards for the Indian population. The study confirms that Indian women get *gestational diabetes mellitus* (GDM) at a much younger age and at a lower BMI compared to the European women. The average birth weight in our GDM pregnancies is 2.9 kg. The epigenetic study suggests that specific pathways are differentially regulated in offsprings of GDM pregnancies, which might influence future risk of cardio-metabolic disease.

In the study at IIIM-Jammu, NIMR, New Delhi, ICGEB-New Delhi, and IISc-Bangalore parasitological surveys have been conducted in cohorts of 300 children and

100 adults from high and stable malaria area of Jharkhand and 300 individuals of all age groups from low endemic area of Mewat in Haryana. Immuno-epidemiological analysis of sera samples collected from tribal region of Jharkhand displayed Naturally Acquired Immunity against malaria.

Finland: The Department partners with Academy of Finland, Finland and TEKES, Finland in areas of biotechnology and till date 41 projects have been funded. Under the Vitalsens project, Healthcare Technology Innovation Centre at IIT-Madras, Chennai in collaboration with University of Turku, Finland have developed an affordable, minimally intrusive wireless ECG patch capable of continuous streaming of 3 channel ECG, accelerometer data and skin temperature information to a gateway device (running custom Android application) with cloud connectivity for use in Neonatal wards, ICU and post-op monitoring. The technology has been transferred to two start-ups HealthSensei and Helyxon.

In another Indo-Finnish project, supported to HTIC, IIT-Madras, Chennai in collaboration with University of Oulu, Finland; three new low cost smart phone supported technology prototypes for vascular health monitoring Vis ARTSENS touch, ARTSENS Mobile and ARTSENS pen have been developed. An extensive clinical validation of these devices is underway in two clinical centres in Chennai and at the hospital in Technology Research Centre, Finland.

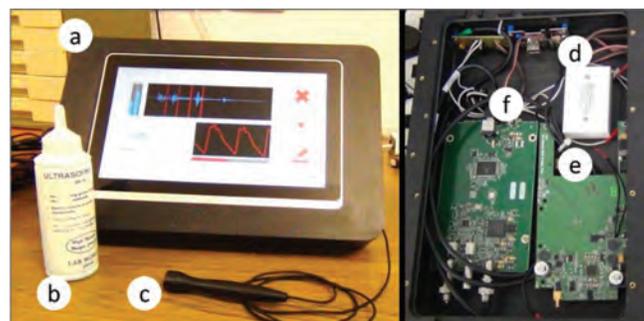


Figure 1. ARTSENS Touch prototype and internal design (a) Hardware prototype (b) Ultrasound gel (c) ultrasound probe (d) Battery (e) ARTSENS analog front end board (f) NI USB 5133 digitizer board.

Germany: Department is partnering with German Federal Ministry of Education, Science Research and Technology (BMBF) and German Research Foundation (DFG) in areas of biotechnology. The project funded to Kasturba Medical College, Manipal, India was beneficial in understanding the genetic basis and establishing a diagnosis for Indian families with osteogenesis imperfecta with the help of an NGS-based gene panel for diseases with low bone mass and exome sequencing.

Russia: Under Indo-Russia collaboration, 9 projects have been supported till date. A second joint call for proposals was announced during the year. Four proposals focusing on Genomics and Proteomics Instrumentation, Nano-Devices and Photosynthesis based Bioenergy & Bio-reagents were recommended for joint support.

Netherlands: The Department collaborates with Dutch organization for Scientific Research (NOW), STW and ZoNMw (Technology Foundations), Government of the Netherlands. The ongoing activities under the partnership include 3 joint projects; improved tolerance to heat and drought, population Based Prospective Cohort Study to Unravel the Causes of Stroke and Cognitive Decline in the elderly population and a joint initiative on “Local treatment of Urban Sewage Streams for Healthy water reuse (LOTUS)”.

The LOTUS^{HR} project by Indian Institute of Technology, Delhi, The Energy and Resources Institute (TERI), New Delhi, National Environmental Engineering Research Institute (NEERI), Nagpur aims at the cleaning of sewage water of the Barapullah drain - the second largest drain in Delhi, while simultaneously recovering resources from it. A foundation stone was laid on the site to mark the beginning of work on cleaning the Barapullah drain on 9 May, 2017 by the Hon'ble Minister of Science & Technology, India, Dr. Harsh Vardhan, Minister of Foreign Affairs, The Netherlands, Mr. Bert Koenders and Lt. Governor of Delhi, Sh.

Anil Bajjal. The first onsite small scale pilot unit, with a capacity of 100 litres/day is now operational. This plant will study the changing microbial consortium and the thermodynamics/flow of the drain water, with the changing weather, through the year. These studies will lead to the final design of large scale pilot with a capacity of 10,000 litres/day, which will be in operation by January 2019.

The Department has partnered with ZonMw and NWO, Netherlands to launch the 3rd joint call for proposal in 2017 in the area of “Technology for a Sustainable Healthcare: Minimally invasive techniques”. Under the call, 5 proposals were approved for funding.



Figure 2. A foundation stone laying ceremony of the LOTUS^{HR} Project by Hon'ble Minister of Science & Technology, India, Dr. Harsh Vardhan, Minister of Foreign Affairs, The Netherlands, Mr. Bert Koenders and Lt. Governor of Delhi, Sh. Anil Bajjal.

Spain: Department collaborates with Centre for the development of Industrial Technology (CDTI), Government of Spain to promote and fund market driven research and technology development as well as to encourage partnerships and business led R&D&I collaborative projects in the field of biotechnology. Under the 4th joint call announced in 2017, 3 projects in the area of brain cancer treatment, novel nano-formulations for leishmaniasis, and bioprocessing of glucose isomerase for enhancing production for use in food industry were approved for funding.

In a study implemented by Natural Remedies Pvt.

Ltd, active fraction of Turmacin was identified and named as Turmerosaccharides. This fraction showed significant reduction in osteoarthritic pain. In another project funded to Jay Research and Biotech India Private Limited, Pune a Bio-organic (microbial + organic or natural) Kit for tomato, soybean, vegetables, pomegranate and table grapes has been developed as per the requirement of farmers (Rain fed, flood irrigation and drip irrigation). Grapes grown using this technology are free of pesticide residue and have been exported to Europe. The technology has been shared with farmers and agri-experts in India and Spain and is ready for scale-up.

Sweden: The Department partners with VINNOVA, Sweden in the area of medical and environmental biotechnology. Under the 3rd joint call, five projects were funded in 2017-18.

In a study at IIT-Kanpur, *oblu* an open-source wearable motion sensing toolkit has been developed. It is a pre-programmed navigation sensor for Pedestrian navigation and positioning, industrial safety, treatment of movement disorders etc. The technology has been transferred to GT Silicon Pvt. Ltd., Kanpur and has been exported to over 20 countries. It is also the recipient of many awards like DST-Lockheed Martin 'India Innovation Growth Programme' (IIGP) and the CII Industrial Innovation award.

In another study at IIT-Guwahati, Guwahati in collaboration with Swedish University of Agricultural Sciences, Sweden, Scientists have developed a bioactive dressing using natural silk fibroin mat top-coated with a thin layer of the recombinant spider silk protein and layered with Human skin (keratinocytes and dermal fibroblast) cells. The wound dressing has shown promising results upon validation in a diabetic rabbit model.

Switzerland: The *Indo-Swiss Collaboration in Biotechnology* (ISCB) is a collaborative research and development (R&D) programme in biotechnology

between the Department and the Swiss Agency for Development and Cooperation (SDC), Government of Switzerland, with the involvement of Indian and Swiss biotechnology R&D institutes and firms. In Phase IV, 4 research networks were funded on pest resistance, yield improvement and climate resistance of cassava, finger millet, chickpea and pigeon pea integrating the socio-economics with the biotechnology components.

Cassava Network Project being implemented at ICAR-Central Tuber Crops Research Institute (ICAR-CTCRI), Thiruvananthapuram and TNAU, Coimbatore transgenic cassava plants for resistance to Cassava Mosaic Virus Disease (CMD) have been developed and tested for resistance in green house. The socio-economic component of the project included analysis of Cassava seed system, cropping system and value chains of cassava products.

BIOFI network project is implemented at Bharathiar University, Coimbatore; Pondicherry University, Puducherry; UAS, Bangalore; ICRISAT, Hyderabad; and MSSRF, Chennai. The network is targeted on development of sustainable pigeon pea and finger millet inter-cropping systems based on the selection of responsive cultivars and validated processes of bio-fertilizers and bio-irrigation particularly for small-holder rainfed farms. Results also revealed that bio-fertilization can improve the yield of both finger millet and pigeon pea, both in mono-cropping and intercropping schemes, and in bio-irrigation trial. Genome-wide variations across pigeon pea lines were assessed in ICRISAT, Hyderabad. Marker trait associations have been identified for transpiration efficiency, total biomass and total water extraction.

The Ragi network being implemented at UAS, Bangalore; St. John's Medical College, Bangalore; and NAARM, Hyderabad is aimed at developing superior Ragi cultivars that have the resilience to stress and are superior in productivity and nutrient availability. The whole genome sequencing of the high

yielding ragi cultivar PR 202 has been completed. This is the first ever report of a hybrid, de-novo sequencing strategy. Breeding and crop improvement strategies have been devised to enhance Ragi yield potential and nutrient bioavailability through molecular breeding. Detailed assessment of Ragi production system, markets and policy was done and strong inter-disciplinary linkage among the partners have been established.

IARI, NBPGR and NRCPB, New Delhi are the Indian partners of the Pigeon Pea network and the project aims at developing high yielding, semi dwarf, short duration, synchronous maturity pigeon pea genotypes compatible with the stakeholders' preferences, including nutritional value. A high-density 62K SNP genotyping chip was designed and used on 384 pigeon pea genotypes. The data so generated have been used for delineating the population structure of pigeon pea cultivars and mapping of fertility restorer gene for the A2 CMS system, which will be useful in hybrid seed production. After evaluation of over 2000 germplasm accessions the high yielding accessions were forwarded for next level multilocation trials and 50 of the panel for yield contributing trait was SNP genotyped at NRCP, New Delhi. Abiotic stress tolerance mechanism was identified and a process patent is proposed. miRNA targets were annotated to find out the genes and pathways being targeted by the predicted miRNAs. Second season evaluation is being carried out with 1200 accessions at Killikulam, Tamil Nadu.

The Department has also partnered with Swiss National Science Foundation (SNSF), Switzerland to develop a joint call for proposal on "Blue sky research/ basic research in the life sciences which is either biotechnology related or biotechnology inspired". The call for proposal has been announced in January, 2017.

United Kingdom: Department partners with Department for International Development (DFID);

INNOVATE; British Council; Academy of Medical sciences (AMS); Cambridge University. It also collaborate with Biotechnology and Biological Sciences Research Council (BBSRC), Medical Research Council (MRC), Natural Environment Research Council (NERC), Economic and Social Research Council (ESRC) through Research Councils U.K. (RCUK) in all major areas of Biotechnology.

Under BBSRC-DBT joint call on Farmed Animal Disease and Health (FADH), a multi institutional network project led the development and evaluation of technologies for detection and typing of currently known 29 serotypes of Bluetongue Virus (BTV) using real time RT-PCR assays; a pan BTV qRT-PCR assay for detecting 4 copies per reaction and Reverse-transcription-loop-mediated-isothermal-amplification (RT-LAMP) assays to detect eastern or western topotype of BTV with analytical sensitivity comparable to real-time RT-PCR, detecting BTV RNA within 60-90 minutes have been developed.

A project being implemented by NIAB, Hyderabad a fine scale gene expression atlas of 220 tissue and cell types collected from adult riverine water buffalo (*Bubalus bubalis*) (Mediterranean, Pandharpuri and Bhadawari breeds) have been developed. This study is the largest gene expression atlas generated in water buffalo to date. In addition, WGS data for 72 Indian buffalo covering six breeds has been done to study diversity between buffalo breeds. Potential variation identified between domestic breeds will form the basis for the development of predictive marker-assisted selection and breed improvement in the buffalo industry.

In another project towards improvement of Nitrogen Use Efficiency in Wheat (INEW), 406 Wheat germplasm lines comprising 199 Indian and 207 UK lines were screened for nitrogen use efficiency (NUE) and adaptation of UK lines to North Indian environments under field conditions as well as precision nutrient was studied. At NBPGR, New Delhi,

activities towards developing bioinformatics data analysis environment (RNASeq NGS pipeline and Wiki Page) to assist analysis of data for NUE experimental partners is being undertaken.

A wheat variety Unnat PBW343 resistant to yellow rust pathogen was developed by pyramiding four rust resistance genes using marker assisted selection and was released at the National level. This is the first MAS based variety to be commercialized for wheat in India.

The DBT-Newton Bhabha funded project is testing the introduction of a new vital sign device CRADLE into routine maternity care at community and hospital level in 10 sites in India, and in 7 African countries. More than 3300 devices have been delivered to hospitals and clinics, and successfully incorporated into routine care, sometimes as the first blood pressure device available in the clinic. More than 1500 health care workers have been trained to use the device. The project was recipient of the first ever Newton award of 200,000 pounds.

United States of America: Under INDO-US Collaborative program on low cost medical devices, a Low Cost Motorized Wheelchair (LOCOMO-WC) (Fig.1) was developed by Indian Spinal Injuries Centre. Compared to the existing motorized wheelchairs, LOCOMO-WC has a suspension system with linear links which lead to all four wheels to operate independently thus making it suitable to handle uneven terrain also. The cost of LOCOMO-WC is estimated at Rs. 45,000 which is far less compared to the imported motorized wheelchair which costs around Rs. 1.5 lakhs.

The Department is partnering with Department of Health and Human Services, Government of USA in the area of vision research. A call for proposals was issued in the current financial year under the research areas of Diabetic Retinopathy, Genetics of Ophthalmic Diseases and Ocular Inflammation. Under

the programme, six joint projects are ongoing. Studies on molecular biomarker role of chemokines in diabetic retinopathy clearly showed the role of MCP-1 (Monocyte Chemoattractant Protein-1) in the progression of Non-proliferative diabetic retinopathy (NPDR) and this is the first study to document the biomarker role of MCP-1 in a prospective study.

Tunisia: Under the joint program of cooperation, project was supported at ICGEB, New Delhi on “Assessment of the protective effect, against Tuberculosis, of a new vaccine composition.” It has been observed that there has been an increase in the incident rates of Tuberculosis partly due to failure of *M. bovis* BCG to impart protection against adult TB. In this project, focus has been to evaluate the effect of FOXO3 activation on the protective efficacy imparted by BCG. MK-2206, an active allosteric Akt inhibitor is in clinical trials for the treatment of solid tumors. Studies have shown that treatment with MK-2206 resulted in inhibition of AKT enzyme, and its downstream signaling *in vitro* and *in vivo*. As expected, pre-treatment with MK-2206 resulted in increased apoptosis in THP-1 macrophages and this induction of apoptosis was observed to be dose-dependent. It has also been observed that pre-treatment with MK-2206 resulted in reduced phosphorylation of AKT and FOXO3 enzymes.

South Africa: Recognizing the importance of collaborative & complimentary research to address regional needs, DBT in collaboration with DST, and Medical Research Council & Dept. of Science & Technology, Govt. of South Africa embarked on a collaborative Research Program on HIV, TB and TB/HIV. This collaborative program is under the framework of bilateral Science & Technology Cooperation agreement between the Department of Science & Technology, Ministry of Science & Technology, Governments of India and South Africa. Three joint proposals in TB, HIV, TB/HIV have been recommended under this collaborative effort.

MULTILATERAL R&D PROGRAMMES

European Union: The Department collaborated with the European Union in all areas of biotechnology, and till date 33 projects have been funded. Under the project entitled 'Targeting the elimination of antineoplastic compounds in hospital wastewaters treatment' being executed by NIT, Durgapur and Central University of Haryana, Mahendragarh; three photocatalysts and photo-catalytic membrane reactor for treating antineoplastic agents in hospital waste water have been formulated. Laboratory scale testing is under progress.

COLLABORATIONS WITH NGOs & OTHER ORGANIZATION

Bill & Melinda Gates Foundation: Under the first GCI call titled "*Achieving Healthy Growth through Agriculture and Nutrition*" five Indian led pilot projects were funded. In a study by the Science for Society, Maharashtra, domestic solar construction dryer has been implemented at community level, to test its impact on ensuring year-wise nutritional food security to Indian women. Under the VeggieLite eKutir, Odisha has piloted a supply chain innovation to assess its impact in improving access to fresh vegetables and fruits to supplement nutrition at affordable prices in rural and peri-urban areas. In a novel approach to reduce zinc malnutrition in rural women and children through agronomic bio-fortification of food crops Amity University, Noida tested an agricultural intervention that used foliar application of zinc on rice and wheat crops to potentially address micronutrient deficiency through supplementation of food crops.

Under the programme "*Reinvent the Toilet Challenge*" six projects were funded under the call. Field testing of off-grid, self-sustained, modular, electronic toilet, with solar energy for Indian weather and integrated with mixed waste processing unit,

developed by Eram Scientific and University of South Florida, USA was carried out. The waste treatment would result in zero discharge and would be pathogen free. The combined technology was piloted at school near Trivandrum, Kerala where it served over 1500 students and people from the local neighbourhood. In another project, BITS Pilani, Goa and Ghent University, Belgium have developed an affordable and simple-to-operate decentralized wastewater treatment system which relies on electrochemical reactions and the production of chlorine, to manipulate the pH of the wastewater to destroy pathogens and helminthes. The system was tested at a household level and then finally scaled up to serve a 100 person hostel, within the campus. The team is now looking to further scale-up the system and deploy it for testing in slums.

HUMAN RESOURCE DEVELOPMENT THROUGH GLOBAL LINKAGES

Newton Bhabha PhD placement programme: For the fourth consecutive year DBT in partnership with British Council India provided funding opportunities to support short-term PhD placements between UK and Indian institutions. Under the scheme 25 Indian PhD scholars were selected to spend a period of their study (2 to 4 months) in UK's higher education institutions in pursuance of their research work of PhD.

Khorana programme for Scholars: The Department is collaborating with University of Wisconsin (UW) Madison, USA and the Indo-US Science and Technology Forum (IUSSTF) to nurture contacts between students of biotechnology and biomedical sciences from India and the US, through a joint training programme in biotechnology and allied areas. The programme acts as a key catalyst to encourage post-graduate students to take up research as a career. In the year 2017-18, 30 Indian scholars were supported under the scheme.

Young Entrepreneur Scheme-India (YES-INDIA): Department in partnership with ABLE is executing a Biotechnology Entrepreneurship Student Teams (BEST) programme for students since last 8 years. BEST-India programme aims at encouraging young postgraduates and doctoral students in developing biotechnology entrepreneurship by exposing them to issues involved in commercialisation of bioscience. Each year ideas of 3 teams of students are funded. The programme has yielded six start-up companies by the winning teams. The call for the year 2018-19 has been announced.

DBT-Stanford programme on Foldscope: Foldscope is a low-cost paper origami microscope developed by Prakash Lab at Stanford University, USA. The programme will open the doors for bringing science to the least privileged in a step towards truly democratizing science. A call for proposals inviting schools, colleges and citizen scientists to apply for Foldscope with application in education and research was announced in 2017 and 520 applications were received. As a first step workshops at municipality Urdu school at Sangharsh Nagar, Dharavi at Mumbai and IIT Bombay were held on August 28-29, 2017 where teachers and students of government schools from across India were trained in use of the Foldscope as a teaching tool.



Figure 3. Foldscope Workshops at Dharavi, Mumbai held on August 28, 2017

EduTech and EduGaming Programme for Rebooting Education: The Department is

developing a programme with Tekes, Finland on “Rebooting education in the Indian Schools” by facilitating long-term collaboration with Finnish Edugaming companies in co-creation of edu-gaming/tech for Indian school systems. As an initial step, the Department organised the bilateral workshop “Edutech and EduGaming: The future of Education” at C-CAMP, Bangalore in October 2017. Thirteen EduTech and EduGaming companies from Finland, 25 Indian companies and 8 schools participated in the workshop. Atal Innovation Mission (AIM), NITI Ayog partnered in the event, which allowed connecting tinkering labs supported by AIM to pilots of the Finnish EduTech.

MEMBERSHIP CONTRIBUTION TO OTHER PROFESSIONAL BODIES

European Molecular biology organization (EMBO): The Department, EMBO and its intergovernmental funding body EMBC, have signed a Cooperation Agreement to strengthen scientific interaction and collaborative research between India and Europe. As an EMBC Associate Member state, researchers working in India are now eligible to participate in all EMBO programmes and activities. In the year 2016, scientist has been selected under the EMBO Young Investigators scheme, 1 has been awarded EMBO Long-Term Fellowships, and 24 have been awarded the EMBO Short-Term Fellowships and 1 EMBO Young Investigator Lecture was organized. Recently, EMBO has established a new cooperation with the Wellcome Trust/DBT India Alliance under which 3 new interdisciplinary meetings in India per year will be organised.

Human Frontier Science Programme organization (HFSP): India is one of the member states of HFSP. The overall objectives of the programme are to support for innovative, cutting edge high risk research at the frontiers of the life sciences and promoting the international collaboration in the spirit of science without borders. HFSP support the

investigator under four categories - programme grant, Long term fellowship, Cross disciplinary fellowship, career development awards. As per HFSP annual report 2016, under four categories India received 1, 5, 1 & 1 awards respectively.

BRICS: Department of Science and Technology, Govt. of India, the nodal agency for the implementation of the programme, has created a working group in Biotechnology, which is jointly coordinated by Brazil and Russia. The coordinating agency from Indian side for this working group is yet to be decided.

INTERNATIONAL MEETINGS

European Molecular Biology Laboratory

(EMBL): Department is exploring collaborations with European Molecular Biology Laboratory. It includes access to EMBL facilities in Europe to Indian scientists and also opportunities for organising joint collaborative research and training for Indian scientists in the areas of bio-imaging, structural biology and bioinformatics. In this context, a 2-day conference titled “Towards India’s Associate Membership of EMBL” was organised on October 12-13, 2017 in Delhi with scientific sessions and panel discussions on recent developments in bio-imaging, structural biology and bioinformatics. The conference was attended by about 100 selected scientists across the country and was also live-streamed to various research institutions across the country.

Agriculture Conclave: In order to develop a roadmap/action plan for setting up of the FarmerZone, an international conclave was organized by DBT on August 30-31, 2017 where, farmers, experts in science and technology, world agri-leaders and policy makers and global companies who work in big-data and e-commerce segments participated. The “FarmerZone” is envisaged as a cloud-service with curated big data, which will cater various needs of the farmer—from dealing with

climate change, weather predictions, matters related to land, soil, disease, pest, water, planting material and marketing. The FarmerZone will also include a MarketZone where farmers can directly sell their produce which can be picked up directly from the farm.

