

Annual Report

2008-2009



Department of Biotechnology
Ministry of Science & Technology
Government of India

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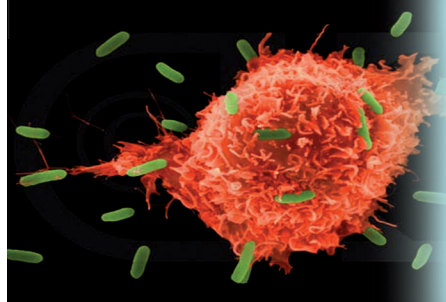
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EXECUTIVE SUMMARY

The year end is an opportunity to reflect on the past and to visualize the future. It has been a year of intense reflection within the Department on how to expand and bring quality to basic sciences, strengthen innovation and promote entrepreneurship. Balancing needs of economic competitiveness with affordable products continues to engage policy makers and the industry. Innovation becomes particularly a serious issue when the value addition is relevant to the health of individuals and the population; and to the food security of the nation. Ecosystem for innovation in the country still has many weaknesses which includes paucity of genuine early-stage funding, lack of dynamic interaction between academia and industry, shortage of right people in right numbers in right working environment specially in the fields of engineering, law, management, technology licensing, IPR etc. To address such issues, DBT has been guided by the National Biotechnology Development Strategy (NBDS) that was approved by the Union Government in 2007. The Department is engaged in delivering on the commitments effectively with the help of multiple stakeholders from the public and private space. DBT itself is undergoing rapid evolution as an organization with likely induction of thirty more officers and an expanded institutional framework for delivery of innovation services through the newly created Biotechnology Industry Research Assistance Council and in partnership with Biotech Consortium of India Limited, Association of Biotechnology Led Enterprises, Federation of Indian Chambers of Commerce and Industry & Confederation of Indian Industry. We present a report card on the implementation of the NBDS of the chapter. As is evident, the implementation has been even ahead of schedule on certain sectors. In addition progress on other critical programmes is briefly reviewed.

Human Resource Development: New Initiatives

People are at the centre of any biotechnology enterprise. The people we create must have high quality and should represent almost 20 different disciplines relevant to biotechnology.

The Biotech Strategy emphasized the need to expand the pool of scientists and expand PhD and Post-Doctoral Programmes; making the

scientific career more attractive and strengthening education at college level. Expansion of human resource is being addressed by the Government through creation of **IISERs**, new **IITs**, six new Biotech Research Institutions and globally acknowledged re-entry package such as the DBT-Wellcome Trust Alliance and the Ramalingaswami Fellowship Programme. The DBT-Wellcome Trust partnership is unique in many ways-a large investment of US \$ 160 million to attract early, intermediate and senior level scientists for career development through

user's friendly management structures. Ramalingaswami Fellowship has been effective in attracting more scientists as compared to similar schemes in the country.

A very innovative scheme launched this year is **Star Colleges** to train students, teachers at undergraduate level. 30 undergraduate colleges were selected across the country and they will get the Star label if they achieve all the reform goals in their education and, experimental work at the end of the two years. The concept of **Star Colleges** to train students and teachers at the under-graduate level has made a beginning and is being extended to North-Eastern states. The imprint of idea generation, creative experimentation and excellence must be made well before the Masters level. India has a huge number of colleges and schools and DBT can only create models and examples. **Innovative Young Bio-technologists Award** scheme launched by the Department as a career-oriented scheme to nurture young researchers with innovative ideas has progressed well and is starting to pay dividends in terms of publications. DBT's **DNA Clubs** (DBT's Nature Resource Awareness Clubs) focusing on schools in each state for hands-on learning as addendum to school curriculum has reached 145 in number spread over 23 states and UTs. National Geographic Channel conducted School Contact Program for 6th – 9th standard to impart awareness on Bioresources and reached more than 4 lakh students over 400 schools across fourteen cities. The **Technologists Training Programme** initiated during the year is going to focus on bio-manufacturing techniques, bio-instrumentation and medical technologies. **All DBT's institutions** cater to the HRD agenda

by providing summer schools, internships, Ph.D and Post Doctoral programmes as well as researcher's training in the projects. Industry placement of Masters students has reached a peak at 800 annually and 34% of these were absorbed by the training companies, a win-win for all. Regional Centre for Science, Education and Innovation in Biotechnology "**RCB**" is specially meant to provide interdisciplinary programmes, but also provide education and training in application and technology relevant courses such as IPR, technology transfer Instrumentation, Policy & Planning, Clinical Research, Fermentation technology and regulation. Special Masters level Translational Science Programmes have been initiated in two medical schools, and in Marine, Animal and Agricultural Biotechnology. In principle, DBT continues not to encourage exclusive biotechnology programme at undergraduate level.

DBT continues to strive to bring quality to Masters programme in the University system (70 Universities), to expand its Ph.D and Post-Doctoral programmes and to support around 300 scientists through long-term overseas training fellowships. **New Masters** programmes have been supported in **marine, agriculture, animal, biomedical, pharmaceutical, industrial biotechnology and molecular human genetics**. The emphasis is clearly on specialized domains rather than general biotechnology.

The young scientists must be particularly nurtured. For scientists below 35 years of age, DBT has started an **Innovative Young Biotechnology Award** scheme. Outstanding people receive an attractive salary as an award, research grants,

flexibility, meetings support and mentorship under this scheme. Similarly, a special research scheme for young scientists in which DBT provides rapid grants within 8 – 12 weeks and mentoring support was initiated.

Strengthening Research in the University System

There is now a unanimous view in the country that research must be nurtured close to the place of education. Every university cannot be research intensive or a hub of innovation. DBT has commenced efforts to help those universities that have potential to become research intensive, to expand the size and depth of the PhD and Post Doctoral programmes, to strengthen institutional framework and mechanisms for interaction with industry and to make innovation and entrepreneurship a part of the educational process itself. The universities are chosen competitively.

Three programmes implemented this year are excellent examples: **UoH-DBT Centre for Research and Education in Biology and Biotechnology at the University of Hyderabad** whereby it is proposed to set up 8 state-of-art laboratories including Biological Containment Facility, Animal House and Green House and Culture (Plant/ Animal/ Microbial) Facilities. The provisions made are expected to result into: increase in number of M.Sc. students from 58 per annum to 150 per annum; PhDs from 26 per annum to 100 per annum; Post-docs from 4 per annum to 50 per annum; R&D projects from 100 per annum to 150 per annum; Publications from

120 per annum to 250 per annum; and about 5 to 10 patents. In addition, about 10 technicians and 50 PhDs with additional skills will be generated.

The **Basic Biological Research Unit at the Indian Institute of Science, Bangalore** was supported with three components: Pathogen Biology; Bio-molecular architecture & interactions and Biological Signaling Mechanisms is an amalgamation of 49 faculty members, 260 Ph.D students, 20 Post-doctoral fellows and 40 Project Assistants in various research activities. The idea here is to sustain quality Ph.D programme and research. The UICT at Mumbai has strengths in chemical science and were supported to develop infrastructure and faculty in biological sciences around a bio-energy programme. The support is tailor made to suit each University's needs and utilize its potential.

Centres of Excellence

To further boost research in the University system and in other institutions, a Centre of Excellence scheme was initiated. The scheme covers basic research as well as translational science and Industrial partnership; Eleven such COEs are under implementation in the areas of: Genome sciences and predictive medicine; system biology and tuberculosis; genome mapping and molecular breeding of *Brassicas*, Stem Cell research, Anti-virals etc. It is envisaged to fund 50 COEs mostly in Universities during Eleventh Plan. The **Programme Support** scheme complements COEs by providing grant to an identified institution/ department in order to strengthen research capabilities on a well-defined research

programme. It enables research programmes to be inter-disciplinary. During the year, five more themes i.e. computational biology, diabetes, research, macromolecular engineering and design, cardio-vascular diseases, discovery of biomarkers for neurological disorders have been added to twenty one on-going themes in areas like transgenic rice, vaccines and biomaterials.

The Department continues exclusive focus on **Biotech facilities and Resource Facilities** such as Primate Resource Centre and Facility on Small Animals at the National Institute of Immunology, New Delhi; International Depository Authority (IDA), at the Institute of Microbial Technology, Chandigarh latter with more than 12000 cultures; database of 38000 records on microbial diversity; and about 200 patent deposits. The year saw the launch of new **Research Resource** on: Toxicology and allergenicity testing labs; GMO detection facilities; specialized centres for screening/ validation; Compositional analysis for GM crop research and services etc. Research resources that have been recently made operational include: Flowcytrometer sorter facility at ILS, Bhubaneswar; P3 facility at JNU, New Delhi; Automatic DNA sequencing and controlled environment growth chamber facility at NIPGR, New Delhi; National Facility for Microarray Genetics and Cell Imaging at IIT, Kanpur; Structural biology of proteins and nucleic acid at the University of Madras; Host-Pathogen biology signaling at IISc, Bangaluru; High-throughput genomic analysis in human complex disorders at JNU, New Delhi; Aerosol containment facility for slow growing and fast growing pathogens and microscopy cum flow cytometry unit at NII, New Delhi. A concept

of **Technology Platforms** in public-private partnership has been promoted. Two such platform established during the year include: **Platform for Translational Research on Transgenic Crops-PTTC** at ICRISAT, Hyderabad and a **Platform for Macromolecular Crystallography** to bring focus of Indian investigators on relevant proteins in infectious organisms i.e. *M. tuberculosis*, *P. falciparum*, Hepatitis and HIV etc. to explore their potential for structure-based drug/ inhibitor design. The newly started **Out reach programmes as extramural activities of DBT's Autonomous Institutes** make select institutions to promote excellence and translational R&D by supporting 'Research Resource Units' in Universities and sister institutions through extramural funding.