Nobel Prize Series, India- 2018: The Department has an ongoing collaboration with Nobel Media AB to hold the Nobel Prize Series in India over five years. The first Nobel Prize Series 2017 was held in partnership with Government of Gujarat on January 9-10, 2017 during the Vibrant Gujarat. The second Nobel Prize Series, India 2018 will be held in partnership with Government of Goa on February 1-2, 2018. The broad theme for the Nobel Prize Series, India 2018 is “*Education and the value of teachers*” emphasizing shaping of future science, technology & innovation.

10

Autonomous Institutions & Biotech Science Clusters

NATIONAL INSTITUTE OF IMMUNOLOGY (NII), NEW DELHI, DELHI

National Institute of Immunology (NII) undertakes research of high caliber in basic and applied immunology to devise strategies for manipulation of the immune system in order to provide protection as well as intervention against diseases. This is undertaken by carrying out innovative research using fundamental tools of biology. The research activities at the Institute are grouped in four broad areas, namely, infection and immunity, molecular design, gene regulation and reproduction and development. The Institute has continued to expand scientific programmes in a multi investigator driven mode to ask challenging questions in biology for improvement of human health. The scientific findings have so far been published as 94 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 (Leishmaniasis, Malaria); chronic disease biology (Diabetes Mellitus, Multiple Sclerosis, Amyloid Diseases); Cancer Biology, Developmental Biology and Genetics, Stem Cell 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: The outcome of basic research which has been published in the frontline journals are: 1) Calcium Dependent Protein Kinases are key effectors of calcium signaling in malaria parasite. Using phosphor-proteomics and conditional knockdown CDPK1 substrates were identified and a cross-talk between CDPK1 and PKA

showing the role of CDPK1 in parasite invasion; 2) RiPPMiner, a novel bioinformatics resource for deciphering chemical structures of RiPPs by genome mining was developed; 3) The Institute has developed a versatile tool - SBSPKSV2 which is for genome mining and analysis of polyketide and non-ribosomal peptide biosynthetic pathways in chemical space; 4) In another study it was shown that inhibitory TNF p100 pathway modulates the adaptive compartment during immune responses; 5) Tumorsuppressor SIRT6 regulation in hepatocellular carcinoma and the mechanism underlying UBE3A-mediated tumorigenesis in the disease was established; 6) a new role for autophagy proteins in directing melanosome movement was elucidated and the unconventional use of the proteins in cellular trafficking pathways was revealed. Such crosstalk between the central cellular function and housekeeping pathway may be a crucial mechanism to balance melanocyte bioenergetics and homeostasis; 7) Another finding showed the efficacy of β -lactam/ β -lactamase inhibitor combination linked to WhiB4-mediated changes in redox physiology of *Mycobacterium tuberculosis*; 8) An immunocompromised mouse model, NOD.SCID-*rd1*, for Retinitis pigmentosa (RP) was developed by crossing CBA/J and NOD SCID mice and selecting homozygous double mutant animals for further breeding; 9) In a study for preparation of a freeze-stable dry powder alum adsorbed antigen stable at frozen conditions it was found that particles maintain their adjuvant potential upon freezing as seen in animal immunization studies; 10) In another study it was shown that autophagy induction by *Mycobacterium indicus pranii* promotes *Mycobacterium tuberculosis* clearance from RAW 264.7 macrophages and 11) Studies demonstrated that daily oral administration of melatonin can increase bone accrual during growth and can cure ovariectomy-induced structural and functional degeneration of bone by specifically increasing bone formation.

Translational Research Activity: The Institute has been engaged in the following research activities to develop products and processes for industrial benefits.

- Freeze-stable alum-adjuvanted vaccine formulation: a freeze-stable dry powder alum adsorbed antigen having stability at frozen conditions was prepared. It was observed that the formulation protects the alum adjuvanted vaccines from cold temperature shock.
- Fabrication of biodegradable composite scaffolds at room temperature for tissue engineering applications: Composite scaffold blends of polymers PDLLA and Eudragit were developed using the novel method of fusion of particles by treatment with methanol. Scaffold with different surface charges can be fabricated, using this method, suitable for cellular interaction.

Intellectual Property: A European patent – “Ig genes specific oligonucleotides and uses thereof” (Patent no 2100970) has been granted on 13/04/2017 while a US patent – “Hemoglobin receptor as novel vaccine for Leishmaniasis” (Application no. 14/648,538) has been accepted in the reporting period. An Indian patent – “Novel immunotherapeutic method for treatment of cancer” (Indian patent no. 284087) was also granted on 08/06/2017. The Institute has filed two patents – 1) Freeze-stable alum-adjuvanted vaccine formulation and 2) A method for fabrication of biodegradable composite scaffolds at room temperature for tissue engineering applications.

Research collaborations: The Institute has signed consulting agreement with EPR Centre for Cancer Research and Bioinformatics Private Limited to provide consultancy on the development of various biosimilars and biologicals. The Institute has also signed MoU with BIBCOLD, PSU of Dept. of Biotechnology, Gol for collaborative research for

developing quality plasma products. The institute will also offer its expertise to BIBCOLD on protein purification and process engineering. Initiatives are being taken to collaborate with Indian Spinal Injuries Centre, New Delhi to set up innovative tissue culture facilities for 3D in-vitro culture of autologous human spinal disc.

New Initiatives: The Institute started working as party to ‘NCR Biotech Science Cluster’ which aims at promoting the cooperation in Research & Development among DBT Institutes around NCR. The R&D facilities, infrastructure and other resources will be shared to promote research collaborations among the NCR institutes. The Institute organized ‘Young Emerging Scientist’ [YES] symposium on 5th-6th October, 2017 at NII. Multiple events were carried out during the symposium and distinguished scientists and students from different institutes (THSTI, ICGEB, NIPGR etc.) participated in poster presentations, talks and seminars.

Academics: The Institute enrolled 21 students during the year for Ph.D. degree with academic affiliation of Jawaharlal Nehru University and 46 graduate/postgraduate students were provided short-term training. NII has provided opportunities to 21 students for short-term training under ‘Science Setu’ conceptualized to enable connectivity between Institute scientists and undergraduate students of 14 colleges of Delhi University and one deemed University of Faridabad. Ten students sponsored by Indian Academy of Sciences, Bangalore were also enrolled as project trainees for six month.

Other notable Achievements: The Institute has discovered SPAG9, a novel cancer antigen that is expressed in reproductive tract, breast and various other malignancies. Human clinical trials employing recombinant SPAG9 have been initiated in Cervical Cancer patients using Dendritic Cell based vaccine at Adyar Cancer Institute, Chennai.

NATIONAL CENTRE FOR CELL SCIENCE (NCCS), PUNE, MAHARASHTRA

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: The national cell repository services at NCCS have supplied six thousand cell lines to four hundred research and academic institutions in India. The repository extended its services further to facilitate human resource development by conducting two national workshops, providing hands-on training in cell culture techniques to researchers from across the country.

Research Activities: Group involved in cancer research, reported that the oncogenic microRNAs, miR-93 and miR-106a, repress FBXO31, resulting in the upregulation of Slug, which was found to be involved in epithelial-mesenchymal transition and cell invasion. The findings have strong relevance to designing improved strategies for controlling malignancy.

In a study on virus and host interactions in HIV-1 infection, differential gene expression analysis was carried out which showed down-regulation of the cyclin F (CCNF) gene. Further investigations revealed that cyclin F has the ability to negatively regulate the expression of the viral infectivity factor (Vif) by inducing its ubiquitination and proteasomal degradation which may lead to restoration APOBEC3G (A3G) expression, providing innate immunity to the host against HIV.

In study related to Vaccinia virus, one of the groups reported that the vaccinia virus complement control protein (VCP) exhibited selectivity in inhibiting the bovine complement pathway (CP) determined by three amino acids which were found to interact with bovine serine protease factor I and inactivate bovine

C4b, the non-catalytic subunit of the CP C3-convertase. Similarly, in Variola virus smallpox inhibitor of complement enzymes (SPICE) contains positively charged residues instead of glutamic acid.

Another group initiated research to gain an insight into the complexity of nuclear pore complex (NPC) macromolecular assemblies and based on the crystal structure and supporting biochemical data, homodimeric and homotrimeric state of Nup62 was observed. In addition, comparative structural analysis showed that the coiled-coil domain of Nup62 was sufficient to interact with other coiled-coil proteins for the formation of parallel triple helix bundles demonstrating the role of this motif in providing plasticity for diverse interactions.

Human Resource Development: During this year, 33 research scholars have received the Ph.D. degree, 21 students have submitted their thesis, and 22 research scholars were registered as Ph.D. students with the University. Besides, 32 new Research Fellows joined the institute and 38 project trainees & 16 summer trainees also received training at NCCS.

CENTRE FOR DNA FINGERPRINTING AND DIAGNOSTICS (CDFD), HYDERABAD, TELANGANA

The Centre for DNA Fingerprinting and Diagnostics (CDFD) is a model autonomous institute with service and research components. The primary objective of the institute is to provide services in the form of specialized diagnostics and DNA fingerprinting, and to carry out fundamental research activities, where both components complement and enrich each other.

Services: Human DNA Fingerprinting: CDFD, being the premier organization in the country for referrals of complex and sensitive cases from various law enforcing agencies has analyzed 430 samples from

119 cases in 2017. These include high-profile cases from MHA, NIA, CBI and State Police forces. CDFD also provides training in the field to different police/forensic personnel.



Figure 1. CDFD analyzed samples from Bhopal-Ujjain train blasts in Madhya Pradesh (left) and Sukhoi Su-30 Fighter Jet crash in Arunachal Pradesh (right)

a) **Diagnostic Services:** The Diagnostics division at CDFD offers diagnosis of genetic diseases as well as prenatal diagnosis for detection of chromosomal abnormalities, single gene disorders and inborn errors of metabolism. About 4753 samples were tested for various genetic disorders. Medical Genetics Department at NIMS is functional under a tie up with CDFD to provide services to patients with genetic disorders as well as for training and research.

b) **Basmati Rice Purity Testing:** Newly established Plant DNA fingerprinting services has been actively offering new purity testing of different rice varieties as well as other commercially important crops. CDFD offers Basmati Rice purity testing to the rice exporters through the APEDA. About 86 samples were tested during 2017.

Research Activities: The Centre undertakes research in several frontier areas of modern biology. The major thrust areas include Microbiology, Cell Biology, Disease Biology, Genetics and Computational Biology.

One of research groups studying cell biology characterized a novel non-canonical function of the Mixed Lineage Leukemia (MLL) protein, a histone methyltransferase during mitosis. It was reported that interaction of MLL complex with kinesin motor protein Kif2A regulates chromosome alignment and spindle assembly. The finding provides novel insight into MLL-rearranged leukemia. Focusing on another aspect of cancer biology, it was found that PTEN, a tumour suppressor, regulates glucose uptake by cells in a phosphatase-independent manner by utilizing its PDZ binding motif (PDZbm) to interact with the PDZ domain of SNX27 preventing recycling of the glucose transporter GLUT1 to the plasma membrane, which leads to impaired cellular glucose uptake.

In a study to investigate role of Inositol hexakisphosphate kinases (IP6Ks) in mice fertility, IP6K1 was found to be a novel component of the chromatoid body and noted that this structure is absent in *Ip6k1* null round spermatids. Furthermore, juvenile spermatids from *Ip6k1* null mice displayed premature expression of the transition protein TNP2 and the protamine PRM2 due to translational derepression, and the aberrant localization of these key sperm-specific chromatin components results in abnormal spermatid and azoospermia in these mice.

A novel defense mechanism against mycobacterial infection that utilizes the histone methyltransferase, SUV39H1 was reported in a study on tuberculosis. Upon infection, the host enzyme SUV39H1 trimethylates the mycobacterial histone-like protein, HupB, this in turn reduced the cell adhesion capability thus reducing the mycobacterial survival inside the host cell. Novel function of cyclic α -(1, 2)-glucan, an intrinsic component of Gram-negative bacteria that is involved in iron homeostasis and protection against iron-induced toxicity by sequestering iron was identified. The study provides a new mechanism of iron uptake in bacteria including important pathogens.

The research outcome of all these studies are in the form of 57 peer reviewed research publications, award of different fellowships including EMBO short term fellowship, awards including B.M. Birla Science Prize and numerous national research and travel grants from the agencies like, DBT, DST, CSIR and ICMR .

Human resource development and outreach

activity: CDFD has about 100 research scholars working for their doctorates in different areas of biology. CDFD also holds a Summer Training Program in collaboration with Indian National Science Academy, Indian Academy of Sciences and the National Academy of Sciences, and about 20 to 25 students every year are benefitted under this Program. Three different fellowship programs have been initiated to impart training to guest workers affiliated to different scientific institutions, hospitals and forensic laboratories.

As a part of outreach activity, CDFD has entered into an MOU with 29 schools and junior colleges in and around Hyderabad under the BRIDGE Program to educate school students in various fields of science.

NATIONAL INSTITUTE OF PLANT GENOME RESEARCH (NIPGR), NEW DELHI, DELHI

The National Institute of Plant Genome Research (NIPGR) has achieved a logarithmic growth in plant genomics research and placed India among the major contributors in the field of plant molecular biology and biotechnology. The Institute has been effective at generating new knowledge that has potential for genetic enhancement of crops for social benefits and in providing higher education as service to academia and society. Through its infrastructural base and knowledge-based resources, NIPGR is poised to contribute towards frontier areas of plant biology and agricultural biotechnology. Currently, 28

scientists, including five who have been recently inducted, are leading independent research groups in four major areas viz. structural genomics and computational biology, plant development and architecture, stress biology and nutritional genomics. NIPGR scientists have been working on major cereals and legumes, several vegetables and oilseeds of economic importance, besides model plants.

Salient Achievements: Over the years, a number of projects have been undertaken to enhance tolerance against biotic and abiotic stresses and growth ability under nutritionally deficient conditions. Sheath blight disease, caused by the necrotrophic fungus *Rhizoctonia solani* AG1-IA, is one of the major rice diseases. It causes huge crop losses worldwide with no source of natural resistance available thus far. In one of the projects, NIPGR researchers have identified a novel *Rhizoctonia solani*-eating bacterium *Burkholderia gladioli* strain NGJ1 and established that a peptide secreted by this bacterium has a broad-spectrum anti-fungal property. This discovery not only showcases high-end basic science research, but it also has potential application in controlling fungal diseases. Insect herbivory is a major biotic stress causing great amount of crop loss, resulting in increased use of chemical pesticides by farmers. Our researchers have identified a potential novel herbivore-associated-molecular-pattern (HAMP) from the oral secretion of the herbivore Spodoptera. Identification of a so far unknown HAMP would accelerate development of herbivore-resistance in plants. Another study focused on phosphorus-use-efficiency in rice. Rice is one of the largest consumers of phosphate fertilizers; however, most of the soil phosphates remain unavailable for the plant's uptake and utilization. Scientists have identified rice genes, which regulate phosphate homeostasis and promote improved growth under low phosphate or on organic manure. Apart from rice, major findings were also achieved for other crop species. Chickpea genes encoding enzymes from inositol metabolic

pathway as well as a tubby-like transcription factor involved in stomatal closure were characterized, that would advance our understanding of molecular mechanisms of abiotic stress tolerance. These candidate genes would be useful in developing new generation crops. In yet another study, strong correlation of sly-miR159 with the tolerant attribute of a tomato cultivar against Tomato leaf curl New Delhi virus (ToLCNDV) infection was demonstrated.

Previously, NIPGR scientists sequenced desi chickpea genome and published a draft genome assembly. During this academic year, NIPGR has published the draft genome assembly of the wild progenitor of chickpea, *Cicer reticulatum*. This wild chickpea species is used for introgression breeding and thus its genome sequence would facilitate identification of beneficial alleles for chickpea improvement. To that direction, our scientists have identified genetic markers for seed size and are using them for marker assisted selection. Additionally, the scientists have successfully carried out whole-genome re-sequencing of four rice genotypes with contrasting seed size/weight [long grain genotypes, LGR and PB 1121 and short grain genotypes, Sonasal and Bindli].

Considerable progress has also been achieved in ongoing programs with a major target to improve protein content and amino acid composition by expressing a seed albumin, AmA1, from *Amaranthus hypochondriacus*. This has been made possible by developing an advanced generation of *indica* rice population expressing AmA1. A detail agro-phenotypic and physiological analysis revealed an enhanced photosynthetic activity, increased yield and 42-67% increase in total protein in the transgenic lines. Significant progress has also been made towards our ongoing efforts to develop low glucosinolate lines in Indian oilseed mustard. The application entitled “Event selection under small scale open field growth condition and substantial equivalence test of the promising low glucosinolate transgenic *Brassica juncea* line” has been submitted

to RCGM for conducting a limited field trial.

Genomics research bridges different branches of natural sciences and has seen enormous growth in the last two decades. It is constantly providing new ways of tailoring crops, medicines and industrial molecules for human benefit. It is hoped that in coming years, the ongoing efforts at NIPGR will allow India to emerge as one of the important national and international resource centres for materials and knowledge in the area of plant molecular biology. Besides this, the scientific human resource being produced by this institute and the training extended to the students and researchers of other organizations through short-term training programs and workshops would immensely contribute in the achievement of such an aspiration.

In terms of publications and patents, the year 2017 was highly productive and scientists were able to publish 103 articles in high impact international journals, and file national and international patent applications.

NATIONAL BRAIN RESEARCH CENTRE (NBRC), MANESAR, HARYANA

NBRC is credited with the mandate of pursuing basic research to understand brain function in health and disease, generate trained human resources with the capability to carry out inter-disciplinary research in neuroscience and promotion of neuroscience in India through networking among institutions across the country.

Major initiatives: The Dementia programme, which is a multi-centre, nation-wide programme, to integrate the social context of dementia in India with the biology of the disease has been initiated this year. It seeks to study the incidence and prevalence of dementia in the context of the community and in both urban and hospital based studies and develop cohorts that can be assessed for various risk and protective factors. Study of known and potential

biomarkers, imaging and genetics would be utilized to understand biology of the disease. The Centre of Excellence (COE) in Epilepsy, a joint programme between AIIMS and NBRC has been recommended for the second phase based on the excellent work done during Phase I and future projections that combine innovative basic and translational research. NBRC offers unique M.Sc. and Ph.D degrees in Neuroscience to train students in the integrated study of brain function that is not provided by conventional courses in various aspects of Biology. The selection of students from different streams apart from biology and biotechnology based programmes including conventional engineering and computer science courses, physics, chemistry and mathematics results in an intellectual churning leading to better creativity.

Salient achievements: In a study related to Japanese Encephalitis it was observed that the host microRNA miR-301a blocks the IRF1-mediated neuronal innate immune response to Japanese encephalitis virus (JEV) infection. The neutralization of miR-301a reinforces host innate immunity by restoring IFN-beta expression, thereby restricting viral propagation in neurons. In addition, JEV induces human neural stem/progenitor cell death by elevating endoplasmic reticulum (ER) resident chaperone GRP78, mitochondrial protein Prohibitin (PHB) and heterogeneous nuclear ribonucleoprotein hnRNP through stress. This unravels a novel mechanism underlying stem/progenitor cell death following viral infection. Significant strides have been made by scientists at NBRC working on various kinds of brain tumours. In addition to highlighting the previously unknown role of telomerase in the regulation of pentose phosphate pathway, studies have indicated the involvement of Nrf2-TERT loop in maintaining oxidative defence responses in glioma. The importance of dysregulated metabolism in immune surveillance has highlighted the importance of Protein arginine methyltransferase 1 in modulating chromatin landscape crucial for facilitating HLAB

gene expression in glioma. In a study to investigate Brain expressed X-linked (Bex) genes, a newer group of tumor suppressor genes which are silenced in different varieties of cancers, curcumin was shown to induced all endogenous Bex genes in N2a cells in a dose and time-dependent manner and also activated p53 prior to Bex genes induction. Most importantly, inhibition of curcumin-mediated induction of Bex genes by pifithrin-alpha (p53 inhibitor) and siRNA for Bex mRNAs also inhibited N2a cells apoptosis suggesting, a direct role of Bex genes in N2a cells apoptosis and the involvement of p53 in the induction of Bex genes. These results suggest that re-expression of Bex genes by curcumin act as tumour suppressors and may provide a new strategy to treat neuroblastomas. In a study to probe how information is processed in the somatosensory and motor systems of different mammalian species, subtle but important differences were observed in the organization of the movement systems in two closely related rodent species mice and rats. Interestingly, mice have more of a mosaic pattern of the movement representation in the cortex as compared to rats. Such differences optimize the survival of these species in their individual niche. In a study undertaken to examine axonal regeneration in peripheral neurons of *C. elegans*, let-7 microRNA was identified for inhibition of functional regeneration by regulating the expression of ced-7 coding for a homotypic cell adhesion protein. Further, the loss of this microRNA promotes repair process by increasing axon fusion events during regeneration. In another study carried out in collaboration with scientists from Indian Association for the Cultivation of Science (IACS), it was found that the nanoparticle form of some of the sugar molecules can significantly enhance their chaperone performance in inhibiting protein aggregation and in lowering of amyloidogenic cytotoxicity. Scientist at NBRC have developed a comprehensive brain signal processing toolbox called "KALPANA" for brain metabolic profiles and quantization, which has a direct application in clinical

settings. NBRC has signed an MOU with Mahatma Gandhi Institute of Education for Peace and Sustainable Development (MGIEP), a type I UNESCO centre, for the advancement of collaborative research. NBRC also signed an MOU (Glue Grant) with the Government of Haryana regarding joint work with Gurgaon General Hospital, Regional Centre for Biotechnology and THSTI (Translational Health Science and Technology Institute).

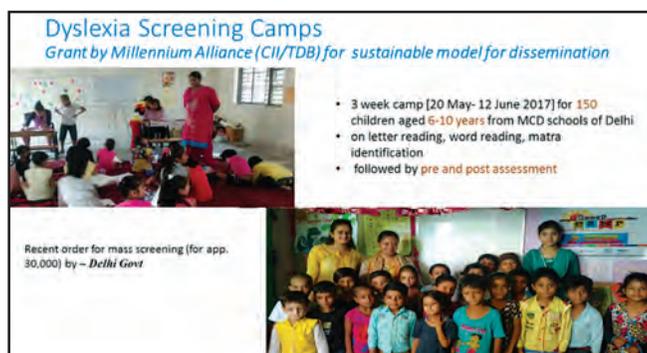


Figure 2. Dyslexia which is a reading disability affects learning in children. A tool to detect dyslexia has been developed at NBRC for early detection of this disability which is now being used in schools

INSTITUTE OF BIORESOURCES AND SUSTAINABLE DEVELOPMENT (IBSD), IMPHAL, MANIPUR

Institute of Bioresources and Sustainable Development (IBSD), Imphal continued its efforts towards bio-resources development and their sustainable use through biotechnological interventions for the socioeconomic growth of the North East Region. During the year, IBSD has published 12 research publications in peer-reviewed scientific journals along with filing of a new patent.