Bioclusters

Bioclustering is a globally recognized innovation and enterprise creation strategy. Clusters create a federation of education, R&D, product development, innovation, innovation services and start-up companies. DBT strategy is to build clusters around existing institutions of excellence and to integrate them deeply into the economic, entrepreneurial and social fabric of the region. Four bioclusters being supported by DBT are: National Health Technology Biocluster, about half an hour away from Delhi; the second at Mohali, Punjab; the third at the University of Agricultural Sciences, Bangalore campus led by National Centre for Biological Sciences and the fourth at the University of Hyderabad who have taken the lead in creating a science bio cluster in their campus. The National Capital Region Cluster is dedicated to Health Science and

Technology and will have the Regional Centre for Biotechnology Training & Education partnered with UNESCO, the Translational Health Science Technology Institute (THSTI) partnered with Harvard-MIT Health Science & Technology programme; a Molecular Medicine Centre in partnership with local medical school in the city; technology platform, concept and design application centre, animal services and science centre, nanoscience centre and several mission centres around vaccines, neonatal & children science, chronic disease biology and so on. The Mohali cluster will have the IISER, the Nanoscience institute, a management school, the Agri-Food and Nutrition Biotech Institute with a bioprocessing unit and a biotech park. The NCBS cluster has UAS, Bangalore, the Agricultural University, National Centre for Biological Sciences, the Stem Cell Institute, Centre for Biomolecular Characterization, Silk and Biomaterials Centre, platform technology centre and the innovation society. ABLE, an industry innovator is closely associated with the New Delhi and NCBS clusters. The challenge is to make the clusters dynamic around a common vision and not simply co-located entities.

Incubation is a crucial part of innovation system. The key to incubation is skilled governance. DBT strengthened the incubation facility at the Hyderabad Park, Bangalore Park and the Lucknow Park and will support two new incubators at Mohali and in the NCR with industry partnership. We will endeavour to achieve quality incubation services. In terms of improving infrastructure, several new biotechnology institutes capable of doing both basic multidisciplinary research as well as

translational work have been approved. These include Biomedical Genomics Institute in Kolkata, Stem Cell Institute at Bangalore and Vellore, the Translational Health Science Technology Institute at Faridabad and Agri-Food Biotech Institute at Mohali. The DBT has been enriched by welcoming Rajiv Gandhi Centre for Biotechnology at Thiruvananthapuram into his family.

Early and Late Stage Innovation Support

National Biotech. Strategy has committed 30 percent of DBT budget by the end of 11th Five Year Plan for research in which industry is a key participant. This includes start up support for small and medium companies and high innovation R&D support irrespective of the size of the company. In order to give encouragement to start up and SMEs the department initiated Small Business Innovation Research Initiative (SBIRI) scheme. DBT received nearly 500 proposals spanning health care, agriculture, industrial products and processes, instrumentation, environmental biotechnology, food & nutrition and bioinformatics; of these 48 projects have been funded. Notable achievements from SBIRI projects are: Production of monoclonal antibodies for RBC phenotyping; Humanized monoclonal antibodies against Epidermal Growth Factor Receptor, a silk protein blend film for burn wound management; a homologous natural biomaterial for treating cancer lesions, burn wounds. The external reviewers appreciated the design of the scheme and considered it to be India's genuine early stage support scheme from the government. They suggested greater accommodation of

broader range of biotech industries and to identify more nationally relevant projects.

Large and medium industries can handle discovery and high end innovation programme in new opportunity areas to maintain our future economic competitiveness. To meet this niche – the **Biotechnology Industry Partnership Programme (BIPP)**. An Advanced Technology Science Scheme” was initiated for discovery and late stage development including clinical trials for companies irrespective of size. Upto 100% grant-in-aid support would be provided for Phase-I, II and III clinical trials of biotech-based research leads; and for limited and large scale field trials in the case of agriculture products. The scheme envisages Indian innovation in technology development. In order to facilitate an interface between Industry-Academia, provide innovation service and help promote start-ups, Department will establish a **Biotechnology Industry Research Assistance Council** - as an Autonomous body. In the interim, “Pilot BIRAP” - Biotechnology Industry Research & Development Assistance Programme has been launched in partnership with Association of Biotechnology Led Enterprises and Biotech Consortium of India Limited.

The Department continues to give equal emphasis to R&D under its **Biotech Product and Process Development** programme and **Food Biotechnology**. Clinical efficacy studies on iron fortified rice premix and wheat flour have generated evidence on using iron fortification for anemia. Indigenous probiotic cultures are being studied as a potential source

of Vitamin B12 and for immuno-modulatory effects in Indian children. Nutraceuticals from underutilized plant sources are being explored. Taking note of need for biotechnological interventions in food processing, the Department has initiated integrated M.Sc./ M.Tech & PhD courses in Food Science & Technology in four institutions during 2008-09 & henceforth. A plan to establish an **Agri-Food Biotechnology Cluster**, Mohali, Punjab has been approved during the year. The cluster would have three constituents: a National Agri-Food Biotechnology Institute ; a Bio-Processing Unit and an Agri-Food Biotech Park & Incubator. It will facilitate bench to market progression of products and services and act as a catalyst of innovation in state of Punjab as well as the entire region.

New Legislation and Regulation Agenda

DBT plays a crucial role in regulation of issues under its ambit and has performed its role significantly. Proposing **DNA Profiling Bill** is an important step to augment and transform forensic investigation and criminal justice delivery system. The proposed legislation envisages to establish standards for laboratories, staff qualifications, training, proficiency testing, collection of body substances, custody trail from collection to reporting and a Data Bank with policies of use and access to information therein, its retention and deletion. Under this Act. Intellectual Property, its early licensing and commercialization need a balanced yet flexible approach. The **Protection and Utilization of Public Funded Intellectual Property Bill, 2008** addresses the same. It is envisaged to create a legal framework that would encourage transfer of the Intellectual Property

created by Government funded research, Universities, academic and research institutions to the industry. It will also have positive consequences in terms of providing adequate incentives to the Intellectual Property Right Creator and getting recognition to the Universities, academic and research institutions and researchers for their contribution in rendering public good.

A smooth and vibrant interaction between different agencies is required for the approval of genetically modified products/processes. The Government of India directed DBT to act as a nodal agency for establishment of a **National Biotechnology Regulatory Authority**. The Department prepared a draft legislation and establishment plan for setting up of NBRA, and has proposed NBRA as an independent, autonomous and professionally led body to provide a single window mechanism for the safety assessment of genetically engineered products and processes. Establishing NBRA will require the promulgation of new legislation, i.e. National Biotechnology Regulatory Act or the NBR Act. A draft bill has been prepared by DBT through consultations. In the meantime, according to the **Biosafety Agenda**, the Department facilitates implementing biosafety procedures and guidelines under Environment (Protection) Act 1986 and Rules 1989 under the Act. A Monitoring-cum-Evaluation Committee has been created under the RCGM and it ensures the agronomic advantage and safety of the transgenic crops to the environment, by on-the-spot monitoring of GM crops in the field trials. During the year, MEC & RCGM played important roles in the release of **142 new Bt. cotton hybrids** by GEAC and providing marketing approval of several indigenously developed r-DNA pharmaceuticals.

Though cotton is the only transgenic crop approved for commercial release in the country so far, the transgenic research is being conducted on several other crops like brinjal, cabbage, castor, cauliflower, corn, groundnut, mustard, okra, potato, rice, tomato etc. for experimental purposes. The department has been successful in further streamlining the biosafety procedures and the total number of **IBSCs touched 379** in various research institutions and industrial R & D units. Protocols for food and feed safety assessment of genetically engineered crops, and Guidelines and Standard Operating Procedures for confined field trials of regulated GE plants were adopted by RCGM and GEAC during the year. Two dedicated, dynamic & interactive web sites on **Indian Biosafety Rules and Regulations** and **Indian GMO Research Information System** to provide information on rDNA research in disseminate statutory requirements to be followed are in operation. The Department in association with MoE&F provided continued support for the capacity building in State Agriculture Universities and organized twelve workshops on management and monitoring of field trials of GE crops.

Research and Development Agenda

Research development is the central activity provided by DBT. The area of emphasis were: Development of staple crops through transgenic approach & MAS, non-staple crops, Plantation & Horticulture, Bio-fertilizers, Bio-pesticides etc; Bioresource Development and Utilization; Infectious Disease Biology, Chronic Disease Biology, Vaccines & Diagnostics; Stem Cells Research; Bioengineering, Implant and Devices; Human genetics and Genome Analysis; Environment Biotechnology; Nano-Sciences and

Nano-Medicine and Agriculture and Energy Bio-Sciences

Health Care Biotechnology

Department's health care agenda has expanded exponentially during later part of the 10th plan and continuing during 11th plan period. There is adequate emphasis towards translation of research leads and consolidation of open ended R&D projects into distinct programs i.e. Centers of Excellence and Public-private partnership. The newer programs/activities include: setting up of a **Vaccine & Infectious Disease Research Centre; a Centre for Molecular Diagnosis & Imaging; and a Health Science Technology Policy Unit** under **THSTI**, New Delhi; developing clinical trial sites; clinical trials of various lead compounds etc. The programmes of Medical Biotechnology are grouped into: Vaccines & Diagnostics; Infectious Disease Biology and Chronic Disease Biology. Under Vaccines & Diagnostics. Candidate vaccines for Rotavirus, Cholera, Typhoid, DNA based Rabies vaccine both for animal & human, Anthrax, Malaria, Dengue, Tuberculosis and Japanese Encephalitis Virus are already into pre-clinical or clinical trial stages. An interesting feature emerging out of the entire **vaccine research** is the India's competence to work in a cost-effective manner for initial candidate vaccine development. The translational limitation for cGMP manufacturing and competence in clinical testing are being gradually addressed by newer public-private partnership structure such as BIPP and the **National Development Services Agency**. The Task Forces on Infectious Diseases Biology and Chronic Disease Biology have supported around 200 R&D projects both on Infectious biology and Chronic Disease biology. Good

publication and patents have emerged from these R&D projects during the year. The progress of indigenously developed vaccines is summarized in **table on page 9**.

Agriculture Research and Development

The focus of R & D in agriculture area is on three main staple crops viz. **rice, wheat & maize**, followed by **pearlmillet, groundnut, pigeonpea** and **cassava**. After initial success of Biofortification programme in main staple crops, Phase-II programme on pearlmillet, groundnut, pigeonpea and cassava for alleviating micronutrient deficiencies has been planned. In all genetic manipulations, the objectives are to define the function of the predicted genes, particularly those affecting yield and tolerance to various abiotic & biotic stresses. Functional genomics of rice for discovery & functional validation of genes and novel genes conferring resistance against biotic stress were supported. India is joining **"International Wheat Genome Sequencing Consortium"** for physical mapping and sample sequencing of wheat chromosome No. 2AL. A **National Plant Gene Repository** has been approved for procuring important plant genes, promoters, vectors and Expressed Sequence Tags in the form of DNA clones etc. and for those cloned by our institutions and maintain them for their long term storage and use. The Department has established a National Plant Gene Repository at NIPGR, New Delhi to facilitate research in Agricultural Biotechnology, plant molecular biology, transgenics, genomics etc.

Under the **National Bioresource Development Board**, a major initiative was the establishment of a **Microbial Culture Collection- Biological**

Success Story on Vaccine front

Rotaviral diarrhoea vaccine (116E)

- *Safe and immunogenic*
- *cGMP material ready*
- *Entered into Phase-III clinical trial*

Malaria Vaccine

- *Three candidates i.e. P. falciparum- PfF2; PfMSP-119 and P. vivax- PvRII; PvMSP-119 developed*
- *P. vivax: PvRII globally accepted candidate for vaccine development*
- *Produced GMP grade material for clinical trials*
- *Establishing partnership with MVI, EMVI, Gates Foundation for clinical Development*

Cholera (recombinant oral)

- *Completed Phase-I &II clinical trials*
- *Being manufactured by M/s Shanta Biotech in a contractual mode*
- *Ready for Phase II/III*

Rabies (combined DNA based)

- *Completed clinical trials*
- *DCGI clearance awaited for launch*

Typhoid Vi-conjugate

- *Technology transferred to USV, Mumbai for GMP production and pre-clinical toxicology studies*

Tuberculosis

- *Antigen 85C, ESAT and SOD-based candidates ready for clinical trials after encouraging animal data*

Dengue (recombinant tetravalent)

- *Accelerated development vaccine through industrial partner*
- *Animal studies being conducted in collaboration with Emory, USA*

JEV (Vero cell based)

- *DBT-NII vaccine transferred to M/s Panacea Biotech*
- *Ready for Phase-I clinical trial*

HPV

- *Indian efforts based on HPV oncogenic are going on*
- *Collaboration with Merck and Wellcome Trust being worked out*
- *Indian Company entered into partnership on one candidate*

Immuvac – An Immunomodulator

- *Based on inactivated Mycobacterium indicus pranii*
- *Shown significant immuno modulatory effects in Leprosy.*
- *Rediscovering for treatment of Tuberculosis and Cancer*

Research Centre at Pune. Provision to hold more than 2,00,000 bacteria and fungi following international standards has been made with gradual up gradation of the facility as an International Depository Authority on microbial collections like ATCC. Under the programme on prospecting of drugs from microbial sources, about one lakh bacterial isolates have been collected and screened. More than two lakh extracts have been prepared and about 7,000 promising hits obtained. Indian Bio-resource Information Network (IBIN) portal was launched by the Hon'ble Minister in 2006. A sugarcane network programme continues to identify genes differentially against pathogens.

Trans-boundary Agenda

The first attractive trans-boundary collaboration on multiple-partner basis was India's commitment through DBT to host India unit of the **International Centre for Genetic Engineering and Biotechnology (ICGEB)** way back in 1987. The centre provides a scientific and educational environment of international standard and conducts innovative research in life sciences for the benefit of developing countries. ICGEB has many notable successes such as lead, malaria candidate vaccine, system biology of tuberculosis, crop improvement, environmental protection/remediation, bio-pharmaceuticals and bio-pesticide production by transferring a number of technologies. The centre provided quality Ph. D programme to a huge number of Indian students and organized short term training in avian influenza, transgenic and tuberculosis .

International cooperation and partnerships are essential for exploring mutually advantageous

science collaboration and achieving global standard and creating industry level linkages, partnership with advanced, emerging and developing countries were supported. The aim was to achieve global best practices, joint IPR generation, harmonization of regulatory processes, smooth trans-boundary movement of biologics and leverage global markets for the products. Strategic partnership was established with **Australia, Canada, Denmark, Finland, Norway, Sweden, Japan, Cuba, Switzerland, UK, EU and USA** with increasing financial commitments during the year. Emphasis has been laid on , basic research as well as technology development while pooling-in the collective knowledge resource of the collaborating countries. DBT and the Wellcome Trust partnered to strengthen the research base of India biomedical science by providing post-doctoral fellowships for early stage, intermediate and seniors. The partnership was launched in September, 2008 by Mr. Kapil Sibal, Hon'ble Minister for Science & Technology. A US\$ 160 million scheme to be jointly shared between the DBT and the Wellcome Trust over 10 years aims to attract world class biomedical research talent to India.

Aquaculture and Marine Biotechnology

The emphasis continued on the development of new technologies and enhancing the production in the area of aquaculture and marine biotechnology. More than 70 neuro-active peptides have been isolated and purified from the crude venom of various species of Indian cone snails and their biological activities analyzed. An anaerobic consortium was developed from marine sediment and biological sludge for the application of wastewater treatment. A multi-centric

programme on cell line development was initiated and primary cell lines developed from hepatopancreas of edible crab; eye muscle of *Etroplus*, grouper, catla and rohu. The blue print for creation of an institution on **Marine Biotechnology** to exploit huge marine resources was finalized.

Animal Biotechnology

In the area of animal biotechnology emphasis was on: Development of quality feed; Animal reproduction; Animal byproducts; and Genetic characterization of indigenous breeds of livestock. In order to provide translational research perspective and product development directive, the Department set up Task Force on “Translational Research and Product Development of Veterinary Vaccines and Diagnostics” during the year. Notable research outcomes are: candidate vaccine against *Haemorrhagic septicaemia*; vaccine against *Clostridium perfringens*; DNA vaccine against bovine brucellosis and vaccines for bovine tuberculosis. Leads from projects on diagnostics are: development of a rapid diagnosis kit for leptospirosis, diagnostic techniques for *Dichelobacter nodosus*, development of molecular methods for rapid detection of Johne’s disease, PCR test for detecting major pathogens of bovine mastitis, diagnostic(s) for chicken anaemia virus for echinococcosis in animals and its environment. Transgenic mice models were developed using a reproducible novel technique for inserting genes in spermatogonial cells through *in vivo* electroporation. Embryonic stem cells were isolated and cultured from inner cell mass of buffalo blastocysts. Two bacterial artificial chromosome (BAC) genomic libraries of male Murrah buffalo were prepared and

characterized. Comparative fiber degradation capacity of various biomaterial of bovine origin for reconstructive surgery in animals was developed and its acceptance as surgical material was also studied.

Basic Research and Modern Biology

Programme on basic research is being supported to enhance the understanding of fundamental principles and theories. Projects were funded under following categories; Genomic and Drug Discovery; RNAi Biology; Proteomics; Systems biology; Computer Modelling, Simulation and Optimization; Molecular Immunology; Gene Cloning and Biochemical studies ; Plant Molecular Science and Nanobiotechnology; Bioengineering and Reproductive health. Currently about sixty projects are going on.

Environment & Climate Restoration

The goal of environmental biotechnology programme is to provide cost-effective solutions for: eco-restoration of degraded habitats, conversion of toxic recalcitrant chemicals into harmless by-products, treatment of wastes, production of value-added products from waste/biomass and effective *ex-situ* conservation strategies. During the year, a comprehensive National Action Plan on climate change using “Mitigation technologies” was prepared and about 250 pre/concept proposals received. Using a novel mechanism of short listing, 44 preproposals have been screened-in. One pilot plant for the large scale production of Oil Zapper was established in The Energy and Resources Institute (TERI), New Delhi with the help of petroleum Industries i.e. ONGC, IOC, HP, and BP. Technology for the

treatment of pulp & paper mill waste was field tested in Uttar Pradesh with the involvement of user industry. Guidelines for bioremediation of oil contaminated sites, oil contaminated water, oily sludge pits, crude oil sludge and oil contaminated drill cuttings etc. were prepared and sent to the Ministry of Environment & Forests for approval. **Energy Bioscience Programme** has Jatropa micromission where in 1615766 plants are in the field covering roughly 693 has at 145 sites across the country. Multi-locational trials of Jatropa have been extended to ten different locations. Network projects are going-on to develop a commercially viable technology for bioethanol production using varied lignocellulosic feed stock as a raw material. Efforts have also been made to build capacity in the Energy Biosciences by establishing **National Energy Bioscience** and **Energy Bioscience Overseas Fellowships** for overseas scientists.

Social Agenda

The social agenda of the Department is to provide cost-effective/income generation solutions. The approach primarily is to use softer biotechnologies and its demonstration for adoption by rural population, women and tribals. The agenda is taken forward primarily in the form of demonstration of proven technologies on: food and Nutrition; use of bio-control agents; bio-fertilizer; health care technologies etc.