Salient achievements: In the Plant Resources Programme, protocols for *in vitro* propagation of *Lilium mackliniae* (Siroi lily) and *Lilium chitrangada* (Dzuko lily) have been developed. Two new species have been identified in family Zingiberaceae. The whole transcriptomic analysis of *Swertia chirayita*

(root and leaf) has been performed and sequences were submitted to NCBI under SRA accession number SRR3530418. Transcripts obtained will accelerate the understanding of metabolite biosynthetic pathways, along with providing new insights to increase the biomass yield. A major programme on mass production of orchids for developing bio-entrepreneurship in North East Region (NER) has been initiated. IBSD has also taken major initiative to promote *Prunus cerasoides* (Cherry Blossom) in different parts of North East (NE), which will boost up the economic potential of these states. A new bioactive compound, Xylosmanoside has been isolated from *Xylosma longifolium*. A process has been developed for extraction of highly stable natural colour pigments from chillies and its characterization is in progress.



Figure 3. Mass production of orchids at IBSD Bioresource Park at Haraorou, Imphal, Manipur

In the Microbial Resources Programme, a total of 21,631 cultures (18777 bacteria, 739 probable actinobacteria, 1881 filamentous fungi and 234 yeasts) originated from various ecological niches of NE India including from untapped ecological niches such as hot springs, high altitude, low temperature mountains, caves, forest, fermented foods etc., have been collected and preserved at the Microbial Repository Centre in IBSD. Molecular surveillance of traditional fermented foods marketed in North East India conclusively established the risk of enteric bacterial pathogens (*Clostridium botulinum*, *Bacillus*

cereus, *Staphylococcus aureus*, *Clostridium perfringens*, *Listeria monocytogenes*, *Escherichia coli*, *Proteus mirabilis*, and *Yersinia enterocolitica*). IBSD has initiated research on the development of a DNAChip based microbial risk assessment platform and identification of critical control points of pathogen entry in fermented foods of Manipur. Microbial pesticide for the control of soil and seed borne fungal pathogens using *Trichoderma viride* (T20) has been developed. *In vitro* antifungal efficacy of indigenous actinomycetes isolate identified as *Streptomyces albidoflavus* RCS243 has been established as promising biocontrol agent.

A major programme on bioenergy from aquatic weeds of Loktak Lake has been initiated during the year. The work has been carried out on the exotic paragrass of Loktak Lake as feed stock for bioethanol production by different pre-treatment and hydrolytic process.

In the Animal Bioresources Programme, a potent AChE inhibitor 2, 3-Dimethylmaleic anhydride has been isolated from *Colocasia esculenta*. Further, the molecule showed significant impairment in the antioxidant enzymes. Therefore, the possible reason of insect toxicity of 2, 3-Dimethylmaleic anhydride might be associated with inhibition of AChE activity and oxidative imbalance.

In the Bioinformatics Programme, around 85 ethno-veterinary plants were selected from the secondary sources followed by primary data from surveys. Compilation of Ethno-pharmacological plants of North East is under process. Rhododendron database of Sikkim Himalaya is also in progress.

IBSD has signed an MOU with Inter American University of Puerto Rico, United States of America for carrying out joint research programmes. The institute has organised Global Sustainable Development Summit 2016 towards United Nations Sustainable Development Goals in association with North East Development Foundation (NEDF) at

Guwahati. The IBSD and Institute of Life Sciences (ILS), Bhubaneswar have jointly organized a National Consultation on Bioresources for Sustainable Development during August, 2017 at Bhubaneswar.

INSTITUTE OF LIFE SCIENCES (ILS), BHUBANESWAR, ORRISA

The major area of research in ILS during the last year focused on infectious diseases biology, various aspects of gene function and regulation, and translational research through technology development. In this year 13 Ph.D degrees are awarded to the students and 30 new students have enrolled for Ph.D. programme.

Salient achievements:

a) *Infectious disease Biology*: Mice with chronic malaria were found to be resistant to endotoxemia, sepsis and *Salmonella typhimurium* infections. This cross- protection to other pathogens appear to offer an evolutionary advantage for persistence of Plasmodia in Human and animal communities.

Studies on biofilm revealed that PIA-independent biofilm formation is a standard feature of *S. haemolyticus* isolates, irrespective of the sources of isolation. Cell lysis enabling DNA release was an essential step for biofilm attachment during initial stages of biofilm development. The DNA and protein remain an important matrix component throughout the process of biofilm maturation. It was also noticed that curcumin reduced the capacity of biofilm formation during initial stages of development and the expression of *Sortase A* transcript decreases with the biofilm age indicating its role in early stages of biofilm development.

Investigations on Chikungunya virus has resulted in the characterization of the interaction between nsP1 and nsP2 proteins of this virus during infection. It was mapped that amino acid residues 170-288 of Chikungunya virus nsP1 directly interacts with amino

acid residues 1-95 of nsP2 and modulates its ATPase activity *in vitro*.

Investigation on bacterial cell division protein showed the interaction of the FtsZ with MinD using microscopy and pull down assays. Moreover, using independent *in silico* and laboratory techniques FDA approved drug library was screened to identify molecules those may inhibit cell division in bacteria by targeting FtsZ. With this approach, it was found that doxorubicin; an anthracycline antibiotic is able to inhibit *E. coli* growth by perturbing FtsZ functions. Monocytes and macrophages represent critical arms of the innate immune system and are considered regulators and effectors of inflammation and innate immune response. The studies showed an unexpected function of LPA that transfigures CD11b⁺ murine monocytes into F4/80⁺ macrophages. LPA stimulated Akt/m-TOR signaling is critical for LPA mediated macrophage development in mice. Additionally, transcriptome analysis reveals that PPAR α is the key transcriptional regulator in the development of LPA induced macrophages. In humans, LPA mediates macrophage formation using similar pathways. These findings identify critical role for LPA in regulating innate immune system.

b) Gene regulation and function: Several studies have been undertaken on host gene expression and regulation associated with cancer at ILS. The GSE4170 dataset analysis showed that EVI1 positively correlates with FUT8 in CML cell lines and patients samples. Furthermore, it was found that EVI1 blocks not only erythropoiesis but also the differentiation of erythroblasts through FUT8 in K562 cell line.

Whole genome sequencing of 15 new bacteria has been completed to elucidate the metabolic model and functional analysis of the genes linked to the phenotypic expression of the bacteria. Genome-scale reconstruction of the metabolic model has elucidated the functional activity of genes involved

in sulfur oxidation pathways in an obligatory mixotrophic bacterium *Thiomonas bhubaneswarensis* strain S10 (DSM 18181^T).

In order to make an ideal promoter system for optimal gene expression, the SA-inducible promoter (CmYLCV: -729 to +137 from TSS) from *Cestrum yellow leaf curling virus* was employed to study the interaction of SA-inducible Arabidopsis transcription factors, TGA3 and WRKY53. *In vitro* and *in vivo* DNA-protein interaction studies suggest that TGA3 and WRKY53 bind to -closely located as-1₁₍₋₆₄₉₎ and W-box₁₍₋₆₄₀₎ cis-elements present in the CmYLCV promoter. This interaction between TGA3 and WRKY53 resulted in the enhancement of CmYLCV promoter activity via NPR1-dependent salicylic acid signaling in Arabidopsis.

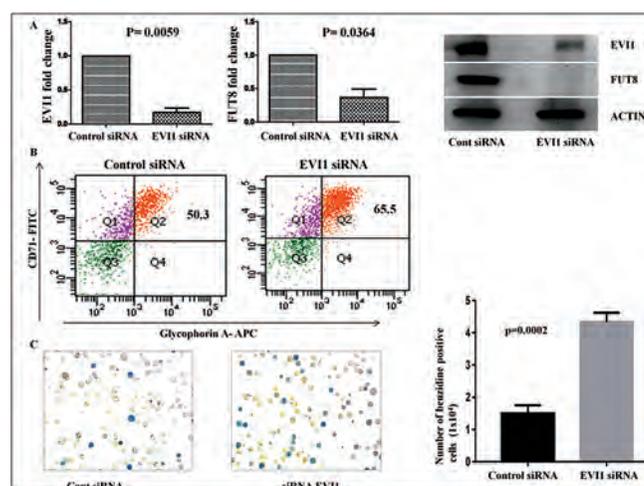


Figure 4. EVI1 and FUT8 block erythropoiesis in CML. A). K562 cells transfected with EVI1 siRNA and control siRNA. B). CD71/Glycophorin A expression. C). Increased number of benzidine-positive cells (blue staining) transfected with EVI1 siRNA with respect to cells transfected with control siRNA.

c) Translational research and Technology Development: A lipid based dual herbal drug loaded nanoparticles was developed which could be a potential candidate for CNS delivery and co-delivery of dual drug loaded Nano medicines to kill cancer stem cells. The cancer group working on *Oral squamous cell carcinoma (OCSS)* have observed that TIGAR (TP53-induced glycolysis regulatory

phosphatase) diverts the shunt towards Pentose Phosphate Pathway (PPP) and this leads to production of NADPH which cancer cell utilize for their survival during stress. The data suggests that TIGAR might have potential tumor initiating role in OSCC and therefore could be potential therapeutic target for OSCC.

In rice more than 250 putative miRNAs were identified. Presence and expression of several rice miRNA involved in salt tolerance were confirmed. In addition, several known miRNAs were also identified to be salt responsive with their expression decreasing more than 50 % in response to exposure of the plant to salt. An initial study on target prediction and validation revealed regulation of expression of the antioxidative enzyme like L-ascorbate oxidase, the expression level of which decreased more in the salt-sensitive rice cultivar Badami compared with the salt tolerant cultivar Pokkali, suggesting that the removal of reactive oxygen species could be one among several strategies being followed by plant for salt tolerance.

A collaborative agreement has been made during with Institute of Bioresources and Sustainable Development (IBSD), Imphal for undertaking research and development efforts for sustainable bioresource management in Odisha and Northeast regions of the country. A dedicated "Science Outreach Centre" was inaugurated during March 2017, with a focus for providing platform and opportunities for young students and scholar for inculcating scientific temper among them and also to organize dialogues and technology dissemination workshops for relevant stakeholders of the region.

RAJIV GANDHI CENTRE FOR BIOTECHNOLOGY (RGCB), THIRUVANANTHAPURAM, KERALA

Rajiv Gandhi Centre for Biotechnology (RGCB) continued with significant success innovative

research across various sectors of Biotechnology with a mandate to understand the underlying biology of human, animal and plant diseases and eventually develop a new complimentary approach to train individuals in translational biology and promote collaborations between clinical, veterinary and agricultural professionals with basic biology scientists.

Salient achievements in key areas:

a) Breast cancer: A novel anti-invasive mechanism mediated by Star-PAP/PIPKI α of key metastatic regulators was reported. Invasiveness of cancer cells was observed to be inversely co-related to cellular Star-PAP levels in breast cancer. This study has opened an avenue for translational research with Star-PAP/PIPKI α nexus as a direct or adjuvant therapeutic target to prevent cancer metastasis.

α -hCG has been shown to promote migration and invasion through TGF β RII signaling predominantly in BRCA1 mutant breast cancer cells. Studies have established that α -hCG induces expression of hemoglobin genes and protects the cancer cells during oxidative stress resulting in drug resistance.

b) Stem cell: It was hypothesized that Aprataxin PNK-like Factor (APLF), with insignificant expression in Embryonic stem cells, could act as a barrier in reprogramming of mouse embryonic fibroblasts (MEFs) to induce pluripotent stem cells (iPSCs). Studies proved that Histone chaperone HIRA is required to maintain the self-renewal status in hESCs. PHB, a metabolite with HIRA could contribute towards retention of pluripotent state of ESC. This study established that α -Keto Glutarate associates with pluripotent nature of both naïve and primed pluripotency.

c) Chikungunya: A proteomic analysis of CHIKV-infected human astrocytic cell line U-87 MG revealed tight interactomes among the modulated proteins, which were further identified. The results also

showed that NPM1/B23, a multifunctional chaperone, plays a critical role in restricting CHIKV replication and is a possible target for antiviral strategies. The analysis of expression profile of Interferon-regulated genes (IRGs) in the brain tissue in a mouse model of chikungunya virus (CHIKV) neurovirulence identified significant upregulation of 269 genes, out of which a predominant percentage (76 %) was IRGs. Concordant modulation of IRGs in both mice and human cells indicates that they might play important roles in regulating CHIKV replication in Central Nervous system (CNS).

d) Dengue: In a study to compare two closely related DENV serotype-2 strains; it was observed that these laboratory strains differed significantly in infecting human microvascular endothelial cells (HMEC-1) and hepatocytes (Huh7), two major target cells of DENV in *in vivo* infections. A comparison of the sequences of the two strains with published sequences of various DENV strains known to cause clinically severe dengue identified a number of amino acid changes which could be implicated as possible key genetic differences.

e) Tuberculosis: Rv3334 protein of *Mycobacterium tuberculosis* is a transcriptional regulator and is upregulated during hypoxia and other stress conditions. Studies have been done to establish that Rv3334 binds to its own promoter and acts as an autorepressor. DNA-binding activity of the protein was abrogated in the presence of certain divalent metal cations. Histone acetyltransferase, an enzyme that is required only in the eukaryotic context was first ever discovered in *M. tuberculosis*. Subsequently by ChIP seq it was demonstrated that the protein is recruited to nine promoters in infected macrophages.

f) A National Facility For Drug Discovery and Developmental Therapeutics: Envisaging the future of drug discovery and therapeutic development with the support from Department of Science & Technology (DST), Rajiv Gandhi Centre for

Biotechnology (RGCB) has established National Facility For Drug Discovery and Developmental Therapeutics (NFDDDT). 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.

g) BioNest: The BioNest is a unique program designed to provide infrastructure and scientific support that helps researchers, inventors, and entrepreneurs looking to transform biology or medical or cosmetic based technologies and innovations into full-fledged commercial enterprises. The facility located in Kochi, which is jointly managed by the Rajiv Gandhi Centre for Biotechnology and the Kerala Startup Mission. BioNest also offers hospitals in the Kochi area access to high end molecular diagnostics for infectious diseases, cancer and cardiovascular diseases at RGCB's NABL and NABH accredited facility, high end bioinformatics & computational analysis, DNA barcoding services for plant based material used in preparation of various nutraceuticals and plant based medicines as well as access to expert advice and assistance in IPR protection and related matters.

h) Services for the Ayurveda/natural medicine industry: RGCB has identified major programme on "Ayurveda Inspired Discovery". The program has clear objectives that include developing a center of excellence for generating knowledge on treatment response and effects on patho-physiological processes in response to Ayurveda based therapeutics.

i) Molecular Diagnostics: Laboratory Medicine and Molecular Diagnostics (LMMD) group dedicatedly works 24x7 to cater to the diagnostic needs of the people of southern Kerala. With high incidence of epidemics in Kerala, LMMD has significantly contributed in accurate outbreak investigations

through 42 viral and 4 bacterial tests assisting patients from various public and private hospitals in the region. Additionally, cancer and cardiovascular biomarker panels are being extensively used at the community level at highly subsidized rates for all and even free of cost for the under privileged. The panels of tumor recurrence prediction and tumor drug response as well as pharmacogenomics assay of Tacrolimus® post renal transplantation have been widely accepted by the medical community.

j) Regional Facility for DNA Fingerprinting: The major service of RFDF is to provide human DNA Fingerprinting services to judicial, crime investigating and law enforcing agencies. RFDF has expanded its DNA Fingerprinting services to flora and fauna including RAPD, AFLP or microsatellite marker-based studies, testing for genetic diversity analysis, species/population/variety discrimination, hybrid seed testing, Cox-1 based molecular identification and DNA bar coding of fauna especially for species identification in wildlife forensics.

k) Training and Education: RGCB holds a unique program “catching them young” for school students selected from various schools to do a three-month project at RGCB during weekends and summer holidays. A total of 110 students graduated from RGCB in the years 2007 to 2016.

l) International collaboration: RGCB and NIH have agreed upon a RO-1 Grant to study response and failure to measles vaccine in South India. RGCB and the International Agency for Research against Cancer & the Gates Foundation have agreed to extend the HOV Vaccine study till 2020.

REGIONAL CENTRE FOR BIOTECHNOLOGY (RCB), FARIDABAD, HARYANA

Regional Centre for Biotechnology (RCB) was established with a vision 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. It provides a platform for biotechnology education, training and research at the interface of multiple disciplines. The programmes of the Centre are designed to create opportunities for students to engage in multi-disciplinary research to provide solutions for human and animal health, agriculture and environment.

Major initiatives: The Centre has continued to pursue the various innovative research programs to create knowledge in the broad areas of biotech science. In study on transcription Regulation: Structure and Mechanism (FleN), a P loop ATPase was identified as a vital protein for maintaining a monotrichous phenotype in *Pseudomonas aeruginosa*. It exhibited antagonistic activity against FleQ, the master transcriptional regulator of flagellar genes. Crystal structures of FleN revealed that it undergoes drastic conformational changes on ATP binding to attain a structural remodeling which facilitated the formation of the functional dimer and helped the antiactivator attain a reversible form that could calibrate FleQ activity to an optimal level. Studies have been carried out on development of nanomaterials for biomedical applications focused on the engineering of the Synthetic Antimicrobial Polymers (SAMPs) derived from biocompatible polyamides for novel therapies to treat Mycobacterial infections.

The India-ESRF partnership: To continue the successful first phase of association with ESRF (2008-2016) a new agreement with the ESRF has been made. The agreement provides access to multiple and much better experimental stations for macromolecular crystallography, small angle X-ray scattering (SAXS) and the cryo-electron microscopy. India has become the 22nd country to join the ESRF. Since the start of this new agreement, scientists from 13 different institutes from all over India have obtained X-ray diffraction and small angle X-ray

scattering data for different macromolecules and macromolecular assemblies. The access to this international facility will enable Indian scientists to formulate innovative solutions to problems faced by the nation in public health and agriculture.

Human Resource Development: Thirteen young scientists are currently mentored by the RCB faculty. A multidisciplinary Ph.D programme has been instituted where 25 students were admitted in the academic year 2017-18. The RCB Act 2016 has also empowered the Centre to conduct an integrated M.Sc.-Ph.D degree program in Biotechnology, which will commence from the academic session 2018-19. An MoU has been signed between Tata Institute of Fundamental Research and participating institutions for conducting Joint Graduate Entrance Examination for Biology and Interdisciplinary Life Sciences (JGEEBILS) examination with a purpose to establish a combined entrance test for Ph.D and, where applicable, M.Sc. in life science and interdisciplinary streams. A joint mini-symposium on “Cellular Mechanisms in Health and Disease” was organized with Advanced Institute of Science and Technology (AIST) of Japan in February 2017. The 5th Molecular Virology meeting was hosted with THSTI in February 2017. The meeting brought together researchers from various Indian institutions working in various areas of virology. The Centre has also been regularly conducting short-term courses and workshops in the frontier areas of Life Sciences benefitting young and mid-career researchers.

TRANSLATIONAL HEALTH SCIENCE AND TECHNOLOGY INSTITUTE (THSTI), FARIDABAD, HARYANA

Translational Health Science and Technology Institute (THSTI) was established with the mandate to integrate multidisciplinary scientific teams from the fields of medicine, science, engineering and technology for generating translational knowledge

and make the biomedical innovations accessible to improve the public health. Scientists at THSTI have secured significant extramural funding from National and International agencies.

The Vaccines and Infectious Diseases Research Centre (VIDRC): The VIDRC is the first Centre of THSTI. Some of the significant achievements include: 1) a demonstration of VapC20 as an obligate homodimer, and its self-association is critical for its folding and activity. Surface Plasmon Resonance experiments suggested that VapC20 interacts with its cognate antitoxin VapB20 to form a stable complex with nanomolar affinity. 2) Scientists at HIV Vaccine Translational Research Laboratory (HVTR) laboratory proved that the broadly neutralizing antibodies elicited in HIV-1+ elite neutralizers typically are unable to reduce viremia in the same individuals from whom they are isolated. 3) A non-radioactive RNA Strand Displacement Assay protocol for measuring the dsRNA unwinding activity of the Hepatitis E virus helicase and also a protocol to assay the RdRp activity of many other viruses has been established. 4) Correlation between lncRNAs and severe dengue phenotype has been established. This would enable its application as prognostic marker for dengue virus-induced disease progression. 5) A new analog of 5-NP, 3-methyl-6-nitro-1, 10-phenanthroline with improved *in vitro* activity and *in vivo* efficacy in mice was designed. 6) Calcimycin was identified as a potent inhibitor of *Mycobacterium bovis* BCG growth *in vitro* and in THP-1 cells as well. 7) Monoclonal antibody pairs have been characterized and translated into rapid immunochromatography tests to specifically detect the viral nonstructural 1 protein antigen and distinguish four dengue virus serotypes and Zika virus without cross-reaction. 8) The ability of zinc salts to block HEV replication by virtue of their ability to inhibit the activity of viral RdRp was discovered. Since high-dose zinc is used in the treatment of Wilson's disease, it might be possible to control HEV-

associated health problems following a similar treatment regimen. 9) A novel STK1-targeted small-molecule quinazoline compound 'Inh2-B1' has been identified as promising antibiotic-resistance-breaker against multidrug-resistant *Staphylococcus aureus*. 10) Scientists at HVTR lab identified a new clade A Env, A5 which is efficiently cleaved on cell membrane, and can be used in DNA prime-protein boost vaccination studies with already identified BG505. 11) Scientists at HVTR lab engineered an HIV-1 B/C recombinant, native-like trimeric Env protein that is highly resistant to CD4-induced conformational changes making it suitable for use as antigenic bait for bnAb isolation, structural studies, and use as potential immunogens. 12) High activity of myeloperoxidase and neutrophil elastase was detected in the plasma samples of the follow-up and recovered dengue patients, the presence of a larger amount of cell-free dsDNA in the dengue-severe patients, suggesting an association of neutrophil-mediated immunity with dengue disease progression. The study has a great translational significance for the prognosis and management of the dengue patients.