Conscious efforts were made to establish market linkage to the beneficiaries for sustainable employment along with training & capacity building. Urban and semi-urban beneficiaries were encouraged to set up their enterprises in sectors like floriculture, medicinal & aromatic plants, bee-keeping, bakery and value added

products from seasonal horticultural crops, sericulture, bio-control agent etc. These projects are implemented either as an individual or an integrated manner in the form of **Biocomplex**. Women network projects were implemented in the form of **Women Bioresource Complex** to benefit farmers for sustainable employment through commercially important local crops, cultivation & processing of medicinal plants and spices, poultry & livestock management, aquaculture along with paddy cultivation and organic cultivation of tea etc. Through these Biocomplex projects, over 7,500 families have been trained in various technology packages and are in the process of establishing their enterprises. The beneficiaries trained in activities like vermicompost, mushroom cultivation, value-added food items, poultry/goat farming have already started marketing their produce. The **Rural Bioresource Complexes** continued their activities during the year and benefited 49,055 families.

North-Eastern Programme

DBT's presence in the North-Eastern (N-E) states has been in the form of its autonomous institution i.e. **Institute of Bio-resources and Sustainable Development (IBSD)**, Imphal; **North East Bioinformatics Network (NEBInet)**; collaboration with IIT, Guhawati and extension of **Star Colleges** scheme to N-E states and establishment of a Biotech. Incubator in Assam. IBSD focuses research using local bio-resources towards entrepreneurship development and socio-economic upliftment. During the year, this institute has brought out fifteen research publications and started a major network programme on microbial bio-prospecting for drug discovery with an industrial partner. Twenty-five

Bioinformatics Centers have been established in Universities, colleges and Institutions at various states of North-Eastern region as part of the BTISnet. During the year, in the first North-East Bioinformatics interactive Meeting, it was decided to establish a **North-Eastern Bioinformatics Network (NEBINet)** for faster network activities, sharing of online lectures, databases, electronic journals, expertise and other resources. There is vision to expand N-E agenda to all medical colleges of the region by strengthening pathology/micro biology/biochemistry labs and establishing clinical trial networks for chronic disease prevalent in the region.

Cell and Tissue Engineering

Stem cell is a scientifically fascinating area with an immense potential for translation and therapeutics. Both basic and clinical research was promoted by the Department using embryonic and adult stem cells such as limbal, haematopoietic, embryonic, pancreatic, neural, cardiac stem cells; generation of human embryonic stem cell lines; use of banana lectins for stem cell preservation; haematopoietic stem cells (HSC) for haplo-identical etc. Project on protein profiling of human ovarian tumour stem cells; differentiation of human fetal pancreatic progenitor cells for potential use in cell replacement therapy for type-1 diabetes; establishment of propagable cell lines from pancreas and adipose tissue of embryo and adult obese rats, *In-vitro* differentiation of hESC and MSC into cardiomyocytes; characterization of cultivated oral mucosal epithelial cells and its application for reconstructing the ocular surface in patients with severe ocular surface disease; MSCs therapy in diabetic induced mice skin wounds etc. have been supported. India is

participating in the Stem Cell Network on Asia Pacific” (SNAP), a conglomerate of seven countries. Stem Cell Guidelines have been submitted to the Ministry of Health and Family Welfare. A CMC-DBT Centre for Stem Cell Research is functional at CMC, Vellore as a translational unit of the “Institute for Stem Cell Science and Regenerative Medicine” that has been approved to be located at Bengaluru to carry out both basic and translational stem cell research.

RNAi Biology programme of the Department uses the knowledge of using small non-coding RNAs, including siRNA, miRNA and piRNA for modulating gene expression at the stage of translation or transcription of specific genes both in plants and animals. The Department started a programme on the “Development of RNAi technology for application in Medicine and Agriculture” two years back that has now forty nine projects exploring applications in agriculture and medicine. miRNA profiling on skeletal muscles of healthy, pre-disposed type 2 diabetics is using multi-targeted RNAi (MTRNAi) effector technology through bioinformatics tools. RNAi technology is also being extended to silence genes of unfavorable traits in Brassica sps., rice and wheat. Similarly, in the areas of **Nanosciences and Nanotechnology**, the Department has taken special initiatives to support scientists across all disciplines with focus on nanomedicine and nanoagriculture. The projects aim to: develop bioconjugates of nanomaterials (NMs) for their applications in cancer therapy; *in vitro* imaging studies in cancer cell lines (HeLa and A549) using metallodendrimers; develop nanoscale material for therapeutic use; develop innovative nano-structured polymer composite materials with surface-tailored properties; model systems for

assessing diagnostic and drug delivery potential of Au NPs etc. Most of the projects are leading into translational results.

Bioengineering programme is to improve the quality of the nation's health by increasing biological knowledge and facilitating the development of novel devices and drugs and integrates physical, chemical, mathematical, and computational sciences and engineering principles to study biology, medicine, behaviour, and health. It advances fundamental concepts; creates knowledge from the molecular to the organ systems levels; and develops innovative biologics, materials, processes, implants, devices, and informatics approaches.

During the period, the department sanctioned 30 projects across various disciplines. On-going projects resulted in publication of research papers in high impact journals.

The Department has taken initiative to promote medical technology innovation in India in collaboration with the Stanford University, USA. **Stanford-India Biodesign (SIB)** programme has been formulated as a collaborative venture of DBT, Indo-US S&T Forum and Stanford University, USA. The focus of the programme is on development of implants and medical devices. Identification of opportunities is done by an interdisciplinary team by real life observations of clinical cases for designing a prototype. The first SIB Centre in India is established jointly at AIIMS and IIT, Delhi.

DBT's Institutional Framework Agenda- It's Autonomous Institutions

The Department has a number of autonomous

institutions under its ambit. Its vision to create the institutions at the time of its inception in 1986 was to address the crucial areas of research that needed special attention or consolidation. After two decades of existence, DBT is in the process of establishing several new institutions and "Bio-clusters". The driving force for the new institutions is need for disease/area-based institutions and also to capture the leads of R&D from existing institutions for translation into usable products.

National Institute of Immunology (NII), New Delhi



*Prof. Avdhesha Surolia,
Director, NII*

NII continues to focus on **basic and applied immunology** research with an aim to develop novel and appropriate biomedical technologies of special relevance to the nation. The research focuses on: Infection and immunity; Host-pathogen interactions;

Developmental & Reproductive Biology; Structural Biology and Chemical biology. New activities initiated during the year include: Chikangunya vaccine development with USV Limited, Mumbai; clinical evaluation of rotavirus vaccine with Society for Applied Sciences, Kolkata; setting-up centre of excellence in infectious diseases and a NMR structural biology. NII initiated collaboration with Drexel University Medical Centre, USA. During the year, four potential technological leads have been obtained through basic research: New insights into mycobacterial polyketide biosynthetic machinery have been made opening

up novel avenues for **drug discovery for tuberculosis**; use of green tea extract and Triclosan have been proven useful in treatment or prevention of tuberculosis; a novel method for **generation of transgenic animals** without sacrificing animals with applicable to other species has been developed. NII also has developed a technology to generate “**Artificial Skin**” using FDA approved biodegradable polymer. NII team has bagged the Second prize at Intel-UC Berkeley Technology Entrepreneurship award in Nov.2008 in U.S.A for the innovation. Seventy nine papers by the scientists and scholars of the Institute were published during 2008-09.

National Centre for Cell Sciences (NCCS), Pune



*Prof. G.C. Mishra,
Director, NCCS*

The NCCS has emerged as a leading centre for fundamental research in Cell and Molecular Biology in the past ten years. Expanding its role from a National Tissue Culture Facility in 1986, the current mandate includes: cutting-edge research activities in stem cell biology, cancer biology, signal transduction, diabetes, insect molecular biology, infection and immunity, chromatin architecture and gene regulation. NCCS functions in a tripartite manner as: a National Cell Repository; centre for Human Resource Development and R&D centre focusing on the frontier areas of biology. The National Cell Repository at NCCS is a major service centre for both public and private sectors. During the last

five years the repository has procured more than 35 new cell lines and has a total culture collection to 1161. Approximately 510 researchers from 275 institutes are registered with NCCS. During the year, NCCS provided more than 1800 cell lines of different cell types to over 100 scientific institutions in the country. It is in the preliminary stage of establishing another centre to conduct application-oriented research with focus on regenerative medicine, neuro-degeneration and developmental biology. A programme for setting up a centre for conservation of microbial diversity is also in progress. Three patents have been obtained during the year. NCCS has on-going collaborations under Indo-French, Indo-German, Indo-UK and Indo-Finnish programmes.

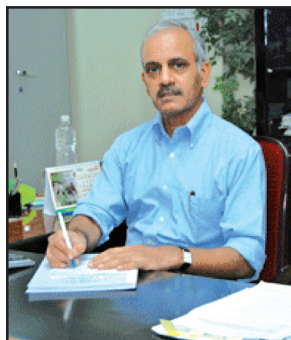
National Brain Research Centre (NBRC), Manesar, Haryana

NBRC is aiming to be a “Centre of Excellence in Brain Research” with state-of-art facilities and adopting a strong philosophy of networking. It has been established by the Department as an “Apex Coordination Centre” for Neuroscience research in India. The focus of research is on: Computational neuroscience, system and cognitive neuroscience stem cell research, developmental neurobiology and basic research towards understanding of neurological and psychiatric disorders.

NBRC has networked with 47 centers and provided access to over 400 on-line journals to scientists at the networked centres. Efforts are on to meet the other requirements of the scientists, such as establishment of centralized facilities and training programmes. In addition, NBRC has expanded its international collaborative

agreements to scientists working at the networked centres, thus providing a unique platform for interaction of scientists from India and elsewhere in the world.

Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad



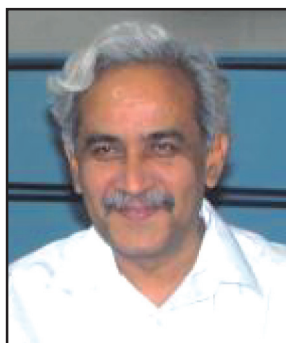
*Dr. J. Gowrishankar,
Director, CDFD*

Set up twelve years ago, CDFD is involved both in services in the areas of DNA profiling for law-enforcement agencies & diagnostic tests for genetic disorders; and **frontier-level research** in various disciplines of molecular biology under fifteen

group leaders. CDFD pursues the research on genetics, molecular and cell biology, cancer biology, pathogen biology, HIV biology, immunology, fungal pathogenesis, plant-microbe interaction etc. CDFD is recognized by the Manipal Academy of Higher Education and University of Hyderabad for pursuing Ph. D programme in life sciences. During the year, 60 papers were published in international peer reviewed journals and a technology related to "Tuberculosis diagnostics" licensed to M/s Arka Nanomeds Pvt Ltd. Two patents have been issued related to "A method of altering levels of plasmid". The Centre has secured the allotment of 13 acres of land in Hyderabad from Andhra Pradesh State Government for its permanent campus. CDFD continues to receive funding from other agencies like The Wellcome Trust (UK), National Institutes of Health (USA), CSIR, IFCPAR, DRDO, etc. on specific collaborative research projects. A large

number of patients diagnostics services are being provided by CDFD at Nizam's Institute of Medical Sciences, Hyderabad under a MoU.

National Institute of Plant Genome Research (NIPGR), New Delhi



*Prof. Akhlesh Kumar Tyagi
Director, NIPGR*

NIPGR continues its research towards **genetic modification** of crop plants for improved **nutritional quality**. The Institute has made significant progress in this area with advances in recombinant DNA methods and transformation procedures. During the year, NIPGR has entered into a MoU with Donald Danforth Plant Science Centre, USA as a collaborative arrangement to use **plant sciences** to improve agriculture, health and nutrition with emphasis on improved planting materials for farmers. Four patents have been granted i.e. Plant variety of *Catharanthus roseus* named "Ili"; A method for tandem cropping of wheat and mustard in Indo-Gangetic plains; Extra-cellular matrix localized ferritin for iron uptake, storage, and stress tolerance; Novel stress responsive transcription factor involved in plant growth and development and methods thereof. The institute looks forward to intensification of research efforts in selected areas like the Proteomics. The establishment of a "National Plant Gene Repository" has been initiated and emphasis on quality human resource development is on the anvil for making NIPGR a resource for plant sciences research with strong element of application.

Institute of Life Sciences (ILS), Bhubaneswar



*Dr. B. Ravindran,
Director, ILS*

The institute aims to develop a cluster of trained and motivated faculty in an ideal scientific cell ecosystem to establish a “National Centre of Excellence” in Life Sciences with focus on the regional advantages. The research focus is on: Infectious

disease biology of *Plasmodium* and cholera; Cancer Biology and Plant Biotechnology. During the year work has progressed well on clinical presentation of ABL kinase domain mutations and secondary events in chronic myeloid leukemia; Dose-dependent cytotoxicity of etoposide containing nanoparticles using Y-79 cells; molecular studies using competitive RT-PCR analysis of relevant genes in rice. A patent was filed for production heat and photo-resistant Catalase was filed and its commercial exploitation will be pursued. The civil part of the construction of R&D Phase-I building, Animal House & Research Scholar's Hostel has already been completed. Construction of Phase-II of R&D building is going on.

Institute of Bioresources and Sustainable Development (IBSD), Imphal

IBSD continued its research activities focusing on bio-resources for entrepreneurs or industries towards employment generation and socio-economic upliftment of N. E. region.

Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram



*Prof. M. Radhakrishna Pillai,
Director, RGCB*

After taking over of the RGCB by the Department in 2007, the center initiated three new ambitious programs during the year i.e. cardiovascular biology, a technology & business culture systems, animal models & human studies.

RGCB and Hindustan Latex Limited have established a joint technology & business incubator for developing newer molecular diagnostics. The primary goal of the translational synthetic biology initiative at RGCB is to clone, express and characterize proteins from non-coding genomic regions of *E. coli* and Yeast. Expression of such novel proteins may lead to discovery of molecules with completely new functional characteristics, many of which are likely to be of interest to basic biology as well as to applied areas such as therapeutics. Recognizing the capability of RGCB to translate biotechnology into industrial and knowledge wealth, the Government of India has sanctioned RGCB, a grant of Rupees 100 crores for building up a unique second campus for Bio- Discovery Cluster for Disease Science & Engineering (BCDSE). The vision statement for the second campus is to be a centre of excellence for translational research in disease biology and molecular medicine, inspired by the operational philosophy of discovering ‘Bench-to-bedside’ solutions. During the year, four patent applications on: Antimicrobial activity of herbal extract of *Kaempferia galanga*; Synthesis and anticancer activity of a novel Cu (II)

coordination complex; Chalcone Synthase (CHS) Gene from Ginger and Assay for Detection of Transient Intracellular Ca²⁺ have been filed. Some of the promising technologies developed include: MCF-7 Bid Ds Red stable cell line for anticancer drug screening; RAGEP marker system; Universal protocol for generating 100 bp size standard for endless usage; a techniques for sensing intracellular calcium transients; Platform for simultaneous detection of dengue and Chickungunya viruses.

Vision for 2009-10

The year **2009-10** has been identified for reforming the competitive grants system and governance. It is aimed to:

- To expand capacity for translation research in health, agriculture,, industry and environment sectors;
- Advancing standards in manufacturing of biologicals;
- Rapidly respond to new opportunities in newer areas i.e. nano-sciences, stem cell biology, genetics and genomics based health-care and agriculture
- Expanding the use of Information Technology
- Focus on young scientists
- Creating a pipeline of products

Remodeling of DBT is on the anvil with 40 new positions being filled up. Past decade built infrastructure so far has supported bottom-up research. However with the current strength, mid- and high-level inventions may result into bed-to-bench technologies. DBT understands the national call and is making efforts to deliver it.

Administration

Administration Section is an integral part of the Department and renders its support through well-laid out schemes for the welfare of the in-house scientists as well as implementation of various scientific programmes. The group ensures successful holding of Scientific and Expert Group meetings by providing logistical support. Latest equipments and multi-media are provided to the individuals and made available in all conference rooms.

Establishment

Establishment Section deals with the personnel matters of the Department.

Finance

Finance division is an integral part of the Department. It manages both non-plan and plan funds of DBT and works closely with the scientific divisions in meeting their financial deadlines. It shares the responsibility of ensuring the smooth expenditure of the department in each quarter and has a record of making use of atleast 90% of the funds allocation each year. The department has the distinction of meeting its financial commitment towards all its schemes. While some hurdles have been experience for the North-Eastern budget, the current year is all geared-up up to take up that challenge for generating relevant projects from that region. The Department of Biotechnology was allocated an amount of Rs.901.50 Crore (Rs. 879.00 Crore (Plan) and Rs.22.50 Crore (Non-Plan) for the year 2008-09. The budget allocation for 2009-10 is Rs.900.00 Crore (Plan) and Rs.24.00 Crore (Non-Plan).

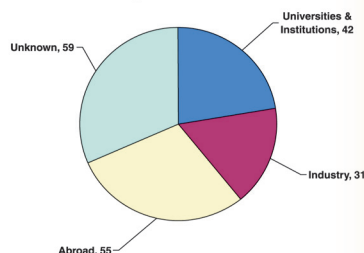
NBDS : PERFORMANCE DURING 2008-09	
AIMS	ACTIONS
BUILDING WORLD-CLASS HUMAN CAPITAL	
Focus on research-education: Re-engineering of existing University departments	<ul style="list-style-type: none"> • DBT-UICT Bio-energy Centre set up at Mumbai. • DBT-Central University, Hyderabad Centre for Research and Education launched for: research in selected areas; PG-teaching and upgradation of training labs. • DBT-IISc, Bangalore programme on Basic Biological Research initiated.
Focus on under-graduate education: “Star Colleges” in life sciences to be up-graded	<ul style="list-style-type: none"> • Already 25 colleges identified for support and strengthen undergraduate life science teaching & infrastructure and training, including training of faculty in select colleges across the country. • Being expanded to North-Eastern States.
Setting-up of the UNESCO Regional Centre for Science, Education and Innovation in Bio-technology (URBS)	<ul style="list-style-type: none"> • Being set up at Faridabad cluster, NCR.
CREATING WORLD-CLASS RESEARCH CAPACITY	
Expanding infrastructure by instituting newer schemes i.e. Centres of Excellence (COE) scheme; Research Resources and Technology Platforms in institutions and labs	<ul style="list-style-type: none"> • COE scheme launched; already eleven COEs established covering different interdisciplinary areas; about twenty five Programme support to institutions on different themes; Biotech facilities expanded; Research Resources & Technology Platforms initiated.
PROMOTING BIOTECH INDUSTRY	
Schemes to promote public-private partnership to be initiated: <ul style="list-style-type: none"> • Biotechnology Industry Partnership Programme (BIPP) to be launched for 	<ul style="list-style-type: none"> • SIBRI already functional for last two years • BIPP Scheme launched and nine projects approved.

achieving global competitiveness and generating IP in frontier biotechnologies	
<ul style="list-style-type: none"> Biotechnology Industry Research Assistance Council (BIRAC) to be set up as an interface between academia and private sector particularly for SMEs and start-ups. 	<ul style="list-style-type: none"> Ground work for BIRAC initiated; an interim Biotechnology Industry R&D Assistance Programme put in place to promote and facilitate industrial research through technology transfer and IP management, technology acquisition and technology forecasting.
ATTRACTING OVERSEAS SCIENTISTS	
DBT-Wellcome Trust Fellowships	<ul style="list-style-type: none"> WT/DBT India Alliance, an independent charitable trust established by the two partners i.e. DBT & Wellcome Trust. A DBT/WT Biomedical Research Career Programme launched with a commitment of US \$ 160 million to attract world class bio-medical research talent over the next 10 years.
Ramalingaswami Re-entry Fellowships	<ul style="list-style-type: none"> A re-entry fellowship to attract high-calibre scientists of India origin to work in Indian labs for up to five years. Twenty five scientists in positions.
CATALYZING SYNERGY AND INNOVATION	
Technology Clusters	<ul style="list-style-type: none"> Three Bio-cluster: Health Biotech Science Cluster, Faridabad (NCR); Agri-food Biotech Cluster, Mohali, Punjab and Bangalore Biotech Cluster, Bengaluru in offing.
SCALING NEW HEIGHTS	
New institutions with area/disease-specific focus	<p>Five new institutions approved</p> <ul style="list-style-type: none"> Translational Health Science & Technology Institute, Faridabad Cluster. Institute of Stem Cell Research and Regenerative Medicine, Bengaluru.