The Pediatric Biology Centre (PBC): The PBC serves 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. Significant achievements are: 1) it was experimentally proved that there is no significant beneficial effect of zinc on the duration of recovery or risk of treatment failure in children with radiologically confirmed pneumonia. 2) Scientists at PBC discovered that addition of TNF to podocytes causes CD80 upregulation, actin reorganization and podocyte injury. Overexpressed CD80 and Neph1 interact via their extracellular domain and this interaction implies possible use of small molecules that disrupt CD80-Neph1 interaction as a potential for treatment of nephrotic syndrome associated with CD80

upregulation.

The Drug Discovery Research Centre (DDRC):

The DDRC is an inter-disciplinary center that works on disease interrogation, target identification and early stage development and also has a focus on metabolic syndromes, particularly diabetes. Some of the significant achievements are: 1) Scientists at DDRC experimentally proved that gap junctional coupling between excitatory and non-excitatory cells of heart muscles plays important role in the calcium dynamics 2) Scientist at DDRC were able to construct a network between biological processes through common genes and data was analyzed to obtain perturbed biological processes at each time point to identify paths linking initial perturbed processes with final perturbed processes which capture progression of metabolic disorders such as obesity and diabetes. 3) A mathematical model predicting host mitochondrial pyruvate transporter activity to be critical regulator of *Mycobacterium tuberculosis* pathogenicity and possible mechanistic target for drug discovery was also developed and validated experimentally.

The Centre for Human Microbial Ecology (CHME):

The CHME focuses on malnutrition, gut microbiota, and multi-drug resistance with ongoing studies on the role of the microbiome in the pathogenesis of type 2 diabetes, its effect on the immune response and the influence of diet and artificial sweeteners on gut microbial composition, role of effector and regulatory T cells in intestinal inflammation and of retinoic acid metabolites in regulation of the inflammatory response. In one such study, scientists at CHME have proved Foxo1 as a key transcription factor that dictates the development and effector functions of Th9, while IL-9-producing T cells could prove beneficial in designing targeted therapies aimed at alleviating the course of autoimmune diseases and anti-cancer therapy.

The Clinical Development Service Agency (CDSA): The CDSA has a unique mandate to provide cost-effective, high quality, not-for-profit technology-based preclinical and clinical product development as well as support services for clinical research conducted by various public institutions, academic institutes and small and medium enterprises (SMEs). A broad range of services offered by CDSA includes regulatory consultation, project management, clinical monitoring, medical writing, safety monitoring, audit, data management and biostatistics. CDSA has been involved in clinical monitoring of various projects such as project on Severe Acute Malnutrition (SAM), Preterm Birth and Reflexology studies, study on indigenously developed surfactant for preterm babies with Respiratory Distress Syndrome etc. It also has a mandate to guide, strengthen, coordinate, undertake and implement human resource capacity building in India for preclinical and clinical development and other related activities by conducting trainings and workshops across the country. CDSA conducted a total of 4 training sessions on Good Clinical Practices across 5 organizations with 228 participants. It has also conducted one training session on Ethical and Regulatory Requirements for clinical trials and research at ESIC Medical College and Hospital, Faridabad with 80 participants.

The Policy Center for Biomedical Research (PCBR): The PCBR was sanctioned with a mandate to bridge the gap between health researchers, who implement and who are impacted by that research by providing analysis on health technologies that could guide strategic planning to meet local health needs.

The Achievements in key identified areas of PCBR are:

a) Point-of-care Diagnostics: PCBR has partnered with DSS, New Delhi for creating a prototype to optimize LED as lighting source for microscopy. PCBR

facilitated Reamatrix, Bangalore for the validation studies, and optimization of ReaTBdx at SGPGIMS, Lucknow. PCBR has created a consortium for LAMP test implementation at Community Health Centers through MoHFW and NIB. PCBR in collaboration with NCDC, ICMR and Manipal Center for Virology in a CDC funded study successfully mapped 750 labs for their capabilities in doing diagnostics work as well as biosafety preparedness.

b) Vaccines: PCBR prepared a Roadmap for cholera prevention and control. The analysis of available data on cholera, led to identification of “hot spots” or regions with high risk of cholera in India. PCBR has been consulted by Global Alliance for Vaccines and Immunization as well as by the WHO’s Global Task Force for Cholera Control for a meeting on Ending Cholera: A Global Roadmap, for 2030. PCBR is also involved in committees set up by the Government for introduction of rotavirus vaccine, to provide inputs in technical issues such as cross over in the use of two different vaccines in the program. PCBR has analyzed global data on influenza and has observed high degree of morbidity and mortality in pregnant women. PCBR has created partnership with INCLIN to collect the baseline data and study the effect of Pneumococcal Conjugate Vaccine in pregnant women in India.

c) Neglected Tropical Diseases (NTDs): A roadmap for vaccine introduction in Kala-Azar elimination program is being created with analysis of shortcomings of four candidate Leishmania vaccines.

INSTITUTE FOR STEM CELL SCIENCE AND REGENERATIVE MEDICINE (INSTEM), BENGALURU, KARNATAKA

The Institute for Stem Cell Science and Regenerative Medicine (inStem) at Bengaluru is India’s first stem cell institute committed to accelerating advances in stem cell biology & regeneration to understanding disease. The thrust on interdisciplinary, thematic

research with translation emphasis has allowed inStem to tackle complex questions in ways that cannot be addressed in individual investigator-driven efforts. inStem has also been engaged with various international universities/institutes to enhance its technical and scientific capabilities. inStem's efforts have focused on building core strengths in stem cell biology and manipulations, in areas such as repair from injury or wounding, disorders of the brain and heart.

Salient achievements: The Centre for Cardiovascular Biology and Disease(CCBBD) at inStem, is establishing a consortium comprising clinicians and researchers across India through which 6000 South Asian heart failure patient samples have been organized and sequencing of protein-coding regions (exomes) of 30,000 genes have been accomplished for 100 donors. The initial analysis has identified possibly novel genes for South Asian specific cardiomyopathies. To understand how these genes function, two transgenic mice models, mimicking the disease in humans were generated. Notably, one of these was made at the state-of-the-art National Mouse Resource (NaMoR) Facility on campus. Studying how these proteins interact with other structural components of the heart, not only informs about differences in proteins from normal and diseased hearts, but also enables the application of this knowledge to develop cost-effective drug screening strategies for repurposing approved drugs.

At Centre for Inflammation and Tissue Homeostasis (CITH), attempts are being made to restore organs in the body that are lost during injury. In recent work, a specialized subset of immune cells in the skin known as $\gamma\delta$ T cells has been shown to play a major role in activating stem cells, so that they can perform their role in rebuilding the skin following a wound. Scientists have identified a protein that appears to cause human cells in culture in the laboratory, to age (Figure 5). Such studies will assist in understanding of how tissue normally functions and

how it breaks down during aging and disease.

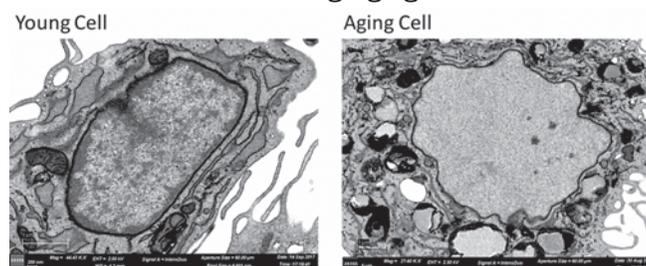


Figure 5. Images to show the shape of the nucleus (the compartment in cells where DNA is stored) in a young cell (left) and the changes in the shape of the nucleus in an old cell (right).

The Technologies for the Advancement of Science (TAS) theme develops technologies and catalyzes new approaches to solve difficult problems in fundamental and applied biology. Scientists in this theme have reported fundamental discoveries in natural light sensing which has shed new light on eye evolution, while helping map functional eye-brain regeneration. New methods for biomaterial delivery was developed that work for model organisms as well for inflammation alleviation. The technology to deliver nucleic acids into flatworms is already paving the path towards uncovering interesting facets of the regeneration process.

Work at the Centre for Brain Development & Repair (CBDR) has established the robust re-programming protocols to generate iPSCs, a biorepository of human LCL and iPSC cell lines and protocols for neural differentiation. Fully operational breeding-colonies of nine new transgenic rat models of highly penetrant single-gene causes of ASD/ID to better animal model systems that can accurately reflect autistic symptoms in humans have been established.

Efforts over the past year at the Centre for Chemical Biology and Therapeutics (CCBT) at inStem, has led to the first exemplification of a new strategy to interrupt intracellular signaling pathways via molecular recognition of phosphorylated proteins. Bractopin, a selective, potent, drug-like inhibitor of the BRCT domain family, had been discovered and characterized chemically and biologically.

A National Cryo-EM facility has been set up under the aegis of a Multi-scale Basic and Applied Research program as a joint effort between inStem and NCBS. The recent installation of the 300 keV microscopes with state of the art detectors and automation is a major technological capability, the first of its kind in India, allowing molecular exploration of biological function and is a major technological capability in campus. The formal inauguration of the facility is scheduled in January 2018.

Centre for Stem Cell Research (a translational unit of inStem, Bengaluru) at Christian Medical College Campus, Bagayam, Vellore: The Centre for Stem Cell Research 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.

Salient achievement:

a) Gene therapy: This program involves two major areas at present – The first is directed towards a clinical trial for AAV vector based gene therapy for haemophilia B: A novel transgene construct was developed and evaluated in human hepatocytes and in haemophilia mice. It is now being tested in various models for dose finding, safety, toxicity and biodistribution. Apart from this, the clinical gene therapy program is also being developed with screening of patients for AAV antibodies and development of the clinical trial protocol. A potential target for the reactivation of fetal haemoglobin has been identified and a CRISPR/Cas9 based ribonucleoprotein system has been developed for genome editing of the identified target. Using the Multiplex genome editing approach, successful cleaving of the target sites both in human embryonic kidney cell lines and human umbilical cord blood-derived erythroid progenitor (HUDEP) cell lines has been achieved. For therapeutic genome editing for hematological disorders, a 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. The group 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. In parallel, ribonucleoprotein based system (RNP) is being used to cleave the target locus in hematopoietic stem cells.

The second part of the gene therapy program involves preclinical models for lentiviral vector based gene therapy through hematopoietic stem cell for the major haemoglobin disorders. New lentiviral vectors carrying the beta globin gene are being tested in human ex-vivo erythropoietic systems developed at CSCR and in parallel experiments in mouse models. A liposomal formulations with anti-oxidant lipid as an efficient delivery system has been developed for enhanced transfection with quenching of Reactive Oxygen Species (ROS) levels. A novel strategy called green transfection in which cationic nano carrier system derivative from vegetable oil, palmstearin (PS-Lips) have been developed. These nanocarriers system could efficiently deliver mRNAs into haematopoietic cells. Work is in progress towards development of first indigenous commercial transfection reagent. Patent filing for novel liposomal transfection formulations is also under process.

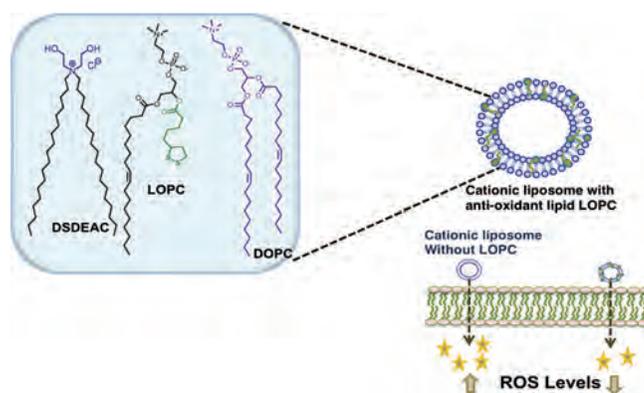


Figure 6. Chemical structures cationic amphiphiles synthesized from Palmstearin. Schematic illustration shows the complex formation between PS-Lips and pDNA.

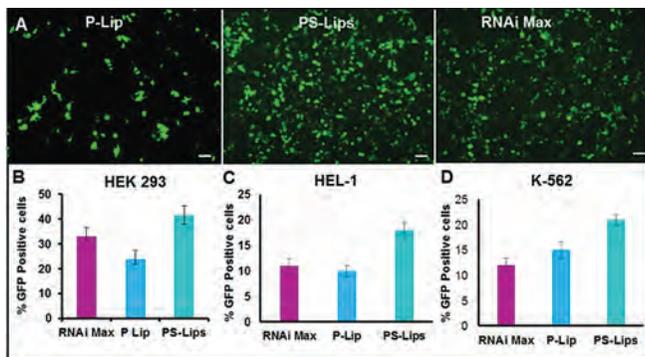


Figure 7. Comparative *in vitro* mRNA transfection efficiencies of PS-Lips & P-Lip in adherent cell line, HEK 293 (A&B); and suspension cell lines, HEL-1 (C); K-562 (D). Lipofectamine RNAi Max was used as positive control for mRNA transfections.

b) Musculoskeletal regeneration: The major focus of this program is on clinical translations related to physis, articular cartilage and bone regeneration. For articular cartilage regeneration, ongoing small and large animal studies have articular defect reconstruction with differentiated MSCs on indigenous scaffolds. In a first of its kind study, reconstructions of bone defects in children with MSCs differentiated to osteoblasts on ceramic scaffolds have shown good outcome in the first 5 cases. Further, a larger trial is being planned to be performed.

c) Haplobanking: A major translational effort has also been initiated towards establishing a “haplobank” as a part of an international consortium called the Global Alliance for iPSC Therapies (GAI_T) for potential use in regenerative medicine in the future.

Other Programmes:

a) Somatic cell reprogramming: iPSC lines from the fibroblasts of a patient with Fanconi anaemia (FA) have been generated by non-integrative methods. Currently, these iPSC lines are being used to understand the molecular basis of Fanconi Anaemia disease pathogenesis.

Novel multifaceted approach to widen the therapeutic window of spinal cord injury in SCID mice

model using FDA approved material, indocyanin green (ICG) a method of labelling of mesenchymal stem cells (MSCs) and *in vivo* tracking of labelled stem cells in mice using live cell imaging system has been developed and a patent application has been filed for this technology.

Tissue Engineering: Studies have been undertaken for design, fabrication and characterization of various nanofibrous-based tissue grafts (flat and hollow-types) suitable for regenerative medicine. Development of biomaterials as a carrier system for the delivery of stem cells, in particular injectable gel-based stem cell delivery systems, for osteochondral and cardiogenic applications is under progress.

NATIONAL INSTITUTE OF BIOMEDICAL GENOMICS (NIBMG), KALYANI, WEST BENGAL

NIBMG was established in 2009 with a vision to enhance knowledge on human health and disease through genomics and translate the knowledge using appropriate technologies for promotion of well-being and improvement of genetics based health care in India. 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, University of Chicago etc. Students and faculty members of the Institute have received national and international awards and

recognitions. The campus is now vibrant and fully functional with most of infrastructure being completed.

Major initiatives: To accelerate genomics in health and disease, the Institute is successfully running a laboratory for collaborative research with clinicians called the Biomedical Genomics Unit (BMGU) for open access to its high-end platforms to national institutions in which such infrastructure is required. Studies are ongoing to understand the role of microbes inhabiting the skin of humans in the development of various skin conditions, such as acne, psoriasis, dermatitis etc.

India gained the status of a founding member of the “International Cancer Genome Consortium” with efforts of NIBMG and DBT. In a study focused on oral cancer, various gene alterations were identified which could be used to predict the extent of survival of an oral cancer patient after surgery by screening just a few genes. In another major study on cervical cancer, HPV16 virus was observed to cause the cancer by acquiring certain genetic and epigenetic changes in the viral genome that correlate with the activation of certain host cell signaling pathways. CKS1B, a gene of this pathway that activates cell proliferation was highly expressed in such cancers but not in those that had integrated HPV16. An inhibitor of this gene which is actually prescribed to patients with manic depression could be relevant for treating such cancers. Studies on infectious disease genomics based on transcriptomic analysis of blood samples revealed up-regulation of gene expression in osteoclast differentiation in human septic shock. In this area, it has also been identified that age and gender can act as effect modifiers in the association of the functional IFNL4-generating polymorphism with allergy and clinical features of asthma in a Polish population. Studies on tuberculosis revealed that key metabolic pathways of the host cell might be more critical for regulating the intracellular mycobacterial load, in the context of

granuloma formation. Life course epidemiology has been initiated with 50,000 recruited individuals to understand the role of environmental factors in modulating the effects of genes. Blood profiles and clinical profiles are being collected repeatedly for in-depth studies on genetic and environmental interactions

Salient achievements:

a) Teaching and Training: One student has acquired PhD degree and two students are awaiting the award of PhD degree. Besides, as part of short term training, a total of 13 trainees were recruited of which, 4 were from the Academy Summer Research Fellowship Program and the rest from various Universities across the country.

b) Establishment and sustenance of CoTeRI: Formidable capacity for massively parallel nucleic acid sequencing was built and two global records of sequence data generation in a single experiment were created. In the last five years, data equivalent to about 10,000 human genomes were generated cutting costs of sequencing using various innovative experimental approaches. To share the infrastructural resources with other researchers in India to facilitate pursuit of genomics, “Core Technologies Research Initiative” program (CoTeRI) has served the genomics needs of researchers in over 40 universities and national institutions, including the laboratories of the NE region. The demand for accessing CoTeRI is increasing steadily.

c) Establishment of Systems Medicine Cluster (SyMeC): NIBMG has catalyzed a collaborative ecosystem by bringing six institutions to work together towards the goal of fostering systems medicine - Bose Institute, Indian Institute of Chemical Biology, Indian Statistical Institute, Tata Medical Centre and the Indian Institute of Science Education & Research. The project has been funded by the Department of Biotechnology under the “Biocluster” scheme. Preliminary evidence of DNA alterations that

drive metastasis in oral cancer has been obtained. Work on many clinically relevant problems that relate to susceptibility, diagnosis, early detection of risk exposures, and new methods to integrate and analyze multiple data types for more robust inferences has been initiated.

d) Outreach Programs: An outreach open house program and panel discussion on flagship programs of Govt. of India such as “Swasth Bharat”, “Digital India” and “Climate Change and Sustainability” was organized which was attended by more than 80 students from different schools. A visit of various laboratories in NIBMG with hands-on experiments has also been conducted in a session for school students where faculty members and research scholars from NIBMG, IISER-Kolkata and Kalyani University participated.



Figure 8. India International Science Festival: Public Outreach & Open Day Program, held on September 18, 2017

NATIONAL AGRI-FOOD BIOTECHNOLOGY INSTITUTE (NABI), MOHALI, PUNJAB

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. Institute is working in the five core areas that includes, (I) Improving cereals for nutrition and processing quality; (II) Improving fruits

for postharvest 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: NABI researchers are engaged in development of designer crops with high nutrition, increased shelf life and processing quality. Research is ongoing to improve the nutritional and processing quality in wheat. Functional genomics strategies for improving micronutrient transport and its bioavailability in wheat have also been employed. Genetic Transformation of Banana for Quality Improvement for enhanced provitamin-A is another prime area where work has been initiated with the support from BIRAC. In the area of bioinformatics development of advanced algorithms, databases, tools and pipelines for data mining and comparative analysis of food crop genomes, transcriptome and small RNA based regulation have been done. Transcriptional regulation of seed development and maturation in plants is also ongoing. NABI has also developed biodegradable and nontoxic coating materials for the post-harvest shelf life improvement of fresh fruits. In the area of food and nutrition, researchers are manipulating the beneficial gut bacteria as a strategy for the management of metabolic disorders. Additionally, fabricated nanomaterials in food for enhancement of micronutrients bioavailability and food safety has also been undertaken and currently its efficacy and its related studies are being performed.

Salient achievements: In a tilling (EMS treated) based approach to develop resistant starch in wheat; mutant lines showing variation in amylose content and resistant starch were developed. Some of high amylose mutants are being used for introgression of high amylose into high yielding varieties as well as for molecular and genetic basis of high amylose. Advance generation (M6) of 101 mutant lines showing variation from 3 to 76% amylose was produced and evaluated for starch,

amylose, and resistant starch. Out of them 24 mutants were evaluated for agronomical traits for producing advanced breeding lines. In an attempt to develop colored wheat lines with high anthocyanin content for nutraceutical applications, several advanced colored wheat lines with bright color and bold seeds have been developed through breeding method. Yield of advanced lines is comparable to high yielding cultivars. The anthocyanin content and antioxidant activity of different colored wheat and its products was in the order of Black<Blue<Purple <White. Colored wheat lines showed anti-obesity effect on high fat treated mice. *In vivo* studies using high fat diet induced obesity models suggested that black and purple wheat lines could effectively prevent fat deposition, improve glucose homeostasis, insulin tolerance, lower the serum cholesterol and free fatty acids levels. To increase the bioavailability of micronutrients in wheat; gene encoding for inositol pentakisphosphate kinase (*TaIPK1*) involved in biosynthesis of PA was targeted for gene silencing to develop low phytate wheat. Towards improving provitamin-A in Banana, several transformation experiments have been performed to generate desirable numbers of transgenic lines. Carotenoid profiling in contrasting cultivars, Nendran and Rasthali were studied for changes in carotenoids in fruit-peel and pulp as collected at unripe and ripe stages. In the area of food and nutrition biotechnology, multiple leads were obtained. Glycoconjugates capped multifunctional Gold nanorod based nano-biosensor was developed to detect food borne bacteria and efficacy of the kit is currently being studied.

Fabrication of the nanomaterials in food for enhancement of micronutrients bioavailability is also been addressed at NABI. In this area, *guanosine diphosphate* (GDP) was encapsulated within the lipid vesicle to increase its delivery, stability, specificity and efficiency along with improved pharmacokinetic properties. Characterization of encapsulated GDP

performed using SEM and TEM showed that encapsulation did not cause any distortion in the structure.

In the area of post-harvest technology development, the composite film formulations containing wheat straw AX and oat bran polysaccharide-fatty acid esters exhibited improved functional properties. These properties included significant reduction in water vapor transmission (~67-85%), improved mechanical strength (~10-13 MPa), thermal stability (> 200 °C) and film transparency (60-75%). The emulsion based composite film formulations were further coated on the surface of fresh fruits (apple) and the studies to determine the efficacy of the coating materials for the postharvest quality improvement are under progress.



Figure 9. Coloured wheat lines generated at NABI and their seed sections. Purple colour is in pericarp and blue colour in aleurone. Black wheat has both the colours.

NATIONAL INSTITUTE OF ANIMAL BIOTECHNOLOGY (NIAB), HYDERABAD, TELANGANA

National Institute of Animal Biotechnology is aimed to harness novel and emerging biotechnologies and take up research in the cutting edge areas for improving animal health and productivity. The mandate of the institute is to develop human resource across the value chain and is developing the human resource through Ph.D programme, project staff training and hosting women scientists

having fellowship in the area of animal biotechnology. Further, the Institute is reaching to the local schools and colleges to connect NIAB scientists with national educational needs of schools and colleges.