	<ul style="list-style-type: none"> • UNESCO Regional Centre for Biotechnology Training and Education, Faridabad Cluster. • Punjab Agri-food Biotechnology Institute, Mohali, Punjab. • National Institute of Biomedical Genomics, Kalyani, West Bengal. <p>Centers in pipeline</p> <ul style="list-style-type: none"> • National Institute of Marine Biotechnology. • National Institute of Animal Biotechnology. • Institute of Silk and Biomaterial Technology.
PROMOTING NEW LEGISLATION	
<p>Protection of IP in public-funded R&D</p> <p>DNA Profiling Bill to augment and transform forensic investigation and criminal justice delivery system</p>	<p>The Protection and Utilization of Public Funded Intellectual Property Bill, 2008 for enactment of legislation introduced in the Parliament.</p> <p>Inter-ministerial consultation is underway for the bill.</p>
STREAMLING REGULATION	
National Biotechnology Regulatory Authority (NBRA) to provide single window biosafety clearance of genetically modified products/ processes	<ul style="list-style-type: none"> • A draft for establishment of NBRA and its legislation is under circulation for inter-ministerial consultation.

Highlights of 2008-09

- *University involvement*
- *Networking of research and development through University*
- *Opportunity to redesign institutions*
- *Entrepreneurship*
- *DBT's entry into economic and social system*



HUMAN RESOURCE DEVELOPMENT

Working on a dual plank of creating “Critical Human Resource” and “Infrastructure” since inception, the Department has been implementing an integrated programme on human resource development at the postgraduate, Ph.D. and post-doctoral levels. There are postgraduate teaching programmes and specialized training of mid-career scientists and faculty in leading national and overseas laboratories that aims at upgrading their skills. Newer activities of the year include “Star college scheme” for improving training of biotechnology at the undergraduate level by faculty improvement, curriculum revision and emphasis on practical training. HRD programmes also aim at preparing India for global biotechnology economy; hence putting adequate attention to training of high quality technicians and technologists in skills required by the industry. Special schemes/programmes to invite Indians from overseas labs have been initiated and strengthened.

Teaching

Expansion of postgraduate M.Sc./M. Tech teaching programme: Initiated in 1985 in six Universities, the PG teaching programme has gradually expanded to over seventy two Universities. There are ten such courses that include: General Biotechnology; Medical, Agricultural, Marine, Veterinary, Industrial, Food, Molecular & Human Genetics, Neurosciences and Pharmaceutical Biotechnology. Selection of students is through a common entrance test conducted by JNU. The programmes are regularly monitored by in-house Advisory Committees and an annual course coordinator's discussion.

During the year, the Department supported M.Sc. Agriculture Biotechnology in Bidhan Chandra Krishi Vishwavidyalaya, Kalyani and Mahatma Phule Krishi Vidyapeeth, Rahuri;

M.Tech Food biotechnology at UICT, Mumbai; and M.Sc. Human Genomics at Punjab University, Chandigarh & Jiwaji University, Gwalior. Fourteen more proposals are under active consideration.

Star Colleges: The Department has laid the foundation to start a scheme of “Star Colleges” to improve teaching of biotechnology by providing specialized infrastructure and consumables to colleges and University departments offering undergraduate courses in life sciences. The programme entails:

- Improving knowledge and skills to teachers in basic life sciences and specialized techniques;
- Generating appropriate infrastructure and making it accessible to students;
- Increasing availability of consumables, reagents and chemicals for students;

HRD Agenda of DBT

Teaching

- *Postgraduate M.Sc/M. Tech Teaching Programme*
- *Star Colleges*
- *Strengthening University/Colleges in North-Eastern region*

Training

- *Short-term Training Courses*
- *DBT Junior Research Fellowship*
- *DBT Post-doctoral Fellowships*
- *Biotechnology Overseas Associateship*
- *Associateship for Specialized Training of Young Scientists in Niche Areas of Biotechnology*
- *Vacation Training Programmes on Bioresources*
- *Biotech Industrial Training Programme*
- *Entrepreneurship Development Programme*
- *Technologists Training Programme*

Fellowships

- *DBT Biology Scholarships*
- *DBT-TWAS Biotechnology Fellowships*
- *Tata Innovation Fellowship*
- *Visiting Scientists from Abroad Programme*

Re-entry Awards

- *Ramalingaswami Fellowship*
- *DBT-Wellcome Trust Fellowship*

Awards

- *Innovative Young Biotechnologist Award*
- *Rapid Grant for young Investigators*
- *DNA Clubs Programme*
- *National Bioscience Award for Career Development*
- *National Woman Bioscientist Award*
- *Biotech Product, Process Development and Commercialization Awards*
- *Distinguished Biotechnologist Award*

Popularization Programme

- *Biotechnology Popularization Programmes*
- *Support to Seminars and Conferences*

Publications

- *Publication of bimonthly issues of IPR biotechnology*
- *AIBA newsletter*
- *DBT newsletter*

- Curriculum revision to enhance science creativity, hands-on experience in designing and conducting practicals by students;
- Summer schools for exposure to platform biotechnologies.

Under the scheme, twenty eight proposals have been recommended and seven shortlisted for inspection by the site-visit.

Strengthening Universities/Colleges in North-Eastern region: In order to strengthen and upgrade biotechnology teaching, training and research in the North-Eastern region, the Department is going to provide support to ten Universities /colleges in that region with the help of the Indian Institute of Technology, Guwahati.

Curriculum revision: In order to match the course contents with the upcoming trends, an exercise to frame model curriculum for ten PG courses has been instituted during the year for its adoption from the next academic session. The curriculum revision exercise is undertaken periodically by the Department to incorporate the latest developments and to rationalize the disparities in theoretical and practical training. A core committee defines the broad outline/basic guidelines to synchronize the curriculum structure of different specializations; and subject-specific sub-committees finalize the curriculum for specialized courses. A set of foundation courses have been introduced across specialization and practical training emphasized by increasing the duration. Latest advancements in upcoming fields such as nano-biotechnology and stem-cell biology have been incorporated in the revised curriculum and special courses on Bio-entrepreneurship, IPR and Biosafety included.

Training

DBT Junior Research Fellowship programme: DBT-JRF programme initiated in 2004 (with revised fellowship from 1.4 2007) has gradually become popular. There is a steady increase in number of applicants. The students are selected through Biotechnology Eligibility Test conducted by University of Pune at seven centers.

DBT Postdoctoral Fellowship programme: DBT-PDF programme initiated in 2001(with revised fellowship from 1.4 2007) is being implemented by the Indian Institute of Science, Bangalore. Though students from all parts of the country take advantage, it is encouraged to avail fellowship in institute other than the one from where they have been awarded the Ph.D. The programme is advertised on All India basis and selection is held two times a year.

Short term training for mid-career scientists/faculty: The scheme for conducting short-term training courses of 2- 4 weeks for mid-career scientists from research laboratories/faculty for undergraduate and postgraduate teaching programmes has continued. During the year, 17 short-term training courses were supported out of 43 proposals received.

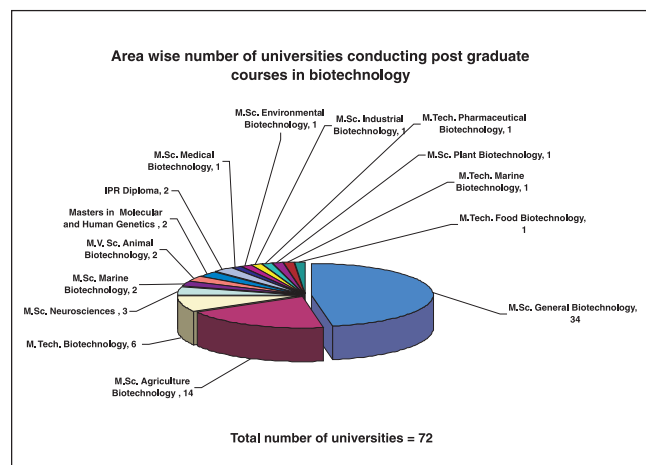
Biotech industrial training programme: The Department supports a Biotech Industrial Training Programme (BITP) for providing practical industrial training to fresh B.E./B.Tech./M.Sc./M.Tech. students in biotechnology for six months. The programme is mutually beneficial to the students and the industry as it provides industrial exposure to the students and an opportunity to the industry to select prospective human resource for their requirements.