Major initiatives: Research at NIAB is focused on infectious diseases, reproductive biotechnology, genetics & genomics, bioinformatics, nutrition & metabolic diseases of livestock and poultry, transgenesis and therapeutic proteins. Towards developing improved diagnostics and vaccines for brucellosis, immunodominant antigens of *Brucella* were identified through immunoproteomics. An antigen BM-5, strongly reacted with sera from infected animals and humans, and not with serum from S19 vaccinated cattle, hence being potentially useful in the differentiation of infected and vaccinated animals. BM-5 antigen was used to develop a prototype Lateral Flow Assay (LFA) device for detection of brucellosis in animals and humans (see figure 10).

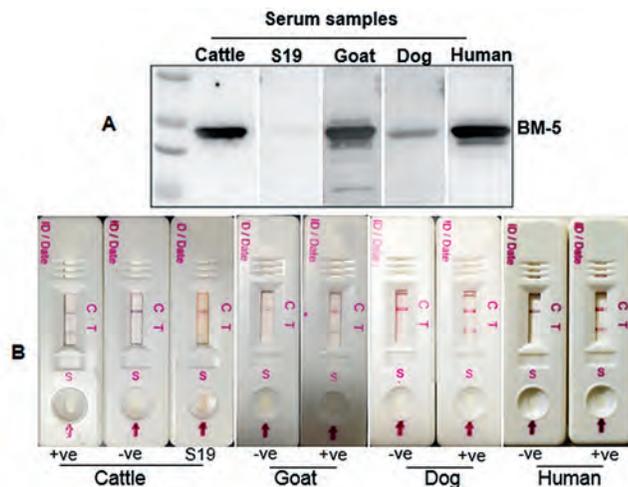


Figure 10. A: Immunoprobings BM-5 antigen with serum samples; B: Testing of LFA device with negative or positive sera.

In an effort to identify and characterize host factors that support the invasion and intracellular replication of *Brucella* in macrophages, *Brucella* protein TcpB was identified which interacted with cellular protein CLIP170, and suppresses Toll-like receptor 2 and 4

signaling, leading to attenuation of the host pro-inflammatory response. The study would be helpful in developing novel anti-*Brucella* drugs and preventive strategies to control brucellosis.

For understanding host immune response and development of vaccine against leptospirosis, several outer membrane proteins of *Leptospira* were cloned and expressed. *Leptospira* proteins Lsa21, LigA and LigB were identified to induce strong innate immune responses in macrophages, through the activation of Toll-like receptors. The mechanisms and their potential to serve as subunit vaccines are currently being investigated. In addition, the institute is embarking on a systematic approach to evaluate different adjuvants/vaccine delivery systems like liposomes, microparticles, nanoparticles, herbal adjuvants, etc., to identify potent adjuvants for animal vaccines.

Studies were undertaken for molecular characterization of non-structural viral proteins of Newcastle disease virus (NDV) to understand their roles in host-virus interactions. NDV genome carries six genes, one of which (the P gene) is co-transcriptionally edited to produce two non-structural proteins V and W. It was found that V protein supports viral RNA replications and shields dsRNA (viral replicative intermediate) to prevent interferon response. In addition, overexpression of W causes apoptosis, the mechanism of which is under investigation. Institute is in the process of setting up a reverse genetics system to mutate the V and W proteins to further understand their functions and to develop novel vaccines.

Microsatellite analysis and genetic diversity studies using immuno-dominant antigens to understand the pathogenesis of *Theileria*, showed polymorphisms and significant sequence diversity between the prevalent strains and current vaccine. Further, screening of 550 cross-bred animals from the endemic areas could identify 181 susceptible and

369 resistant/tolerant animals based on microscopy and qPCR. Further, genotyping analyses using the Illumina/Agilent Bovine chip for identifying the disease related markers/loci are being carried out. In order to understand host-parasite interactions, *Theileria* infected bovine cell lines were established from the peripheral blood mononuclear cells of infected animals. Studies have also been initiated on profiling of exoproteome and total proteome of the selected virulent isolates of mastitis-associated *Staphylococcus aureus* for identification of the virulence genes.

In a study to understand the role of novel cell cycle regulators orchestrating the unique cell cycle and transcription of *Toxoplasma gondii*, the role of Cdk-related kinase, Crk9 was identified in transcription elongation, mediated through phosphorylation of conserved serine residue in the heptapeptide repeats of C-terminal domain of the large subunit of RNA polymerase II, TgRpb1. Multiple modes of TgCrk9 regulation indicating an overall unique molecular mechanism of transcriptional control to cater to the special needs of the parasite was established. The study could lead to rational drug design programs.

In another study *Sphingobium fuliginis*, a prominent organophosphate degrading microorganisms which affects animal health and production was sequenced, assembled and two novel chromosomes (3.8Mbp and 1.2Mbp) and four plasmids (27 to 224 kb) were identified. The two chromosomes were shown to harbor 5100 protein coding genes, 9 rRNA and 55 tRNA genes.

NIAB has initiated a program on the development of an easy method of transgenesis of farm animals, as well as *in vitro* maturation and fertilization of goat oocytes. The healthy embryos, once obtained, would be used for male pronuclear DNA injection. Testicular transgenesis establishment in farm animals is underway.

In order to conserve indigenous breeds and to

implement genomic selection to increase milk yield, a program to decipher the genetic makeup of indigenous cattle breeds has also been initiated.

CENTER OF INNOVATIVE AND APPLIED BIOPROCESSING (CIAB), MOHALI, PUNJAB

The Center of Innovative and Applied Bioprocessing (CIAB) is working on development of processes and products from secondary agriculture produce. Institute is also developing bioprocesses and innovative technologies to meet the translational need of industries. Institute is significantly contributing towards human resource generation by imparting training to students in the areas of bioprocessing and secondary agriculture.

Salient achievements: A thermo-stable and recyclable magnetic nanobiocatalyst has been developed for bioprocessing of agro-industrial residues and D-allulose synthesis. The nanobiocatalyst was employed for treatment of fruit pomace wash, resulting in D-allulose production from the low-cost feedstock. A liquid whey beverage product named CIAB-NAVITA has been developed. The liquid whey, which is rich in protein and lactose, is transformed into a nutraceutical beverage enriched with prebiotic dietary fibers derived from fruit processing residues such as kinnow pulp. An efficient process based on xylanase and magnetic-xylanase CLEA for xylo oligosaccharides production from agro biomass has been developed. Interestingly, hydrolysis of rice straw and corn cob by both types of enzymatic forms was found to produce predominantly xylopentose and xylohexose. A 'Farm Gate Technology' for the recovery of the natural tartaric acid from geranium biomass (*Pelargonium graveolans*) was developed. Iron fortified turmeric- a value added product for every house to improve iron deficiency has been developed. An efficient process of production of

bacterial cellulose from tomato juice has been developed and characterized for purity. Levulinic acid (LA) was produced in a co-solvent, biphasic reactor system consisting of dilute HCl (aqueous) and dichloromethane organic solvent. The modified protocol achieved a 15% wt. LA yield through the synergistic effect of using a mineral acid and acidic products (auto-catalysis) and the solvent system which allowed facile recovery of LA from the organic phase. Further purification of the resulting extractant was achieved through conventional column chromatography and charcoal treatment. Furthermore this system allowed the solvent to be easily recovered, in excess of 90%, which was shown to be able to be recycled up to 5 recycle runs without significant loss of final product concentrations. Convenient, safe, and scalable chemical processing has been developed for the production of citronella essential oil variant with respect to citronellol. Almost complete conversion of citronellol to *cis/trans*-rose oxide has been achieved in citronella essential oil variant. A mix blend of fragrance with high sensory ranking could be produced by mixing native citronella essential oil with rose oxide value added citronella oil.

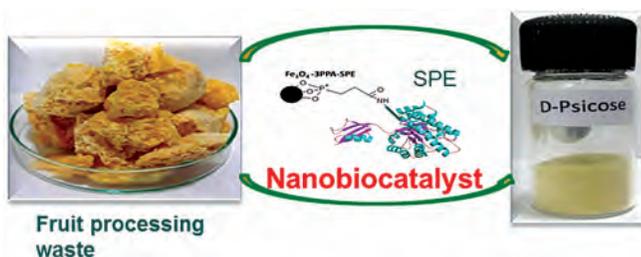


Figure 11. D-Psicose production from fruit processing waste by using Smt3-D-psicoe 3-epimerase

Technology Transferred: Low calorie sugar (D-psicose) from fruit processing residues/ fructose (Patent Appl. No. 201611003411) was transferred to Nagarjuna Fertilizers and Chemicals Limited, Hyderabad and CIAB-NAVITA: Liquid Whey Health Drink (Patent Appl No. 201711008368) was transferred to Diovita Foods Pvt. Ltd., New Delhi.

BIOTECH SCIENCE CLUSTERS

Systems Medicine Cluster (SyMec), Kalyani, West Bengal:

A cluster for multi-dimensional research to enable Systems Medicine: Acceleration using a Cluster Approach (SyMeC), at Kalyani, West Bengal was formed with six participating institutions; National Institute of Biomedical Genomics (NIBMG) [Core Institution], Bose Institute (BI), CSIR-Indian Institute of Chemical Biology (IICB), Indian Institute of Science Education & Research (IISER), Indian Statistical Institute (ISI) and Tata Medical Centre (TMC) to investigate and understand the dynamic systems of the human body as part of an integrated whole, and identify perturbations that cause disease, in order to implement Systems Medicine using cancer as an exemplar; provide improved tools for prediction, prevention and treatment of diseases using a Systems Biology approach; create a platform for multi-disciplinary training to build a cadre of scientific, clinical and technical personnel required to drive and to sustain Systems Medicine. During the year, a multi-institutional approach was evolved to excavate biological systems that precipitate disease and correlated outcomes. Preliminary evidence of DNA alterations that drive metastasis in oral cancer has been obtained. Many clinically relevant problems that relate to susceptibility, diagnosis, early detection of risk exposures, and new methods to integrate and analyze multiple data types for more robust inferences have been initiated.

NCR Biotech Science Cluster, Faridabad: The NCR Biotech Science Cluster has been established at Faridabad by the Department with an overall objective 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 cluster has established an 'Advanced Technology Platform Centre (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. A biotechnology Incubator has been established as part of the Biotech Science Cluster in partnership with BIRAC. This state of the art facility 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. Highly-equipped common facilities including BSL-3 facility have been set up at NCR-BSC taking into account the complex nature of research being undertaken by the cluster partners. An engineering workshop was conducted to support the cluster partners in generating fine mechanical/electronic designs for a wide range of biotechnologies to integrate medicine, engineering and physical sciences towards applications in bio-design and engineering. An Office of Connectivity was set up to serve as a nodal point to facilitate establishing an effective scientific network.

Bangalore Life Sciences Cluster, Bengaluru:

A multi-scale Basic and Applied Research in Biological Sciences (B-LIFE) Cluster has been set up to advance Multiscale Basic and Applied Research in Biological Sciences. The goal is to leverage the strengths that exist in the cluster institutions made of The Institute for Stem Cell Biology and Regenerative Medicine (inStem), National Center for Biological Sciences (NCBS) and the Center for Cellular and Molecular Platforms (C-CAMP) to create new initiatives that cannot be carried out as a single institutions mandate. The strength of the partner institutions in the Bangalore area like the Institute for Bioinformatics and Applied Biotechnology (IBAB), The University of Agricultural Sciences, Indian Institute of Science, National Institute of Mental Health and Neuro Sciences will all contribute to the success of

these programs.

A facility with a state of the art 300 KV electron cryo-microscope was physically installed. Using the microscope some images of ribosomes were collected to test the quality of the microscope. Scientist from UCLA has been working as a visiting scientist and has contributed to setting up of a state of the art membrane protein expression, purification and crystallization facility. The facility has been used to initially express a sialic Acid transporter, whose structure has now been determined and manuscript writing is in progress. Two eukaryotic membrane proteins, one that diffracts to 3.5Å resolution and other to 7.0Å resolution have been crystallized. Structure determination of these proteins is under progress.

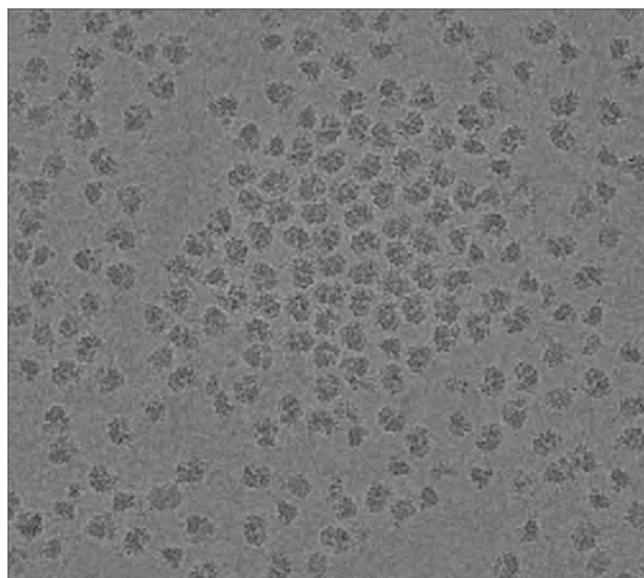


Figure 12. Electron micrograph of Planarian 80S ribosome collected at Bangalore

Under B-Life programme, the Govt. of Karnataka's Dept of IT, BT and S&T appointed IBAB as the nodal centre for the B4 programme (Boston-Bangalore Biosciences Beginnings). About 25 students have been trained in different labs in big data projects. Under the ambit of the grant, three short courses on Computational Neuroscience (Computational

Approaches to Memory and Plasticity) have been conducted, which prompted several students to take data and computational science research in neuroscience. In addition to manpower development, project personnel under B-Life have worked on the multiscale neuronal simulator MOOSE. MOOSE is now at release 3.1.1. In collaboration with another DBT-funded project (CNS) and the University of Edinburgh, MOOSE is being used to develop a detailed signaling model of synaptic function in health and disease. This model already incorporates over 500 reactions and molecules. Currently modelled pathways target autism spectrum disorders. This model development process is designed to be scaled up to incorporate many other signaling pathways involved in other neuronal disorders.

11

Public Sector Undertakings

BHARAT IMMUNOLOGICALS AND BIOLOGICALS CORPORATION LIMITED (BIBCOL)

Bharat Immunologicals and Biologicals Corporation Limited (BIBCOL) is a Central Public Sector Unit (PSU) promoted by the Department of Biotechnology (DBT), Ministry of Science & Technology, Government of India with primary objective of eradication of Polio from the country. With continuous support of Department of Biotechnology, BIBCOL has achieved this vision of Government of India and now Company is in diversification mode to include another vaccines and pharmaceuticals.

S. No.	Year	Turnover	Profit before tax
1	2013-14	202.75	11.0
2	2014-15	146.22	2.01
3	2015-16	128.03	(7.07)
4	2016-17	124.18	9.45

In addition to bOPV in vaccine segment, BIBCOL has been manufacturing and marketing dispersible Zinc Tablet in Pharmaceutical segment, and now launching the RUTF in commercial market. BIBCOL is in process of developing a vaccine candidate like Oral Cholera Vaccine and setting up the facility for production of plasma fractionation for production of plasma derived medicines (PDMs).

BIBCOL has contributed in the vision of Government of India to eradicate the polio from the country. BIBCOL has ambitious plans not only for its long term sustainability and better growth but making significant contributions for the better health of the masses of our country. The company is trying to establish a facility for the production of life saving drugs for the country at very affordable prices.



INDIAN VACCINES CORPORATION LIMITED

Indian Vaccines Corporation Limited was incorporated in March 1989 as a Joint Venture Company promoted by Govt. of India (Dept. of Biotechnology) Pasteur Merieux Serum & Vaccins (PMSV). France and Indian Petrochemicals Corporation Ltd. (IPCL- a PSU) taken over by Reliance Industries Limited (NON-PSU) with a paid up capital of Rs. 18.78 crores, with the objective of manufacturing vaccines based on Vero cell Technology to be supplied by PMSV France. The company came into existence 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. exited from the J.V. in 1998 by selling its shares to DBT.

IVCOL is presently being controlled by a board of

Directors, with two Directors representing RIL and Two Director representing GOI (DBT). Company has been incurring losses for the last two years (Rs.164.37 laces for 2014-15 and Rs.208.22 for 2015-16) and has accumulated losses of Rs.996.39 laces as of 31.03.2017.

Shareholding of IVCOL at percent 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 Section 8, Schedule B, Public Sector Enterprise, set up by the Department of Biotechnology (DBT), Government of India as an Interface Agency to strengthen and empower the emerging Biotech enterprises specially the start-ups and SME's to undertake the strategic research and innovation, addressing nationally relevant product development needs. BIRAC has been taking into consideration the recent scientific advances and commercial successes which have captured the attention and aspirations of policy makers, business people, and investors consequently. This in turn has further propelled the growth of biotechnology sector by supporting factors responsible for entrepreneurship activity, productivity, and sustainability.

BIRAC's vision is primarily to act as a boon for the bioeconomy of India as well as its global partners. There are three main verticals in which BIRAC operates to accomplish its mission viz.:

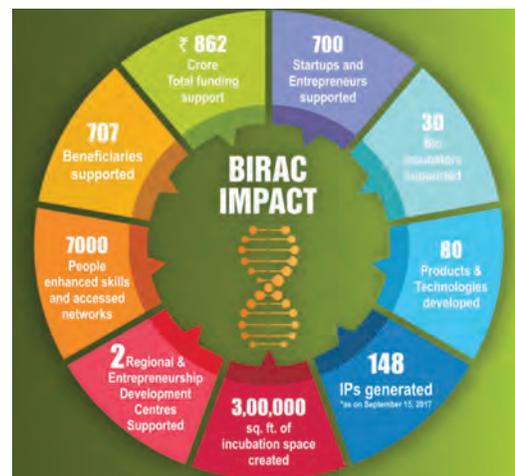
- *Investment: Providing risk capture across the Product Development value chain*
- *Entrepreneurship Development: Nurturing the ecosystem by providing the enabling environment*
- *Strategic Partnership group: Leveraging and*

fostering global and national partnerships

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, taking forward to its validation and scale up, and then right upto pre-commercialization. There are also special product development missions. The *Entrepreneurship Development* domain of BIRAC 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. BIRAC's *Strategic Partnership group* works closely with all the national and international partners including government departments and concerned 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.

→ **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 has been able to create the following impact:



During the year 2017, BIRAC has supported a total of 715 different projects across multiple domains of biotechnology. 32 new projects were supported from April 2017 to December 2017 along with the commercialization of 11 new products and 17 new IPs being filed during this period.



Investment Schemes - The Backbone:

a) Biotechnology Ignition Grant (BIG): BIG is the flagship early stage funding program of BIRAC, which has motivated and ignited more than 250 ideas over last 5 years of its operationalization. So far, more than 2300 applications have been received under 11 calls of BIG. BIG has facilitated creation of more than 75 new start-ups, supported more than 50 women entrepreneurs, and generated more than 700 high skilled workforces. More than 90 IPs have been filed by the BIG grantees during the course of their projects. Another major highlight of the success of this programme is the ability of BIG grantees to secure further follow-on funds through other government and private sources.

b) Small Business Innovation Research Initiative (SBIRI): SBIRI has prioritized early stage funding for high risk innovative research. The projects with high societal relevance supported under the programme have resulted in prominent outcomes in the form of products which have already come to the market.

Till date 229 projects have been supported under this programme.

c) Biotechnology Industry Partnership Programme (BIPP): BIPP is an advanced technology scheme which supports high risk, high innovation accelerated technology development 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 184 projects involving 144 companies and 47 academic institutes. In the current year, 2 calls were announced under BIPP scheme through which 5 projects have been supported and 2 are under consideration.

d) Promoting Academic Research Conversion to Enterprise (PACE- AIR and CRS): To encourage/support academia to develop technology/product (up to PoC stage) of societal/national importance and its subsequent validation by an industrial partner, BIRAC has launched Promoting Academic Research Conversion to Enterprise (PACE) Program on 15th June 2017. The Programme has two components as below:

d.1) Academic Innovation Research (AIR):

The objective of Academic Innovation Research (AIR) programme is to promote development of Proof-of-concept (PoC) for a process/product by academia with or without the involvement of industry.

d.2) Contract Research Scheme (CRS):

Contract Research Scheme (CRS) aims at validation of a process or prototype (developed by the academia) by the industrial partner.

So far, 28 projects have been supported under CRS. During 2017-18, one general call and one special call for proposals on developing novel tools/technologies/processes and product optimization/Scale up of "Anti Snake Venom" have been launched under SBIRI as well as under CRS.

The Entrepreneurship Development- Fostering Innovation: In order to foster innovation, BIRAC has taken several initiatives to promote entrepreneurship and has achieved considerable success.

a) BIRAC BioNEST (BIRAC–Bioincubation: Nurturing Entrepreneurs for Scaling up Technology): Under the BioNEST programme, BIRAC has established 30 world-class bio-incubators across the country and has created around 300,000 sq. ft of incubation space. These incubators offer incubation space and office space to start-ups and entrepreneurs, provide access to high end instrumentation and analytical services, advisory services, IP services, facilitate technical and business mentorship, establish connects between industry and academia and enable interactions for efficient exchange of knowledge and help start-ups gain access to various SEED grants.

Through these Bioincubator facilities, BIRAC has supported skilled manpower for the smooth management of these incubators. A total of about 120 jobs have been generated through these incubators and around 300 start ups have been supported. BIRAC has supported 10 Bio incubators during 2017-18.

b) SITARE (Students Innovations for Advancement of Research Explorations): BIRAC has partnered 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 (Gandhian Young Technological Innovation) Awards (wherein INR 15 lakhs is given for 2 years) and BIRAC-SRISTI Appreciation Awards (wherein INR 1 lakh is given) have been constituted to support and mentor the young innovators working at universities and schools. As on date, we have 34 projects running under GYTI category and more than 120 students have been awarded under Appreciation award category. This year SRISTI is also organizing 21 days workshops

for students called as Biotech Innovation-Ignition School (BIIS), wherein 40-50 students (preferably girl students, and where possible, school students, rural youth) would work to co-create solutions for extreme affordability and mass social applications.

c) eYUVA (Encouraging Youth for Undertaking Innovative Research through Vibrant Acceleration): The University Innovation Cluster (UIC) programme of BIRAC has helped in creating pre-incubation space where innovators (students with a Master/Ph. D degree) with entrepreneurial ideas can perform preliminary studies and bring the same to (pre) proof-of-concept stage. The programme has been running successfully since 2013. Through BIRAC support, each UIC has created a dedicated incubation space ranging from 2500 to 3000 sq. ft. Two post-doctoral and 4 post masters fellows are funded at each UIC, who receive fellowship as well as a one-time grant to conduct R&D.

d) SPARSH (Social Innovation programme for Products Affordable & Relevant to Societal Health): SPARSH highlights the need of Innovative solutions to society's most pressing social problems. The fifth Call of SPARSH announced in January 2017 "Innovate for Agriculture" focussed on developing Innovative Diagnostic tools for Soil and Plant Health. The latest Call of SPARSH i.e. 6th Call "Waste to Value" was launched to address the challenge due to the increased urbanisation and population growth and focussed towards the mandate of Swatch Bharat Mission. The Social Innovation Immersion Program (SIIP) of SPARSH till date has supported 18 social innovators who are trying to develop solutions for most pressing problems in the field of Maternal and Child Health (MCH). Most of the Social Innovators who are mentored through the program have been successful in raising follow-on funding or starting their own enterprises.

e) BIRAC SEED Fund: The SEED (Sustainable Entrepreneurship and Enterprise Development) Fund is aimed at providing capital assistance to start-ups

with new and meritorious ideas, innovations and technologies. The SEED support is positioned to act as a bridge between promoters' investment and Venture/Angel investment. BIRAC operationalized the SEED fund in 2016 and implements it through the Incubators, wherein startups are provided up to INR 30 lakhs in lieu of equity held by the incubators. Till now, two rounds of Seed Fund have been completed, under which 7 incubators including Venture Centre, Pune; C-CAMP, Bangalore; IKP Knowledge Park, Hyderabad; FIIT, IIT Delhi; SIDBI, IIT Kanpur; KIIT Technology Business Incubator, Bhubaneswar and Society for Innovation and Entrepreneurship, IIT Bombay have been supported.

f) BIRAC AcE Fund: The novelty of AcE Fund policy is to create a fund of fund to support daughter funds including Early Stage Angel Funds & Ventures in the area of Biotechnology and Life Sciences. AcE Fund shall enable creation of an ecosystem for providing risk capital to young enterprises to undertake research and development in high priority technology areas. It will, in the process, enrich the intellectual property in the country and encourage more entrepreneurs to work towards product and technology development of high quality at affordable economies in a sustainable manner. The core focus of daughter funds would be to develop domestic innovation & manufacturing capabilities. This will promote innovation, research & development within the country.

Affordable Product Development-Discovery Research Translation:

a) National Biopharma Mission - Innovate in India for Inclusiveness: This year, BIRAC forged a very important partnership with World Bank for implementing the National Biopharma Mission, an Industry-Academia Collaborative Mission of Department of Biotechnology (DBT) for accelerating early development of Biopharmaceuticals. The Mission Programme is a Pan-India Programme with the main aim of making India a hub for design and

development of novel, affordable and effective biopharmaceutical products and solutions. The National Biopharma Mission was approved by the Cabinet for implementation in May 2017 with a total cost US\$ 250 million which is co-funded by World Bank (50%). 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. This Mission is 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.

b) Early Translation Accelerator (ETA): BIRAC supported Early Translation Accelerators (ETAs) to focus on catalyzing transformation of young academic discoveries (publications/patents) with possible commercial and societal impact into economically viable ventures and technologies. The proposed set up will collaborate with academic investigators, will engage industry and will leverage international translation ecosystems. Following three projects are under validation at the healthcare ETA supported at C-CAMP

- b.1). Platform for improved erythropoietin (EPO) production
- b.2). Validation of novel compounds in neuro-degenerative diseases
- b.3). Validation of novel Self-assembled short peptide based nanomaterials for Glioblastoma therapy.

ETA in the area of Industrial biotechnology has been funded to IIT-Madras and selection of the projects is in progress.

Mentorship: The Capacity Building:

a) BRIC (BIRAC Regional Innovation Centre) 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. The study was conducted in two phases and covered various regions in Southern, western and central India. The study conducted as Phase-1 and Phase-2 came out in the form of a report that summarizes the findings of the study and intends to provide inputs for framing policies for sustained development of life sciences innovation ecosystems. During 2017-18 BRIC organized 4 tech showcase events and 6 half day workshops to create awareness among startups and entrepreneurs on funding, regulatory and IP related issues.

b) BREC (BIRAC Regional Entrepreneurship Centre) at C-CAMP: The Regional Entrepreneurship Centre at CCAMP, Bangalore has been set up as an extended arm of BIRAC and is mandated to carry out various activities with an aim to spread a wave of entrepreneurial culture in the biotech sector across the country. The Centre is expected to help BIRAC realize one of its important goals, i.e. massive scaling of entrepreneurship in the Biotech community. During the year, 4 awareness workshops were organized for students, 2 workshops for existing entrepreneurs and 2 events for “Meet the Investor series”. In addition a National Entrepreneurship Challenge Award was launched this year, under which more than 1500 applications were received. BREC also organized a 3-day long boot camp for entrepreneurs this year, involving experts from across the globe.

c) IGNITE Boot Camp: BIRAC has channelized the participation of 5 BIG grantees (every year) for last 5 years in the CfEL’s (Centre for Entrepreneurial Learning, Cambridge Judge Business School) mentorship and capacity building programme. The response from previous batches has been very encouraging and participants have emphasized that the programme helped them in honing their business skills, improvising their business plans and networking for the advancement of their innovation

to next level. Till date, 24 BIG grantees have participated in the program. The program provides the participants access to the Cambridge start up ecosystem and an opportunity to learn from the same and build relevant connects.

d) Roadshows and IP Management Workshops: BIRAC is keen to achieve its mandate of creating awareness among the stakeholders about the activities of BIRAC by conducting IP and Grant Writing Workshops. One such workshop, at Jaipur, Rajasthan has been conducted in the present financial year and target is to conduct 3 more workshops by March 2018.

e) Regulatory Facilitation: BIRAC in collaboration with Clinical Development Services Agency (CDSA) organized ten Regulatory Workshops under the series ‘Demystifying Indian Drug regulations for Product Approvals’ in North and South India. These workshops focused on regulations of ‘New drugs’, ‘Biopharmaceuticals’, ‘Phyto-pharmaceuticals’ and ‘Medical Devices & Diagnostics’. Two more regulatory workshops are being planned in the area of ‘Devices and Diagnostics’ during 2017-18.

The Biotech Ecosystem: Empowerment & Scale-up:

a) Make in India (MII) Facilitation Cell: DBT established the Make in India Facilitation Cell at BIRAC in September 2015. The cell regularly interfaces with DIPP and other Ministries to provide information and updates on DBT’s and BIRAC’s plans for boosting Make in India as well as the Startup India programme. The cell prepares brief industry analysis reports to track new Government initiatives and market trends related to biotechnology and startup ecosystem and provide all inputs to Biotech industry and budget related queries during the year. A dedicated website has been developed for the information dissemination and handholding start-ups <http://birac.nic.in/mii/index.php>. This year MII Cell prepared a two year achievement report of

Biotechnology sector, which was published by DIPP in Jan 2017. MII Cell at BIRAC also organized a Strategy Meet in June 2017 to discuss the road map for the Make in India and Start up India in Biotechnology and also to discuss the specific 3 year action plan for BIRAC. MII Cell has contributed to the Innovation Market Place at BIRAC's sixth Innovators Meet in Sept 2017 and ICMR exhibition in March 2017 at the RashtrapatiBhawan with the aim to showcase the products, indigenously developed by the innovators supported by BIRAC to relevant investors and stakeholders.

b) Start-up India Action Plan: BIRAC has an integral role in the Start-up India initiative of the Government. The launch of Startup India has given an impetus to the BIRAC's role for the biotech industry. Under the purview of Startup India Action Plan, BIRAC endeavours to scale up the number of start-ups in the sector by nurturing approximately 300-500 new start-ups each year to have around 2000 start-ups by 2020. Towards an effort to meet the target, 30 Bio-incubators and 3 bioclusters have been supported. BIRAC has launched ACE Fund and SEED fund to provide capital assistance to start-ups and act as a bridge between promoters' investment and venture/angel investors. BIRAC has also setup two regional centres BIRAC Regional Innovation Centre (BRIC) at IKP Hyderabad and BIRAC Regional Entrepreneurship Centres (BREC) at CCAMP Bangalore.

c) Swachh Bharat: BIRAC has taken many initiatives in promoting the Swachh Bharat mission. The foundation for development of safe and affordable sanitation was laid when DBT and BIRAC partnered with the Bill and Melinda Gates Foundation in announcing the Reinvent the Toilet Challenge-India. The grant was awarded to 6 teams of scientists and entrepreneurs to build next-generation toilets based on innovative, sustainable and affordable sanitation technologies. A special call for Technological interventions for conversion of

fecal sludge and MSW to energy and other product was also launched and 4 projects have been funded which are in different stages of development.

c.1) Bio-toilets in Schools in North East India:

BIRAC is involved in the management of a project funded to the TERI, north Eastern office for phase-wise installation of 100 bio-toilets in schools in north eastern region of India. The short listing of schools in the 7 states has been completed, covering both public and private schools including residential schools and 50 toilets have been installed. Data collection from the digesters is ongoing.

c.2) SOCH(Solutions for Community Health):

BIRAC has launched an Innovation Challenge Award BIRAC-Solutions for Community Health (SoCH) Award '17 on the MyGov portal which is aimed at propelling the Indian innovators towards combating the challenges of community health sector. SoCH is designed to offer recognition and financial support to technology innovators and entrepreneurs who have been working in the community health sector and/or facilitate a promising technology idea that can be converted into a handy technology addressing the issues of community health in a defined time limit. SoCH 2017-18 has been announced based on two themes: 1. Platform technologies for reducing the burden of Diseases (Communicable and Non-communicable diseases). 2. Sanitation and Waste Recycling

National and International Alliances:

a) 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. The unit is also supported by USAID & Wellcome Trust.

b) Grand Challenges Explorations – India (GCE-India): DBT and BMGF as funding partners, BIRAC and IKP as implementation partners launched GCE-India to encourage and nurture innovation in areas that impact global health. In 2016-2017, one round of the call, GCE- India Round 2 was completed with 5 projects having been selected for funding. These projects are currently undergoing final due diligence checks. GCE-Round 3 was announced in June 2017. The Mandate for Round 4 is now under consideration, to be announced in February 2018.

c) Knowledge Integration and Translational Platform (KnIT): Launched in 2016, is an initiative that aims to provide evidence and experience-based guidance to accelerate progress, equity and input in the development of health systems in India.

d) Healthy Birth, Growth and Development Knowledge Integration (HBGDki - India): This is a unique platform promoted by the foundation globally where the foundation is partnering with major countries in Asia, Africa, and South America to improve maternal and child health through development of interventions.

e) Immunization Data- Innovating for Action (IDIA): This program, launched in 2017 aims to address the challenges in immunization data systems in India that are different from current approaches and stretch the frontiers of the existing programmes. The solutions submitted to this GCI may deal with integrated health information, or may focus specifically on immunization only and should have the potential to be scaled up in multiple settings. The call for proposals was launched on 15th November 2017 and will close on 15th January 2018.

f) DeitY-BIRAC Industry Innovation Program on Medical Electronics (IIPME): The project ‘Industry Innovation Programme on Medical Electronics’ is a collaborative project between the “Ministry of Electronics and Information Technology”, Government of India and BIRAC. Two calls were

announced till date under this collaboration and 36 projects were selected for funding in three categories i.e. Seed Grant, Early Transition and Transition to Scale.

- Two projects have completed successfully
- One of the product from IIPME scheme, Sohum (Hearing screening device), has been commercially launched. Three projects (hand-cranked Defibrillator, Hexapod Couch for LINCA machine and Tabplan X-ray to 3D software) have reached TRL-7. Industrial Design registration has also been done for Jeevtronics defibrillator



Figure 1. 3D Surgery Planning Software and Patient Specific Instrument

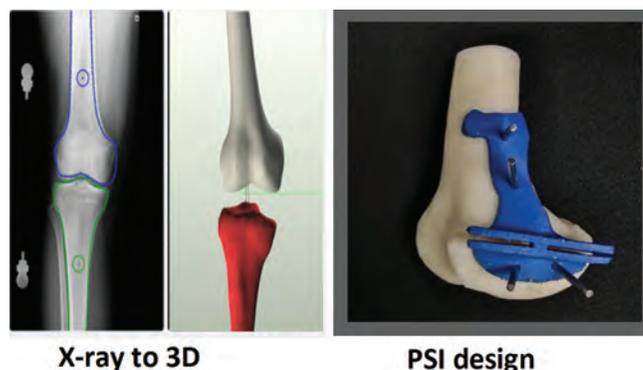


Figure 2. Hand-cranked defibrillator

g) 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.

h) 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. Two calls have been launched till now. A total of 6 projects have been supported out of which 3 projects are now being scaled up.

i) New Partnerships: During the year 2017 BIRAC continued its efforts for establishing partnerships with like-minded organizations and culminated four such collaborations:

i.1) Indian Angel Network (IAN):

BIRAC has signed a MoU with Indian Angel Network to facilitate funding, mentoring and market access for biotech entrepreneurs and start-ups. BIRAC through IAN aims to help start-ups trouble shoot the problem of market access and secure angel investment. The first BIRAC-IAN pitching session was organized in September 2017, where 6 BIRAC supported grantees pitched in front of angel investors.

i.2) Indian Science & Technology Entrepreneurs Parks and Business Incubators Association (ISBA):

BIRAC has entered into an agreement with ISBA with the objective of training managers/professionals working in BioNESTs, conducting awareness programs in institutions/organizations with potential to establish incubators and to organize conferences/events for BioNESTs.

i.3) ICMR:

MoU has been signed with ICMR in 2017 – 18 to establish a collaborative framework under which both BIRAC and ICMR can carry out activities related to the exchange of best

practices and setting up of coordinated support measures to foster technology and knowledge transfer and cooperation for validation studies.

i.4) TATA Trust:

Tata Trusts have supported the formation of the Foundation for Innovation and Social Entrepreneurship (FISE). Social Alpha is the 'ecosystem architecture' created by the FISE to nurture start-up teams through their lab to market journey. Tata Trusts through FISE will support selected innovators to implement social innovations and provide infrastructure assistance for scale up.

Industry-Academia Interaction: Bridging The Gap:

a) 5th Foundation Day of BIRAC: BIRAC completed 5 years of its journey this March and celebrated its 5th Foundation day at India Habitat Centre, New Delhi on 20th -21st March 2017, with a special theme: "BIRAC@5: Impacting the Biotech Innovation Ecosystem". The occasion was celebrated with great enthusiasm by the BIRAC community along with dignitaries representing the Government, academia, industry, start-ups and budding entrepreneurs. Some of the products and technologies developed successfully with support from BIRAC were also showcased during the event.

b) BIRAC's 6th Innovators Meet: It was organized on 21st-22nd September 2017 at New Delhi. 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 event. A major attraction of the event was the Bio-Innovation Fair, where more than 60 products and technologies across different segments of biotechnology (healthcare, agriculture, industrial etc.) were showcased.

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**International Centre for
Genetic Engineering and
Biotechnology**

International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi encourages innovative research in life sciences for the benefit of developing countries. Keeping focus in the three theme areas viz., Molecular Medicine, Plant Biology and Integrative Biology, the centre continues to be very active in research and maintains a high annual publication output, which covers a wide spectrum of scientific investigations. The Centre has taken several initiatives in promoting emerging and interdisciplinary areas, in developing active and close collaboration with research institutions worldwide and in enabling enhanced interactions with the industry through knowledge sharing, translational research and technology transfer.

MOLECULAR MEDICINE

The major efforts in Molecular Medicine were in malaria, tuberculosis, dengue, chikungunya and immunology. Significant progress has been made in all these areas.

Tuberculosis: The findings of the group focusing towards tuberculosis research opened up an entirely new dimension of host-pathogen interactions by suggesting that changes in splicing pattern of infected macrophages helps bacterial survival within the macrophages. Untargeted metabolomics approach was used to establish the TB drug metabolism phenotype at population levels towards studies on tuberculosis detection.

Dengue and Chikungunya: A major focus of the virology research at ICGEB has been on dengue virus infection. Centre continues to invest efforts on development of novel, safe, affordable and effective recombinant dengue vaccine candidates. Considering the criticality of the disease, efforts are also being made to understand the dynamics of CHIKV/DENV co-infections in vector and host. Studies are being carried out to identify virus derived virulence factors that could be playing important roles in enabling virus to fight insect immunity.

Malaria: In malaria biology, proteins of food vacuole protease complex, especially falcipain-2 and heme detoxification protein (HDP) are being targeted towards the development of new anti-malarials. Recently, using *in silico* analysis, mutagenesis and biochemical approaches, two heme binding sites as well as a hemoglobin binding site were identified in HDP. Based on the findings that the treatment of *P. falciparum* 3D7 parasites with peptide corresponding to the hemoglobin binding domain in HDP resulted in food vacuole abnormalities similar to that seen with E-64, a cysteine protease inhibitor, pharmacophores that bind to these HDP sites are being screened and tested for their effects on Plasmodium in culture. To understand functional biology of *P. falciparum* proteases, recently a novel deubiquitinase like protease in the parasites has been identified and characterized. In continuance of the work on helicases from *P. falciparum*, emerging functions of helicases in regulation of stress survival in the parasite in comparison with human host is addressed. On another front, medicinal plants from India and Nigeria have been examined for both *in vitro* anti-plasmodial activity and *in vivo* mouse malaria curative activities.

INTEGRATIVE BIOLOGY

As a leading discovery, differentially regulated metabolites during mono and co-infection of chikungunya and dengue viruses with overlapping clinical symptoms have been identified by NMR spectroscopy. It is shown that many metabolites in the serum are differentially regulated during chikungunya mono-infection and chikungunya co-infection with dengue. These finding may lead to identification and validation of biomolecules, which can be exploited as biomarker candidates for diagnosis of such infections.

A novel mechanism of antigen recognition was deciphered from the crystallographic analysis of single chain antibody 2D10 (scFv 2D10) bound to a

disaccharide moiety. It appears that the molecular crowding leading to supramolecular associations acts as a specificity determinant and could be naturally exploited to bind diverse antigens enhancing the recognition repertoire of antibodies and therefore allows the humoral response to deal with the threats posed by plethora of antigens.

In another study, it was found that microalgae face several challenges in acquiring CO₂ from the environment process by ribulose biphosphate carboxylase-oxygenase (Rubisco). An industrially important oleaginous chlorophyta *Parachlorella kessleri*-I with the heterogeneous inorganic carbon transporters to enhance the supply of CO₂ to Rubisco has been successfully engineered.

PLANT BIOLOGY

The major focus of the research in plant biology is to develop plants resistant to abiotic and biotic stresses. Continuing the earlier work, the metabolic and transcriptomic profiling of rice during a hypersensitive-mediated resistance response has now been completed. These studies will help to evolve novel strategies to control important insect pest gall midge of rice.

It is also understood that in-depth knowledge of the components of stress response pathways is crucial to develop climate-resilient crops. In this direction,

two breakthrough discoveries related to methylglyoxal and its detoxification pathways have been made. Short pathway to Methylglyoxal detoxification discovered for the first time in rice. The presence of unique glyoxalase III enzymes (DJ-1) in plants which catalyze the Methylglyoxal detoxification in a single step showing the existence of a shorter route for methylglyoxal detoxification has been reported for the first time.

Efforts were made to express the gene encoding for phosphite dehydrogenase in plants to enable them to metabolize PO₃ by oxidizing to PO₄. It was shown that the transgenic plants able to metabolize PO₃ as a P fertilizer but simultaneously can act as herbicide to control the non-transgenic weeds and also pathogens in agriculture.

Based on the work carried out during the year, the centre published more than 100 research papers in highly acclaimed scientific journals and filed 3 Indian Patent applications. ICGEB has conducted twin events “International Vaccine Conference & Malaria Workshop” to celebrate its 30th Anniversary. Around 300 national and international researchers have attended the event. At present, around 21 international personnel are on board participating in various research activities. As in the past, several faculty members of the Institute have won national and international awards and honors in recognition of their contributions.

List of Indian Patents:

Sr. No.	Application No.	Title of the invention	Date of filing
1.	201711019184 (Provisional)	Fungal strain with impaired catabolite repression for lignocellulosic degradation	31.05.17
2.	201711031010 (Provisional)	Novel insecticidal molecules, compositions thereof, methods of preparing thereof	01.09.17
3.	201711038417	Phytase enriched tomato fruit	30.10.17

13

**Promotion of
Biotechnology in North
Eastern States of India**

The North East Region (NER) of India is a biological treasure trove that has not been fully explored. In fact, NER constitutes one of the richest hotspots of biodiversity of the country, and most of it remains to be characterised for its medicinal, aromatic, edibility, ecological and ornamental values. Besides, the sublime climatic and rich soil conditions are just excellent for agriculture, plantations and sericulture. Thus, NER offers unique potential for biotechnology-based interventions for overall development of the region. In 2009-10, the Department set up the North Eastern Region-Biotechnology Programme Management Cell (NER-BPMC) for coordination and monitoring of biotechnology programmes in the North Eastern States of India as part of its commitment towards the promotion of biotechnology activities in the North Eastern Region. The Department has made intensive efforts in setting up of basic and state-of-art infrastructure for biotech research and initiating human resource development (HRD) schemes for the benefit of entire North Eastern Region of India.

RESEARCH AND DEVELOPMENT PROGRAMMES

Of the several programs launched by the Department since 2009-10, the R&D *Twinning Programme* has made a huge impact by catalysing vibrant collaborations between institutions from NER and those from the rest of India, evolving NER-specific projects and their implementation across all eight states of the region. More than 480 twinning projects have been implemented, addressing issues in Healthcare (Medical biotechnology), Agriculture (Agri-biotechnology), Livestock & Fisheries (Animal and Aquaculture Biotechnology) and in the areas of Environment, Medicinal and Aromatic Plants (MAP) with specific relevance to developmental needs of the region; nearly 250 research papers have been published in peer-reviewed journals and more than 1000 young scientists of NER have been trained in advanced biotechnology.

With a view to recognize promising mid-career scientists in NER, a programme of awarding *Unit of Excellence* (U-Excel) grant has been initiated so as to enable them to pursue their innovative research in frontier areas of biotechnology. So far, 22 Units of Excellence have been established.

A major network project involving five institutes from NER and DDRC/THSTI-Faridabad has been implemented to harnessing the traditional herbal medicines of NER for developing novel therapeutic strategies for metabolic syndrome.