Entrepreneurship development programme in Biotechnology: With an objective to train the prospective entrepreneurs on different aspects of business management and to promote setting-up of new commercially viable enterprises, six Entrepreneurship Development Programmes were organized at Shimla, Indore, Tripura, Goa, Chennai and Pune in micropropagation, biofertilizer & biopesticide, enzyme production, bioremediation, probiotics, immunodiagnostics, prawn culture and hatchery, biofuels etc. 260 prospective entrepreneurs have been trained.

New Industry-oriented Initiatives

Technology Transfer and IP-related Capacity Building: Keeping in view the requirements for translating scientific leads into useful products and processes, a new national initiative to build capacity in TT and IPR is under consideration through:

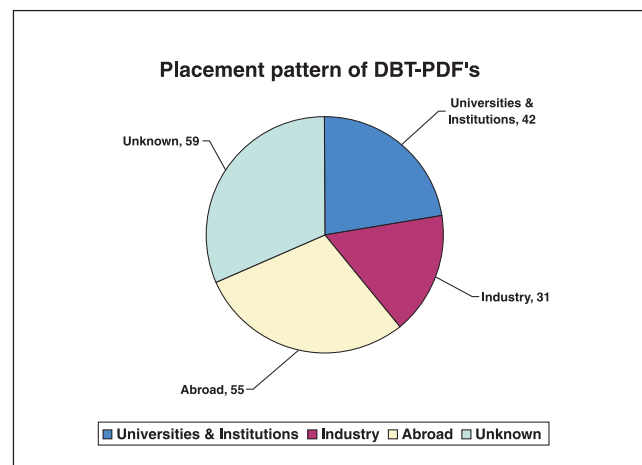
- Training of personnel from the national and regional centers linked to University departments at ten locations across the country
- Special programmes for overseas training



Technologists Training Programme: It is proposed to start HRD-TTP such as biomanufacturing techniques, life science laboratory instrumentation, micro-propagation technology, medical technologies through the financial support to the public funded institutions as well as non-profit organizations with core competence in the subject area. While the diploma programme would provide general technical skills in biotechnology, the post-graduate diploma would address specific skills.

Five new Technologists Training Programmes were initiated during the year. The institutes shortlisted for support in the next four years are:

- Madurai Kamaraj University, Madurai, Tamil Nadu for Post M.Sc Advanced Diploma course in Plant Genetic Engineering;
- North Lakhimpur College, North Lakhimpur, Assam for Post B.Sc Diploma course in Plant Tissue Culture and Micropropagation;
- Alagappa University, Karaikudi, Tamil Nadu for Post M.Sc Advanced Diploma course in Molecular Diagnostics;



- Aligarh Muslim University, Aligarh, UP for Post M.Sc Advanced Diploma course in Plant Tissue Culture and Micropropagation;
- Bharthidasan University, Trichirapalli, Tamil Nadu for Post M.Sc Advanced Diploma course in Molecular Diagnostics.

Need Assessment Study by the Ernst & Young:

The report entitled “Key interventions and projections: Human Resources for the Biotech Industry in India” and “Current state assessment of Indian Biotech Industry” focuses on the existing human resource in academia vis-a-vis current demand of the biotech industry. The report has made an effort to assess the gaps between the demand and supply by inviting feedback from about 186 companies across various sectors with low, medium and high turnover. It emphasizes on the need for academia-industry collaboration, industry’s involvement in training & placement and sharing responsibility to promote academic excellence by creating Chairs in Universities & providing internship to the students.

Biotech Popularization

The objective of biotechnology popularization programme is to bring awareness about the potential of biotechnology and its application amongst students, scientific community and the general public. During the year 2008-09, four popular lectures were organized. The Department participated in four exhibitions in India and two international events held in the USA and Japan. Seventy two national and international seminars/ symposia/conferences were supported and ninety four scientists provided support for international travel.

Support for Publications

The Department is supporting Waterfall Institute of Technology Transfer (WITT), New Delhi for publication of bimonthly issues of IPR Biotechnology and All India Biotech Association (AIBA), New Delhi for publication of bimonthly issues of AIBA newsletter. It also publishes DBT’s newsletter quarterly for information dissemination of major events and programmes of DBT.

DBT Biology Scholarships and Awards

DBT Biology Scholarships: 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.

Distinguished Biotechnologist Award:

Distinguished Biotechnologist Award Scheme has been instituted to utilize the expertise of superannuated distinguished scientists, who are still scientifically active and capable of making significant research contributions in biological sciences, biotechnology and related fields. Three awards were given during 2007-08.

Biotech Product, Process Development and Commercialization Awards:

The Awards upto five are given each year 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 in the areas of biological sciences covering including agriculture, biomedical and environmental sciences. One

Department's Popularization Schemes

- *Organizing popular lectures by experts in Biotechnology;*
- *Publication of popular books in biotechnology in English and other Indian languages;*
- *Publication of science research journals in the area of biology/biotechnology;*
- *Celebration of National Science Day by Institutions and Universities;*
- *Participation in S&T exhibitions and trade fairs held in India and abroad;*
- *Support to Universities and R&D institutions for organizing national/international seminar/symposia/conferences in various areas of Biotechnology;*
- *Travel support to scientists for attending overseas international conferences.*

award was given on 11th May, 2008 under this programme.

National Women Bio-scientists Awards (NWBA): NWBA is given in two categories:

- Senior Category(1) to a senior women biologist for life time contributions;
- Young Category (2) for outstanding contributions of women scientists below 45 years of age in basic and applied biosciences with potential for product and technology development.

National Bioscience Award 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.

Tata Innovation Fellowship: Tata Innovation Fellowship is open to Indian scientists below 60 years. It aims to promote innovation in science,

especially biotechnology, to find path-breaking solutions to major challenges by way of recognizing scientists with an outstanding track record in biological sciences and, a deep commitment to finding innovative solutions to major problems in health care, agriculture and related areas. During 2008-09; 4 candidates were selected for the award. So far 13 scientists have already joined.

Innovative Young Biotechnologists Award (IYBA): This new award scheme was launched by the department in the year 2005 as an attractive career-oriented scheme to identify and nurture outstanding young researchers with innovative ideas and desirous of pursuing research in frontier areas of biotechnology. So far, 24 IYBA Awards have been provided.

Role for DBT's Autonomous Institutes

A new role is visualized for autonomous institutions of DBT to promote excellence in R&D and manpower generation in addition to their in-house programmes. Selected institutions are being

DBT's Scholarship for students

From year 2007-08, the total number of scholarships has increased to 100 out of which 44 students are from CBSE, 4 from the Council for Indian School Certificate Examinations and 52 from State Boards, 2 scholarships each from 26 State Boards.

Regional Biotechnology Centre

Regional Centre for Science, Education and Innovation in Biotechnology which is being established at Faridabad, Haryana has approved plans for creating and nurturing high-quality inter-disciplinary human resource. RCB creation is a partnership between DBT and UNESCO.

- *Globally-oriented education and training;*
- *Training for physicians intending to enter biology and short-term exposure to biologists and engineers through hospitals and medical schools;*
- *Courses with focus on industry –oriented training in Regulatory Affairs;*
- *Courses on Biomedical Enterprise/Business Development in biotechnology;*
- *Courses on Biomedical Quality Systems and Product Development;*
- *Courses on Bioinformatics;*
- *Courses on Technology Transfer and Commercialization;*

financially empowered for promoting excellence in and translational R & D by supporting 'Research Resource Units' in Universities and sister institutions through extramural funding. The funds would be used through a management mechanism independent of the institute administration. The idea is to encourage DBT's autonomous institutes to develop efficient and powerful R&D networks and partnership programmes.

Role of Centres of Excellence

COE's facilitate various biotechnology programmes by putting together new research groups or through creating synergy between related departments or by augmenting the

capacity of existing groups to create inter-disciplinary teams. Development of high quality human resources is an integral component of COE initiative. This is sought to be achieved by a variety of mechanisms including creating adjunct faculty positions and inviting scientists from other countries to work with Indian institutions. This enables the COEs to also serve not only as centers of training but also as loci around which research collaborations and networks can be organized.

Biotechnology Overseas Associateship and Associateship in niche areas of Biotechnology

In an effort towards capacity building of technically trained human resource, DBT initiated the Biotechnology Overseas Associateship

Programme in 1985. Over the years the programme helped create a skilled human resource base that has not only emerged as one of India's the major strengths but has also taken Indian Biotech sector even closer to the competitive edge of the world of science.

In the year 2008-09, 171 applications were received for the Biotechnology Overseas Associateship Award, of which 65 were shortlisted by a screening committee and finally 50 were recommended for the award.

The Specialized training of young scientists in niche areas of biotechnology was also advertised during the year. Seventy-one applications were received and finally twenty-one candidates selected by a screening-cum-selection committee in the areas of medical genetics, stem cell research, nanobiotechnology, transgenic animal models, agriculture biotechnology, bioengineering: tissue engineering, biosensors, biomaterials, medical devices & implants and bioenergy/energy bioscience.

Visiting Scientists from Abroad Programme

Under Visiting Scientists from Abroad Programme (VSAP), eminent scientists working in the frontier areas of biotechnology in research laboratories abroad are invited for a period upto three months to research institutions/universities in India to initiate collaborative research programmes or conduct training courses or to participate in teaching activities. The visits also provide opportunity for dissemination of information on various cutting edge sciences. During the year 2008-09, two scientists from Canada and USA visited NRCPB, New Delhi and Amravati University, Amravati, respectively.