Mega consortia project on “NER-Scented Rice” involving 28 institutions from NER and other parts of the country with the aim to improving Joha and Black rice of NER was initiated. NER possess a rich diversity of aromatic rice that are of high value due to their unique and delicious edible medicinal properties. In recent times, an export market for these rice varieties is emerging gradually. But these rice varieties are poor yielders and susceptible to pest attacks. Hence, biotechnological intervention is required to ameliorate the agronomic characteristics of these aromatic rice.



Figure 1. The aromatic Black and Joha rice of NER

Another project on consortium mode on “NER-Banana” was also initiated during the year. Banana is the top most horticultural crop in NER especially Assam. However, its productivity in NER is well below the national average. In order to address the need to conserve, characterize and expand the germplasm stock, a consortium based banana research program has been initiated to cater to the biotechnological needs of banana production in NER. The research aspects of the consortium are Banana Biodiversity;

Pathogen detection and control; Tissue culture; Value addition; Post-harvest loss minimization and Downstreaming and processing. 48 projects involving more than 80 scientists from NER and other parts of the country are involved in this mega consortia project.

Ducks are the second most important species next to chicken, reared for table egg and meat production in NER. Majority of ducks are desi or non-descript type having low production potential. Therefore, a major consortium programme for “NER Duck Improvement” to enhance duck production and productivity through innovative technologies has been implemented in NER involving six projects and 20 scientists from NER and others parts of the country.

In the area of Animal Biotechnology, DBT has 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, “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.

SOCIETAL PROGRAMMES FOR THE NORTH EAST REGION

Healthcare/Medical Biotechnology: In order to enhance the quality of patient care and diagnostic services, DBT has initiated a program on Development of Molecular Diagnostic Laboratories in 11 Medical Colleges of NER. The program is now operational in all 11 medical colleges/institutions in four states of the Region, namely Assam, Nagaland, Tripura and Manipur. Labs at 11 medical institutions 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. DBT’s 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. These diagnostic labs have conducted more than 4.50 lakh diagnostic tests of NER patients.

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.

Recognizing that accurate and precise diagnosis is the cornerstone of any successful cancer treatment, DBT has established the “Molecular Diagnostic Laboratory” at the Mizoram State Cancer Institute, Aizawl. The laboratory contributes towards enhancing the quality of comprehensive cancer care. It also serves as a hub for 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: a). Chronic myeloid leukemia (BCR-ABL translocation); b). Breast cancer (HER2/neu), and c). 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). This facility 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. Around 1000 diagnostic tests for cancer have been conducted by this facility

Agriculture Biotechnology: A multi-centric programme on value addition in jackfruit and commercialization of its processed products which aims at identification of superior genotypes of jackfruit and their molecular characterization, and validation and commercialization of technologies for value added products from Jackfruit is being implemented in collaboration with University of Agricultural Sciences (UAS) GKVK, Bangalore. The programme has identified more than 40 elite jackfruit genotypes from Karnataka, Assam and Tripura for culinary or table purposes. Training workshops for farmers on existing jackfruit technologies, and production of value added products like pickle, curry, bhaji, tikki, chips, squash, wine, jam, papad, etc. have been organized. Marketing and supply chain is being developed through involvement of farmers and entrepreneurs.



Figure 2. Value-added products of Jackfruit

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 in collaboration with NRC for Citrus (ICAR), Nagpur. Under the programme, more than 2000 seedlings of rough lemon have been raised, Khasi mandarin and sweet orange have been successfully grafted, and processing of citrus juice

from NER varieties has been standardized. A Poly-house for multiplication of NER citrus rootstocks has also been constructed.

A multi-centric network programme has been implemented for promoting eco-friendly agriculture practices in 14 districts across all NE states, with emphasis upon the application of bio-inputs (biopesticides, biofertilizers) for organic farming of key high value crops 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. A considerable yield increment has been reported by providing 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. This programme is aimed at amelioration and eco-restoration of Jhum lands in North East India.

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 (namely nuggets and bites, sausages, patties, kebabs, samosa, momo, slices etc.) and to refine & standardize the technologies for producing a wide range of value added pork products to provide variety to the pork consumers. Commercial production of pork sausages has already been initiated.

CENTRES OF EXCELLENCE IN NER

A “DBT-AAU Centre for Agriculture Biotechnology in NER” has been established at the Assam Agriculture University, Jorhat. 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; Development of drought tolerant rice variety (Ranjit) is in progress; Seven acid tolerance genes have been found to be up-regulated in *Bacillus megatarium*; Biofertilizers and biopesticides generated at headquarter and at satellite centres are being distributed to the farmers. Nine PhD students enrolled in Agri-biotechnology at Assam Agricultural University are awarded fellowships. Centre has also funded 9 innovative projects to the PIs from various organizations at NE India and conducted 6 scientific workshops on biotechnology and several training workshops on bio-input production involving researchers of N E India as well as other parts of the country. The Centre will eventually be an accredited laboratory for quality analysis of farm inputs and products for the North east region.

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. Its main 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 & capacity building and R&D on feed development.

BIOTECH FACILITIES, TECHNOLOGY PLATFORMS AND RESEARCH RESOURCES

Sophisticated biotech infrastructural facilities have been created at National Research Centre on Mithun at Jharnapani, Medziphema (Nagaland) and National Research Centre on Yak at Dirang (Arunachal

Pradesh), for strengthening research dynamics for desirable gains in Mithun husbandry, Yak husbandry and improving research activities on genomics and conservation.

DBT has established “X-Ray Crystallography Facility” at IIT Guwahati. This facility is now fully functional and available to all NER researchers for their experimental use.

A state-of-the-art, Regional Animal House Facility has been set up at Regional Medical Research Centre (RMRC), Dibrugarh to provide well-equipped lab space for researchers from entire NER for carrying out research in medical science and herbal medicine. The facility would ensure 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 “*Technology Incubation Centre for Entrepreneurship Development in Mushroom Culture and Farming*” at Bodoland University. A number of farmers have been trained for production of value added products such as Soup, Cake, Custard and Pakora from Mushroom. The centre has also produced mushroom spawn. The centre has trained more than 100 people in mushroom cultivation and supported few entrepreneurs.

HUMAN RESOURCE DEVELOPMENT IN NER

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. Together these hubs have conducted more than 600 training programmes and supported more than 500

PG and PhD students.

In order to create awareness in the field of biotechnology at the school level, DBT has initiated a scheme for establishing “*Biotechnology Labs in Senior Secondary schools (BLISS)*” across all states of NER. A basic set of laboratory equipment along with recurring support is being provided under this scheme. In the first round, 88 Senior Secondary Schools from NER have been selected by DBT for support under the BLISS scheme, and 100 more are in pipeline.

The Overseas Associateship Scheme for NER Scientists supports scientific research/training in overseas laboratories for short term as well as long term. So far, 205 scientists have been awarded the Associateship. This Overseas Associateship has resulted in more than 50 research papers in peer reviewed journals and has also enabled more than 35 laureates in getting extra-mural funding for their R&D projects besides training in-house scientific human resource of NER.

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. Scientists/faculties from reputed institutions in India have shown their interest in sharing their domain expertise with NER institutions through this scheme. In the first phase, 32 scientists/faculties have been selected for VRP.

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)* to provide latest IT equipment to support the research activities of the host institutions in NER. Two new bioinformatics centres at College of Fisheries, Central Agricultural University,

Lembucherra, Tripura and National Research Centre on Mithun (ICAR), Nagaland were established last year.

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.

An online human resource repository of Biotechnology and Bioinformatics Resources of North East India (BABRONE) has been created and located at College of Veterinary Sciences (AAU), Khanapara, Guwahati (Assam). It is a freely accessible e-learning server developed as a common platform for uploading learning materials, sharing of information and as an online discussion forum at <www.babrone.edu.in>. Details of more than 1300 researchers, faculty and teachers from NER are available on the portal.

14

**Administration &
Finance**

ADMINISTRATION

The Department's administration is responsible for providing 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. Being a scientific department, large number of meetings, interactions and quick referral with technical experts, specialists, academicians and scholars from far reaching places across the world are held regularly, for which technical support was provided.

Swachh Bharat Abhiyan - Swachhta Action Plan: The Swachhta Action Plan (SAP) for the Department for the year 2017-18 has already been finalized for an amount of Rs. 2.25 crore. The SAP activities finalized are as follows:

- Toilet & Road Renovation: Renovation of toilets in the Department at Block-2, CGO Complex and BIBCOL (Bharat Immunologicals and Biologicals Corporation Limited), Bulandshahar. Road repair, BIBCOL, Bulandshahar.
- Cleanliness Drives: Modernization of Canteen, Pest Control Services, repair/re-fitment of old furniture

e-Office in DBT: The e-Office is one of the Mission Mode Projects (MMPs) under the Digital India Programme of Government of India being implemented in the Department. Following steps have been taken in this regard:

- Scanning of active files has been completed
- A Help Desk has been established
- Continuous training to the officers / staff is being imparted
- Scanners provided to the Sections / Divisions for the purpose
- Digital Signature Certificates (DSC) are being procured from NICS

Government e-Market Place (GeM): During the financial year 2017-18, the Department has made the following procurements of goods and services through GEM.

- 43 Scanners at the total cost of Rs.12,51,330/-
- 37 Personal Computers and equal numbers of printers with latest configuration at the total cost of Rs.26.00 lakh.
- 620 Reams of Photocopier paper
- Annual contract of hiring of vehicles on regular basis.
- Procurement of stationary items through GeM is under process.

Renovation work: Comprehensive renovation of all the three floors of Block-2 including corridors (floorings & ceilings), toilets and conference room has been undertaken with the help of CPWD at a total cost of Rs. 1.00 crore.

Video Conferencing / Audio-Visual: Modern video conferencing system procured and installed in conference Room no 727, Block-2 with the help of NICS. Similarly, modern audio-visual system installed in conference Room no 503, Block-3.

ESTABLISHMENT

Establishment Section in the Department is entrusted with the following functions:-

Recruitment and promotion to various posts: Two vacancies of Scientist 'H' were revived with the approval of Department of Expenditure. Appointments of two eligible Scientists have been made to the posts of Scientist 'H' on direct recruitment basis.

One more vacancy of Scientist 'H' arose due to superannuation of the incumbent to the post on 31/1/2017. It was decided to fill-up this vacancy on direct recruitment basis, reserved for Scheduled

Caste Category Candidate. The process to fill-up this vacancy is under way.

The eligible Scientists have been promoted to their next higher grade under Modified Flexible Complementing Scheme.

Recruitment Rules: 12 Posts in the grade of Scientist 'C' have been revived in the Department w.e.f. 27.07.2017. It was decided to fill up these vacancies on direct recruitment basis. The proposal to make necessary amendments in the Department of Biotechnology (Group 'A', Scientific Posts) Recruitment Rules, 2012 is under process with the DoPT.

Modified Assured Career Progression Scheme: The cases for grant of Modified Assured Career Progression Scheme to eligible officials are being processed from time to time.

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.

Grant of Advances and Reimbursement: The cases of grant of various advances, medical reimbursement and other allowances were processed as per rules in a time bound manner.

Miscellaneous: The Staff Selection Commission (SSC) has forwarded the dossiers of 08 (Eight) candidates for filling up the 08 (Eight) vacant posts of Junior Technical Assistants in Department of Biotechnology. This Department is in the process of issuing 'Offer of Appointment' to the selected candidates.

The category wise position of posts sanctioned and filled as on 31.12.2017 is as under:-

Category of posts	Post sanctioned	Post filled
Group 'A'	74	54
Group 'B'	98	67
Group 'C'	77*	46
Total	249	167

*including 01 Group 'D' post

PROGRESSIVE USE OF HINDI IN THE DEPARTMENT

Hindi Division ensures progressive use of Hindi implementation of Government policy on Official Language in the Department. An Official Language Implementation Committee constituted under the Chairmanship of the Joint Secretary (Admin.) in the Department reviews the progressive use of Hindi in every quarter and suggests corrective measures for promoting the use of Hindi. During the year, all documents issued under section 3(3) of the Official Languages Act, 1963 were in bilingual form and letters received in Hindi were replied to in Hindi only. In order to strengthen the monitoring system of progressive use of Hindi, the officers who sign the papers have been made the check- points Under Rule 8(4) of the Official Language Rules, 1976, Establishment, Administration, PPVC, Cash section and Library in the Department have been notified to do their 100% work in Hindi, during the year, 50 officers and employees were imparted training in Hindi workshop. Hindi fortnight was organized in the Department during 01-15th September 2017, in which 10 different competitions namely, Vaigyanik shodh par bhashan, Noting & Drafting, Hindi Typing, Antakshari, General Knowledge competition in hindi and Hindi Vyavahar Competition, Noting/Drafting, Debate, essay, Recitation competition were held. The competition for general knowledge was especially held for encouraging the multitasking staff and speech on scientific thesis for all scientists of the department and in addition to this Hindi Typing test

for project staff was also organised. 60 officers/ employees participated in various competitions, out of which 45 officials won different prizes.

Successful participants of the different competitions of Hindi Pakhwara were awarded in a prize distribution ceremony. The first prize of Rs.5000/-, second prize of Rs.3500/- third prize of Rs.2500/- and 5 Consolation prizes of Rs.1500/- each have been awarded. With a view to encourage writing of original books of biotechnology related subjects in Hindi, the Department has been implementing an award scheme namely “Dr. Jagadish Chandra Bose Hindi Granth Lekhan Puraskar Yojna” since 2002. Under the scheme, first prize of Rupees one lakh rupees, second prize of rupees fifty thousand, third prize of rupees twenty five thousand and consolation prizes of rupees ten thousand each are given. During the year 2017-18 under the said scheme have been awarded First, Second and Third prizes for the scheme of 2016.

PARLIAMENTARY MATTERS

The meeting of the Parliamentary Standing Committee on Science and Technology, Environment & Forests was held on 15.02.2017 in the Parliament House Annex, to consider the Demands for Grants (2017-18) of the Department.

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 grievances on the website of Department of Administrative Reforms & Public Grievances. A total of 206 grievances were received by the Department, from 01.04.2017 to 17.01.2018, through the CPGRAMS portal, out of which 148 have been disposed.

VIGILANCE UNIT

A Vigilance Cell is functioning in the Department to

handle vigilance and complaint cases expeditiously. Complaints received from various sources were processed in-time. In pursuance of the instructions of the ‘Central Vigilance Commission’, a Vigilance Awareness Week was observed in the Department and the Autonomous Institutes (AI) and Public Sector Undertakings (PSUs) under its administration from 30th October, 2017 to 4th November, 2017. An office-wide integrity pledge taking was organized in the Conference Room of the Department, which was administered by senior officer. A banner was displayed at the entrance of the Department, to facilitate focus on the theme of “My Vision-Corruption Free India”, which was adopted by the Central Vigilance Commission (CVC) as theme for the year 2017.

A meeting of the Vigilance Officers of the Autonomous Institutes and Public Sector Undertakings of the Department was convened on 27.12.2016 by the Chief Vigilance Officer of the Department, to take account of the activities done by the Vigilance Officers of the Autonomous Institutes and Public Sector Undertakings.

FINANCE

Department of Biotechnology was allocated as Amount of Rs. 2222.11Crore in the Budget Estimates 2017-18. This was revised to Rs. 2260.11 Crore (Rs. 2229.77 Crore under Major Head 3425: other Scientific Research and Rs. 30.34 Crore under Major Head 3451: Secretariat – Economic Services). The Financial Statement showing the details of Actual Expenditure during 2016-17, B.E. & R.E. of 2017-18 and BE 2018-19 in respect of various Programmes/ Schemes are given in Annexure I.

STATUS OF C&AG AUDIT PARAS

The Status on Action Taken Notes (ATN) on pending C&AG Paras pertaining to the department is as per Annexure II

Details of Actual Expenditure during 2016-17, B.E. and R.E. of 2017-18

(Rs. in crores)

S. No.	Name of the Programme/ Scheme	2016-17 Actual Expenditure			BE 2017-18	RE 2017-18	BE 2018-19
		Plan	Non-Plan	Total		Total	
1	2	3	4	5	6	7	8
	REVENUE SECTION	1874.59	20.90	1895.49	2222.11	2260.11	2411.53
1	Secretariat Economic Services						
1.01	Secretariat	0.00	22.90	20.90	30.00	30.34	32.31
2.01	Biotechnology Industry Research Assistance (BIRAC)	25.00	0.00	25.00	30.00	30.00	31
2.02	Support to Autonomous R&D Institutions*	649.06	0.00	649.06	708.53	724.53	748.98
3.00	Assistance to other Scientific Bodies	726.74	0.00	726.74			1350
3.01	Biotechnology Research and Development, Human Resource Development, Research Resources Facilities	285.89	0.00	285.89	1250.58	1252.42	
4.01	Industrial and Entrepreneurship Development	187.90	0.00	187.90	203.00	222.82	249.24
	TOTAL = Revenue Section	1874.59	20.90	1895.49	2222.11	2260.11	2411.53

* Institute includes 16 Autonomous Bodies namely National Institute of Immunology, New Delhi, National Centre for Cell Science, Pune, Centre for DNA Finger Printing & Diagnostics, Hyderabad, National Brain Research Centre, Gurgaon, National Institute 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, National Institute of Biomedical Genomics, Kalyani, Regional Centre for Biotechnology, Faridabad, National Agri-Food

Biotechnology Institute, Mohali, Institute for Stem Cell Research and Regenerative Medicine, Bengaluru, National Institute of Animal Biotechnology, Hyderabad, Centre of Innovative and Applied Bioprocessing, Mohali, International Centre for Genetic Engineering and Biotechnology, New Delhi.

Annexure II**Position of Action Taken Notes(ATN) on C&AG Audit Paras**

S. No.	Para Number and Year of report	Number of Paras	No. of para settled during year	Present Position
1	C&AG Audit Para No. 3 of Report No. 5 of 2003	One (Containing 157 sub-paras)	84 sub-para has been settled	Based on the ATN submitted twice the Audit has asked for additional information in respect of only 29 sub-paras and ATN for remaining sub-paras accepted. Furnishing of revised ATN in respect of remaining sub paras is under process.
2	Chapter no. 3 of Report No. 12 of 2016- (Irregular Administrative and entitlements operations)	One	-	ATN once furnished to C&AG. Vetted ATN received from Audit. As required by Audit revised ATN is being furnished.
3	C&AG Audit Para No. 3.1, of Report No. 17 of 2017(Irregular expenditure on premises transferred to another organisation)	one	-	ATN has been furnished, vetted ATN received, they have sought further information, as required by Audit revised ATN is being furnished.
4	C&AG Audit Para No. 3.2 of Report No. 17 of 2017 (Unauthorised expenditure due to excess appointment and grant of advance increments to employees)	one	-	ATN has been furnished, vetted ATN received, they have sought further information, as required by Audit revised ATN is being furnished.
5	C&AG Audit Para No. 3.3 of Report No. 17 of 2017 (Overpayment of transport allowance)	one	-	ATN has been furnished, vetted ATN received, they have sought further information, as required by Audit revised ATN is being furnished.

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Mission Programmes

BIOTECH-KRISHI INNOVATION SCIENCE APPLICATION NETWORK (BIOTECH-KISAN)

This programme aims to work with small and marginal farmers especially the women farmer for better agriculture productivity through scientific intervention and evolving best farming practices in the Indian context by linking available science and technology to the farm by first understanding the problem of the local farmer and provide solutions to those problems. It is proposed to establish Biotech-KISAN Hubs in each of the 15 agro-climatic zones in 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. The programme includes conducting training programmes for farmers in laboratories of scientific research institutions and training programmes for scientists in agricultural farms. During the year under report, a Biotech-KISAN Hub has been established at Himalayan Environmental Studies and Conservation Organization (HESCO), Dehradun to cover the agro-climatic zone of Western Himalayan Region. The Sub-Hubs have been created at Almora, Chakrata and Chamoli, which are connected to the Central Hub in Dehradun. Three Polyhouse facilities have been created in each of the three Sub-Hubs to promote protected cultivation of improved varieties of vegetables sourced from GB Pant University of Agriculture and Technology, Pantnagar and Indian Agriculture Research Institute, New Delhi for enhancing the production, quality and profitability to the marginal farmers. A mushroom production-cum-training centre has also been established at Karbari village near Central Hub. Seven days training programme on promotion of horticulture crops and beekeeping have so far been organized at Sub-Hubs located at Chakrata, Chamoli and Almora.



Figure 1. Training Programme on Beekeeping at Sub-Hub Chakrata

SPACE MISSION ON BIODIVERSITY CHARACTERIZATION

Department of Biotechnology and Department of Space have initiated a joint initiative on biodiversity characterization at Landscape Level using Remote Sensing and Geographical Information System. Under this study, a national level assessment of biodiversity richness was undertaken for the first time in India using spatial data to identify and to map potential biodiversity-rich areas in the country. So far 84% of the Country's forest cover has been characterized. The study has brought out a Spatial

Database, first of its kind, adding spatial explicitness to understanding of vegetation formation; it provides a wall to wall mapping of natural habitats.

A new initiative is being launched towards intensive mapping of hot-spots and National Coral Reefs Mapping Mission. These initiatives have been conceptualized based on the action plan that emerged from the “National Meet on promoting use of Space Technology in Governance and Development” which was held on September, 2015 at New Delhi. The Mission activities will include the creation of new geospatial inventory of coral reefs covering 172 grids of Indian coral reef regions at 1:25000 scale which in turn would greatly help in developing appropriate strategies for their conservation and sustainable utilization. Development of space based biodiversity monitoring system will benefit both national imperatives and reporting to international commitments.

MISSION INNOVATION IN CLEAN ENERGY

Mission Innovation (MI) is a global initiative of 22 countries and the European Union to accelerate global clean energy innovation. MI was announced on November 30th, 2015 as world leaders came together in Paris during COP-21. As part of the initiative, participating countries have committed to seek to double their government’s clean energy research and development (R&D) investments over five years. The second Mission Innovation Ministerial (MI Ministerial) was held in Beijing China (in June 2016), where leaders of MI countries announced following seven innovation challenges for advancement of clean energy technologies. Indian delegation participated in the inaugural MI session led by Hon’ble Minister of Science and Technology Dr. Harsh Vardhan.

Mission Innovation Challenges and objectives

1. Smart Grids Innovation Challenge – to enable

future grids that are powered by affordable, reliable, decentralized renewable electricity systems

2. Off-Grid Access to Electricity Innovation Challenge – to develop systems that enable off-grid households, communities to access affordable renewable electricity
3. Carbon Capture Innovation Challenge – to enable near-zero CO₂ emissions from power plants and carbon intensive industries
4. Sustainable Biofuels Innovation Challenge – to develop ways to produce, at scale, widely affordable, advanced biofuels for transportation and industrial applications
5. Converting Sunlight Innovation Challenge – to discover affordable ways to convert sunlight into storable solar fuels
6. Clean Energy Materials Innovation Challenge – to accelerate the exploration, discovery, and use of new high-performance, low-cost clean energy materials
7. Affordable Heating and Cooling of Buildings Innovation Challenge – to make low-carbon heating and cooling affordable for everyone.

India is a member of the Steering Committee and also member of all seven innovation challenges. DBT has been assigned responsibility for coordinating all Mission Innovation activities for India with regular interaction with 22 MI member countries.

Country workshops were held for all above seven Innovation Challenges in 2017. Four of these were arranged by DST and rest three by DBT with support from MI India Unit set up by Department of Biotechnology, at ICGB New Delhi. The major deliverables of each workshop were current status of the technologies in terms of commercialisation status, R&D gap areas, plans and timelines to address the identified gap areas. A dedicated web

site (<http://www.mission-innovation-india.net>) for disseminating MI-India activities has been developed and is regularly updated.

PUBLIC PRIVATE PARTNERSHIP PROGRAMME

The Department through its inter phase agency, Biotechnology Industry Research Assistance Council (BIRAC), a Public Sector undertaking set up by the Department implements Public Private Partnership Programme to strengthen and empower emerging Biotech Enterprises specially startups and SMEs. The details of the Public Private Partnership Programmes being implemented by BIRAC is given in the Chapter: Public Sector Undertakings.

MAKE IN INDIA

DBT has established the Make in India (MII) Facilitation Cell at BIRAC in September 2015. 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 Indiaprogramme.

Make in India has specific relevance to the biotechnology sector in India, owing to the fact that the country's biotechnology industry is in the phase where the opportunities are immense. The MII Cell is responsible for creating an enabling ecosystem in the country for promoting the manufacturing capabilities of the Indian biotech sector. The objectives of Make in India Facilitation Cell at BIRAC are:

1. Contribute to Make in India growth through identifying and promoting new areas in Biotechnology
2. Co-ordinate activities of Make in India with DIPP, Government of India
3. Catalyze the growth of manufacturing industry by mapping incentives and opportunities

provided by Central and State Governments

4. Facilitate Startups, SMEs and companies by communicating the policies and incentives extended by the Government for the programme
5. Support the Make in India Programme by addressing the queries from various stakeholders

Major Activities:

1. A brief industry analysis report has been prepared to track new Government initiatives and market trends related to biotechnology and startup ecosystem and provide all inputs to biotech industry and budget related queries during the year.
2. 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>>
3. MII Cell has also prepared a two year achievement report of Biotechnology sector which was published by DIPP in Jan 2017.
4. MII Cell at BIRAC has organized a Strategy Meet in June 2017 to discuss the road map for the Make in India and Start up India in Biotechnology and also to discuss the specific 3 year Action Plan for BIRAC.
5. The Cell also plays a major role in DBT and BIRAC's Outreach, communication and publications in the area of Bio-entrepreneurship.
6. MII Cell also helps startups and entrepreneurs to connect with the relevant Departments of Govt. and facilitate them by resolving their queries.

7. MII Cell has contributed to the creation of Innovation Market Place at BIRAC's sixth Innovators Meet in Sept 2017 and ICMR exhibition in March 2017 at the Rashtrapati Bhawan with the aim to showcase the products, indigenously developed by the innovators supported by BIRAC, to relevant Investors and stakeholders.

Also a detailed Action Plan 2.0 has been formulated in 2017 under Make in India where DBT/BIRAC has set targets and objectives to achieve which are broadly given below:

1. Entrepreneurial Support to around 150 start-ups/entrepreneurs each year through funding and incubation
2. Creation of shared infrastructure for biopharmaceutical development and development of products
3. Setting up of Manufacturing Fund for startup and SMEs
4. Working with existing Bio-clusters to set up Research Parks & Bio-manufacturing Facilities for attracting FDI
5. Building and strengthening domain specific knowledge management and entrepreneurial skills in Biotechnology

STARTUP INDIA

Startup India is a flagship initiative of the Government of India, intended to build a strong eco-system for nurturing innovation and Startups 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 Prime Minister of India formally launched this initiative on January 16, 2016.

Following are the major achievements in

Biotechnology Sector under Startup India Action Plan:

1. Presently 30 Bio-incubators have been setup across India with world class facilities.
2. Department is supporting 3 Bio-clusters (NCR, Kalyani and Bangalore) and approval of Pune Bio-cluster is in advance stage.
3. BIRAC has launched ACE Fund and SEED fund to provide capital assistance to start-ups and act as a bridge between promoters' investment and venture/angel investors. Seven incubators have been provided funding under the SEED Fund programme
4. BIRAC has setup two regional centers *BIRAC* Regional Innovation Centre (*BRIC*) at IKP Hyderabad and *BIRAC* Regional Entrepreneurship Centres (*BREC*) at CCAMP Bangalore.
5. Bengaluru-Boston Biotech Gateway to India has been formed. Through this initiative, a range of institutes in Boston (Harvard/ MIT) and Bengaluru are able to connect and share ideas and mentor the entrepreneurs and young scientists especially in the areas of Genomics, Computational Biology, Drug Discovery and New Vaccines.

INDUSTRY-ACADEMIA COLLABORATIVE MISSION FOR ACCELERATING DISCOVERY RESEARCH TO EARLY DEVELOPMENT FOR BIOPHARMACEUTICALS - "INNOVATE IN INDIA (I³)"

An Industry-Academia Collaborative Mission of Department of Biotechnology (DBT) for Accelerating Early Development for Biopharmaceuticals; to be implemented by BIRAC, was approved by the Cabinet for implementation in May 2017 with a total cost of

Rs. 1500 crore (50% grant will be arranged through world bank loan). The Mission I³ is “Innovate in India” for Biopharma. It will create an ecosystem for innovative indigenous product development by Researchers, Startups and SMEs and make Indian Biotech Industry Globally competitive.

In a bid to create a globally competitive biopharmaceutical industry that addresses the country’s major concerns around barriers to affordable healthcare, Hon’ble Minister Dr. Harsh Vardhan, Union Minister of Science & Technology launched the *Innovate in India* (I³) program on 30th June 2017 in New Delhi.

The Mission is a PAN India programme involving all stakeholders and BIRAC as a Product Development Partnership (PDP). The Program Management Unit established at BIRAC is functioning as an operational and functional arm for effective execution of the mission activities. The oversight to the program is being provided by the Inter-Ministerial Steering Committee comprising of members from various Ministries; and also supported by Program Technical Advisory Group comprising of global and national leaders from industry and academia.

The Mission is 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 is focussing on the following:

1. 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
2. Establish and strengthen shared infrastructure facilities and product discovery/validation and manufacturing

3. Develop 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.
4. Creating and enhancing technology transfer and intellectual property management capacities and capabilities in public and private sector.

It is envisioned that the Mission would aid in preparing India’s technological and product development capabilities in the biopharmaceutical sector to a level which is globally competitive over the next 10-15 years, and will transform the health standards of India’s population through affordable product development. The Mission will provide a holistic and integrated approach to strengthen and support the entire product development value chain for accelerating the research leads to product development. This will help not only in immediate product development addressing public health needs, but will also help to create an ecosystem which will facilitate development of a continuous pipeline of products.

ABBREVIATIONS

AAU	:	Anand Agricultural University
AAV	:	Adeno Associated Virus
ACTREC	:	Advanced Centre for Treatment, Research and Education in Cancer
ADBS	:	Accelerator program for discovery in brain disorders using stem cells
ADF	:	<i>Acid Detergent Fiber</i>
AD-MSC	:	Adipose derived-mesenchymal stem cell
AIDS	:	Acquired Immune Deficiency Syndrome
AIRCP	:	All India Research Coordinated Projects
AIST	:	Advanced Institute of Science and Technology
ALP	:	Alkaline Phosphatase
AMF	:	Arbuscular Mycorrhizal Fungi
AMP	:	Antimicrobial Peptide
Amph	:	Amphetamine
APC	:	Adenomatous polyposis coli
APR	:	Adult Plant Resistance
ARF	:	Agricultural Research Fund
ARI	:	Ahrakar Research Institute
ASHA	:	Accredited social health activists
ASHD	:	Accelerating the application of stem cell technology in human disease
ATP	:	Adenosine triphosphate
ATPC	:	Advanced Technology Platform Centre
AX	:	Arabinoxylan
AXIN	:	Axis inhibition protein
BAC	:	Bacterial artificial chromosome
BHKcz	:	Body Hamster Kidney Cell Zellen
BIOFI	:	Biofertilization and Bioirrigation for sustainable mixed cropping of Pigeon Pea
BIRAC	:	Biotechnology Industry Research Assistance Council
BL	:	Burkitt Lymphoma
BLAST	:	Basic Local Alignment Sequence Tool
BM-MSC	:	Bone marrow derived mesenchymal stem cell
BMP	:	Bone Morphogenetic Protein
BMSCs	:	Bone Marrow Stromal Cells
BSL:3	:	Biosafety laboratory 3
Bt	:	<i>Bacillus thuringiensis</i>
Cas9	:	CRISPR associated protein 9
CBDR	:	Centre for Brain Development and Repair
CCBD	:	Centre for Cardiovascular Biology and Disease
CCBT	:	Centre for Chemical Biology and Therapeutics
CCCH	:	Three conserved cysteine residues & one histidine residue

CD	:	Circular dichroism
Cdc	:	Cell division cycle
cDNA	:	Complementary Deoxyribonucleic acid
CDS	:	Coding Sequences
CDSCO	:	Central Drugs Standard Control Organization
CHH	:	Crustacean Hyperglycemic Hormone
ChiLCV	:	Chilli Leaf Curl Virus
CHO	:	Chinese Hamster Ovary
CIFA	:	Central Institute of Freshwater Aquaculture
CIFE	:	Central Institute of Fisheries Education
CIMAP	:	Central Institute of Medicinal and Aromatic Plants
CiRA	:	Center for iPS Cell Research and Application
CITH	:	Centre for Inflammation and Tissue Homeostasis;
CMD	:	Cassava Mosaic Disease
CMS	:	Cytoplasmic Male Sterility
CO 1	:	Cytochrome Oxidase I
COL18A1	:	Collagen Type XVIII Alpha 1 Chain
CORVET	:	Core Vacuole/Endosome Tethering
CP	:	Complement Pathway
CPE	:	Cytopathic Effect
CPV	:	Canine Parvo Virus
CRISPR	:	Clustered Regularly Interspaced Short Palindromic Repeats
CS:induced	:	Cigarette Smoke Induced
CSCR	:	Centre for Stem Cell Research
CSIR	:	Council of Scientific & Industrial Research
CTCRI	:	Central Tuber Crops Research Institute
CTNNB	:	Catenin Beta
Cyp19A1	:	Cytochrome P450, family 19, subfamily A, polypeptide 1
DBH	:	Dopamine beta: hydroxylase
DBT	:	Department of Biotechnology
DC	:	Direct Current
DCFR	:	Directorate of Coldwater Fisheries Research
DGKZ	:	Diacylglycerol Kinase Zeta
DNA	:	Deoxyribonucleic Acid
DST	:	Department of Science & Technology
E. coli	:	Escherichia coli
EGF	:	Epidermal Growth Factor
EGFP	:	<i>Enhanced Green Fluorescent Protein</i>
ELISA	:	Enzyme: Linked Immunosorbent Assay

EMS	:	Ethyl Methane Sulphonate
ESC	:	Embryonic Stem Cell
ESRF	:	European Synchrotron Radiation Facility
ET calves	:	Embryo Transfer
ETH	:	Eidgenössische Technische Hochschule (Swiss Federal Institutes of Technology)
FACS	:	Fluorescence Activated Cell Sorting
FANCI	:	Fanconi Anemia Group J Protein
FCR	:	Feed conversion ratio
FDA	:	Food and Drug Administration, USA
FGF	:	Fibroblast Growth Factor
FM	:	Finger Millet
FOG	:	Fats, Oils, and Grease
FOS	:	Fructooligosaccharides
FRP	:	Reinforced Plastic hatchery
FSH	:	Follicle: stimulating hormone
FTIR	:	Fourier Transform Infrared Spectroscopy
FUCCI	:	Fluorescence Ubiquitination Cell Cycle Indicator
FZD	:	Frizzled Class Receptor
GABA	:	Gamma Aminobutyric Acid
GAiT	:	Global Alliance for iPSC Therapies
GBPIHED	:	Govind Ballabh Pant Institute of Himalayan Environment & Development
GBPUAT	:	Govind Ballabh Pant University of Agriculture & Technology
GFAP	:	Glial Fibrillary Acidic Protein
GH	:	Growth Hormone
GMP	:	Good Manufacturing Practice
GNPs	:	Gold Nanoparticles
GO	:	Gene Ontology
GWAS	:	Genome wide association studies
hCG	:	Human chorionic gonadotropin
HCV	:	Hepatitis C Virus
HESCO	:	Himalayan Environmental Studies and Conservation Organization
HFD	:	High Fat Diet
HIV	:	Human Immunodeficiency Virus
hMSCs	:	Human Mesenchymal Stem Cells
HPLC	:	High performance liquid chromatography
HPV	:	Human Papilloma Virus
Hsp	:	Heat Shock Protein
HSP90B1	:	Heat Shock Protein 90 Beta Family Member 1

IAA	:	Indole-3-acetic Acid
IARI	:	Indian Agricultural Research Institute
IASRI	:	Indian Agricultural Statistics Research Institute
IBDV	:	Infectious Bursal Disease Virus
IBR	:	Infectious Bovine Rhinotracheitis
ICAR	:	Indian Council of Agriculture Research
ICMR	:	Indian Council of Medical Research
ICRISAT	:	The International Crops Research Institute for the Semi: Arid Tropics
IC-SCR	:	Institutional Committee for Stem Cell Research
IFI16	:	Interferon Gamma Inducible Protein 16
IGF1	:	Insulin-like growth factor 1
IGF1R	:	Insulin-like growth factor 1 Receptor
IGKV	:	Indira Gandhi Krishi Vishwavidyalaya
IICB	:	Indian Institute of Chemical Biology
IIPR	:	Indian Institute of Pulse Research
IIRR	:	Indian Institute of Rice Research
IISc	:	Indian Institute of Science
IISER	:	Indian Institutes of Science Education and Research
IISR	:	Indian institute of Sugarcane Research
IIT	:	Indian Institute of Technology
IL-6	:	Interleukin-6
IND	:	Investigational New Drug
inStem	:	Institute for Stem Cell Biology and Regenerative Medicine
IPK1	:	Inositol Pentakisphosphate Kinase
iPSc	:	Induced Pluripotent Stem Cells
IRES	:	internal ribosome entry site
IRRI	:	International Rice Research Institute
ISCB	:	Indo-Swiss Collaboration in Biotechnology
ISG15	:	Interferon-Stimulated Gene 15
IVDMD	:	<i>In vitro</i> Dry Matter Digestibility
IVRI	:	Indian Veterinary Research Institute
JAC	:	Joint Apex Committee
JGEEBILS	:	Joint Graduate Entrance Exam for Biology and Interdisciplinary Life Science
JNU	:	Jawaharlal Nehru University
KLF-4	:	Kruppel Like Factor 4
KM	:	Kodo millet
KVK	:	Krishi Vigyan Kendra
LAMP	:	Loop Mediated Isothermal Amplification
LFA	:	Lateral Flow Assay

LH	:	Luteinizing Hormone
LHC	:	Light-Harvesting Complexes
LIF	:	Leukemia Inhibitory Factor
LLP	:	Limited Liability Partnership
LPS	:	Lipopolysaccharide
MAB	:	Marker Assisted Breeding
MALDI-TOF/TOF	:	Matrix Assisted Laser Desorption-Time of Flight
Map2	:	Microtubule Associated Protein 2
MAPK	:	Mitogen Activated Protein Kinase
mESC	:	Mouse Embryonic Stem Cells
MF	:	Multiplication Factor
miRNA	:	MicroRNA
MnSOD	:	Manganese superoxide dismutase
MPA	:	Multiple Party Agreement
mRNA	:	Messenger RNA
MSSRF	:	M. S. Swaminathan Research Foundation
mtRNA	:	Mitochondrial RNA
NAARM	:	National Academy of Agricultural Research Management
NABL	:	National Accreditation Board for Testing and Calibration Laboratories
NAC-SCRT	:	National Apex Committee-Stem Cell Research and Therapy
NAHD	:	Novel approaches to hematological disorders
NaMoR	:	National Mouse Resource Facility; iPSC: Induced pluripotent Stem Cells;
NBFGR	:	National Bureau of Fish Genetic Resources
NBPGR	:	National Bureau of Plant Genetic Resources
NBRC	:	National Brain Research Centre
NCBI	:	National Center for Biotechnology Information
NCBS	:	National Centre for Biological Sciences
NCR	:	National Capital Region
NDF	:	<i>Neutral Detergent Fiber</i>
NDM-5	:	New Delhi metallo- β -lactamase 5
NII	:	National Institute of Immunology
NIMHANS	:	National Institute for Mental Health and Neuro Sciences
NIPGR	:	National Institute of Plant Genome Research
NIVEDI	:	National Institute of Veterinary Epidemiology and Disease Informatics
NOX4	:	Nicotinamide Adenine Dinucleotide Phosphate Oxidase
NPC	:	Nuclear Pore Complex
NPV	:	Nuclear Polyhedrosis Virus
NRCPB	:	<i>National Research Centre on Plant Biotechnology</i>
NRRI	:	National Rice Research Institute

OAS1	:	Oligoadenylate Synthetase 1
OBC	:	Other Backward Class
OcHKT1-5	:	<i>Oryzacoarctata</i> sodium transporter HKT1-5
OCT-4	:	Octamer-binding transcription factor 4
OIE	:	Office International <i>des</i> Epizooties
PAN	:	Presence Across Nation
PAU	:	Punjab Agricultural University
PBMC	:	Peripheral blood mononuclear cells
PcNHX1	:	<i>Porteresiacoarctata</i> (<i>Oryzacoarctata</i>) vacuolar antiporter1
PCR	:	Polymerase Chain Reaction
PGF _{2α}	:	Prostaglandin F2: alpha
PGFM	:	Prostaglandin F2: alpha metabolite
PGM2	:	Phosphoglucomutase 2
PGPR	:	Plan growth promoting rhizobacteria
PKB	:	Protein Kinase B
PKC	:	Protein Kinase C
PMMA	:	Poly Methyl Methacrylate
PMSCs	:	placentaderived mesenchymal Stem Cells
PMU	:	Programme Management Unit
PO	:	Phenoloxidase
PPRV	:	Peste: des: Petit Ruminants Virus
ProPO	:	Prophenoloxidase
PSY	:	Phytoene synthase
PTEN	:	Phosphatase and tensin homolog (PTEN)
qRT:PCR	:	Quantitative Realtime Polymerase Chain Reaction
QTL	:	Quantitative Trait locus
R&D	:	Research and Development
RAF	:	Rapidly Accelerated Fibrosarcoma
RBPT	:	Rose Bengal Plate Test
RCB	:	Regional Centre for Biotechnology
RCF	:	Regulation of Cell Fate
RNA	:	Ribonucleic Acid
RNAi	:	RNA Interference
RNP	:	Ribonucleo Protein
ROS	:	Reactive Oxygen Species
RS	:	Roberstsonian Translocation
RT-PCR	:	Reverse Transcription-Polymerase Chain Reaction
RT-qPCR	:	Reverse Transcriptase-Quantitative Polymerase Chain Reaction
SAGE	:	Scientific Advisory Group of Experts

ERID	:	External Relations and Institutional Development
TRAIN	:	Translational Research Award in Infectious diseases
VIDRC	:	Vaccine and Infectious Disease Research Centre
DDRC	:	Drug Discovery Research Centre
CHME	:	Centre for Human Microbial Ecology
CDSA	:	Clinical Development Services Agency
HVTR	:	HIV Vaccine Translational Research laboratory
BMGF	:	Bill and Melinda Gates Foundation
bnAbs	:	Broadly-Neutralizing Antibodies
dsDNA	:	Double stranded deoxyribonucleic acid
RNA	:	Ribonucleic Acid
IL9	:	Interleukin 9
BCG	:	Bacillus Calmette–Guérin
HEV	:	Hepatitis E Virus
TNF α	:	Tumor Necrosis Factor α
CD80	:	Cluster of Differentiation 80
mPOCT	:	Multiplexed Point-of-Care Test
SAMPs	:	Synthetic Antimicrobial Polymers
SAP	:	Stress Associated Proteins
SAXS	:	Small angle X-ray Scattering
SC/ST	:	Scheduled Caste/ Scheduled Tribe
SCI	:	Spinal Cord Injury
SCID	:	Severe Combined Immuno Deficiency
SDC	:	Swiss Agency for Development & Cooperation
SDS	:	Sodium Dodecyl Sulfate
SEC	:	Scanning Electron Microscopy
SHG	:	Self Help Group
SNP	:	Single Nucleotide Polymorphism
SNV	:	Single <i>Nucleotide</i> Variation
SOD	:	<i>Superoxide Dismutase</i>
SOX-2	:	(sex determining region Y): box 2
SPICE	:	Smallpox Inhibitor of Complement Enzymes
SVP	:	Sub Viral Particle
TANUVAS	:	Tamil Nadu University for Veterinary Animal Sciences
TAS	:	Technologies for the Advancement of Science;
TAU	:	Technology Advancement Unit
TB	:	Tuberculosis
TCA	:	Tricarboxylic Acid
TEM	:	Transmission electron microscopy

TGFBR3	:	Transforming Growth Factor Beta Receptor III
THSTI	:	Translational Health Science and Technology Institute
TIGS:CI	:	Tata Institute for Active Genetics & Society (Centre at inStem)
TMX4	:	Thioredoxin Related Transmembrane Protein 4
TNAU	:	Tamil Nadu Agricultural University
TRL4	:	Toll like Receptor 4
TRPVB	:	Translational Research Platform for Veterinary Biologicals
TSNAX	:	Translin Associated Factor X
UAS	:	University of Agricultural Sciences
UDSC	:	University of Delhi South Campus
UPR	:	Unfolded Protein Response
UTI	:	Urinary Tract Infection
UTR	:	Untranslated Region
VCP	:	Virus Complement Control Protein
VEGF	:	Vascular Endothelial Growth Factor
VLP	:	Virus Like Particles
Wnt	:	Wingless Integration Site
WNT	:	Wingless: Type MMTV Integration Site Family Member
WSSV	:	White Spot Syndrome Virus
ZnF	:	Zinc Finger
ZnSO ₄	:	Zinc Sulfate
β:G	:	β:glucan
β:GBP	:	β:1,3 Glucan Binding Protein



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