Specialized niche areas under Biotechnology Overseas Associateship Programme

- *Medical Genetics*
- *Stem Cell Research*
- *Nanobiotechnology*
- *Transgenic Animal Models*
- *Agriculture Biotechnology*
- *Bioenergy*

Re-entry Programmes

Innovative re-entry packages in terms of fellowships and R&D support are being offered to young and senior scientists of Indian origin to return to Indian laboratories and pursue research on national priorities. Major schemes include:

- Ramalingaswami Fellowship instituted in 2007-08 as a re-entry grant for scientists of Indian origin provides fellowship for at least five years. Fellows have the freedom to work in any of the scientific institutions/Universities in the country and are also eligible for regular research grants. DBT facilitates to place them in a suitable host institute. During 2007-08 fifteen outstanding scientists of Indian origin from across the world have been selected for the fellowship.
- DBT-Wellcome Trust Fellowship is a bi-directional partnership between Wellcome Trust and DBT for augmenting Biomedical Research Career. DBT and WT have committed to invest £ 8 million per annum to support seventy post-doctoral fellowships under early, intermediate and senior categories every year over the next ten years.

BIOTECH FACILITIES, TECHNOLOGY PLATFORMS AND RESEARCH RESOURCES

In order to take advantage of the predicted US \$ 5 billion biotech market by 2010, India needs to prepare itself in terms of appropriate human resource and the state-of-the-art infrastructure. The Department has been supporting establishment of Biotech Facilities in Institutes/Universities to undertake production and supply of biologicals, reagents, culture-collections and experimental animals since 1986. The National Biotech Development Strategy (NBDS) adopted by the Department in 2007, envisaged further expansion of such facilities as well as initiating new schemes for establishing infrastructure. DBT implemented its “Centers of Excellence (COE) in Biotechnology” scheme wherein research teams having complementary backgrounds, skills and expertise are expected to get engaged in thematic research through collaborative programmes. The COE initiative is aimed to realize full potential in the field of biotech research, manufacturing and services. NBDS has also recognized need for setting-up such “Technology Platforms and Research Resources” as interface infrastructures for translating research leads towards regulatory testing, product scale-up, formulation development, validation, field and clinical trials besides continuing the ongoing instrumentation grants.

Centres of Excellence in Biotechnology

COE program envisages identifying priority areas of research; and bringing together institutions excelling in those areas to collaborate. There is flexibility in human resource recruitment and an in-built system for long-term funding. Current focus is on: Advanced basic research; Advanced sciences with Translational Research; and Industrial partnerships. During 11th Plan, 50 COEs are planned mostly around Universities. Institutions receiving COE grant are expected to:

- Improving scientist density and faculty research capabilities;
- Enhancing research infrastructure and innovativeness;
- Putting together new research groups through synergy between related departments or by

augmenting the capacity of existing groups to create inter-disciplinary teams;

- Developing high quality human resources by creating adjunct faculty positions;
- Inviting scientists from other countries to work with Indian institutions;
- Creating loci around which research collaborations and networks could be organized;

Three new Centres of Excellence have been supported during the year.

Salient achievements of on-going COEs

Genetics and Genomics of silkworms at CDFD, Hyderabad: Several microsatellite markers have been developed for muga and tropical tasar

COEs in Operation

Advanced Basic Research

- *Tuberculosis Drug Resistance (Indian Institute of Science, Bangalore; The Foundation of Medical Research, Mumbai; Birla Institute of Technology & Science, Pilani)*
- *Designing inhibitors against infectious agents (National Institute of Immunology, New Delhi)*
- *Basic Molecular biology of a model microorganism, E.coli (Centre for DNA Fingerprinting and Diagnostics, Hyderabad)*

Advanced Science with Translational Research

- *Systems Biology of Tuberculosis and Drug Development (International Centre for Genetic Engineering and Biotechnology, New Delhi; University of Delhi South Campus, New Delhi; Central Research Institute of Jute & Allied Fibres, Barrackpore, W.B)*
- *Genetics and Genomics of Silkworms, (Centre for DNA Fingerprinting and Diagnostics, Hyderabad)*
- *Antivirals Against Hepatitis C (Indian Institute of Science, Bangalore & others)*
- *Mesenchymal and Adult Stem Cell Therapies (Christian Medical College, Vellore)*
- *Platform Technologies for Designer Crops (International Crop Research Institute for the Semi-arid Tropics, Hyderabad)*
- *Stem Cell Research: Basic and Translational (All India Institute of Medical Sciences, New Delhi)*

Partnership with industry

- *Heterosis Breeding in Rice (University of Delhi-South Campus, New Delhi & Mahyco Ltd., Jalna)*
- *DBT-University Institute of Chemical Technology (Energy Biosciences Centre), Mumbai*

silkworm. Phylogeography of these wild silkworms has been studied using these markers.

Coordinated research on Tuberculosis: Development of alternate strategies jointly at ICgeb, New Delhi and UDSC, New Delhi:

Twenty novel Mtb-specific antigens have been characterized and cloned into suitable constructs for use in DNA-based immunization protocols. The results revealed that the survival axis remains unaltered even after the acquisition of a drug resistant phenotype by Mtb which represent excellent targets for the development of chemotherapeutic strategies.

Novel paradigms of inhibitor design against key metabolic pathways to decimate infectious agents at NII, New Delhi: Studies have been carried out on biotin protein ligase as a potential target for anti-mycobacterial drugs. Reduced affinity of MtBPL does not alter enzyme kinetic parameters suggesting that enhanced binding affinity in EcBirA probably contributes to repressor activity.

High-throughput allele determination for molecular breeding at International Crop Research Institute for the Semi-Arid-Tropics, Andhra Pradesh: High throughput genotyping

and phenotyping facilities have been established at the centre. The Diversity Array Technology platform for whole genome profiling has been created. A Target Induced Local Lesions in Genomes population for pearl millet has been developed. The centre has provided SSR markers services for several research and breeding programmes in the country. A total of 77 Indian scientists working on diverse crops have been trained.

Development of high throughput approaches to understand molecular basis of heterosis in rice for precision breeding jointly at University of Delhi South Campus, New Delhi and Maharashtra Hybrid Seed Company Ltd., Jalna: A comparative transcriptomic analysis to reveal differences in the expression profiles of individual genes between two parental lines of rice and their hybrid has been completed for four stages of vegetative and three stages of seed development. An inhouse database of 2000 SSR markers has been generated, which are being screened for polymorphism in two inbred parental lines. A number of gene expression profiles have been generated for root-specific expression, which will be validated for their function in transgenic system in collaboration with the industrial partner.

Tuberculosis research at IISc, Bangalore, BITS, Pilani and the Foundation for Medical Research, Mumbai: A structure-based algorithm to identify functionally important segments in proteins has been developed. This has unveiled new sites in *M. tuberculosis* proteins that can be targeted to inhibit function.

Research on Hepatitis C Virus at IISc, Bangalore; ICGEB, New Delhi; UDSC, New

Delhi and ACTREC, Navi Mumbai: New targets for antiviral therapeutics based on computational modeling have been identified. Enzyme assays have been developed for viral enzymes that can be used for screening inhibitors. HCV replication assay in cell culture system has also been established. The screening of synthetic and herbal compounds has been initiated.

Microbial Biology at CDFD, Hyderabad and CCMB, Hyderabad: The major focus of the centre is to formulate and test novel hypothesis in the physiology of *Escherichia coli* with particular reference to cell division, gene expression, protein folding and stability, replication and genome fidelity, membrane transport and adaptation to different forms of environmental stress.

Genome Science and Predictive Medicine at UDSC, New Delhi; NII, New Delhi; University of Delhi, Delhi; IASRI, New Delhi; AIIMS, New Delhi; Dayanand Medical College & Hospital, Ludhiana and Sri Venkateshwara College, New Delhi: The aim of the centre is to carryout genome-wide association studies for rheumatoid arthritis and ulcerative colitis using the commercially available high density Single nucleotide polymorphism /Copy number variation arrays. The data generated would be the feeder for supporting projects of novel pathway analysis, functional genomics and lead molecule design.

Genome Mapping and Molecular Breeding of Brassicas at UDSC, New Delhi and University of Delhi, Delhi: The focus is on fine genetic analysis and gene identification for complex yield components for improvement of mustard. It also aims to use transgenic approaches towards developing frost and aphid resistant *B. juncea*.

Multidisciplinary approaches aimed at interventions against tuberculosis at University of Hyderabad, Hyderabad; ILS, Hyderabad; CDFD, Hyderabad; NIN, Hyderabad; LEPRABPRC, Hyderabad and Bhagwan Mahavir Hospital & Research Centre, Hyderabad: The goal of the centre is to understand the functional role of some candidate proteins in the pathogenesis of tuberculosis along with development of interventional strategies.

Programme Support

Institutional Programme Support scheme is given contradictory to an identified institution/department in order to strengthen research capabilities at University or institutional level for a well-defined research question and given to a number of investigators from different disciplines. It is also given to investigators from the same discipline with focus on a common research problem. It enables research programme to be inter-disciplinary addressing specific question.

Five concepts- projects have been supported during the year on:

- (i) Macromolecular engineering & design jointly at Anna University, Chennai and Madurai Kamraj University, Madurai;
- (ii) Computational biology at IIT, New Delhi;
- (iii) Research in diabetes at Madras Diabetes Research Foundation, Chennai;
- (iv) Molecular pathogenesis, risk identification and prevention of cardiovascular disease at Thrombosis Research Institute, Bangalore and
- (v) Neuroproteomics for Proteomic Investigation of Neurological Disorders jointly at Institute

of Bioinformatics, Bangalore and National Institute of Mental Health and Neurosciences, Bangalore.

Salient achievements of the ongoing activities are:

- Efforts continued on developing second generation variant forms of therapeutic proteins – thrombolytic cytokines and human monoclonal antibodies at IMTECH, Chandigarh. Murine monoclonal antibodies have been raised against TNF-alpha and EGFR for eventual use in a human sequence framework. The genetic framework encoding IgG human heavy and light chains are being constructed / synthesized.
- A novel methanol-inducible zinc-finger protein has been identified in *Pichia pastoris* at Indian Institute of Science, Bangalore.
- Peptides specifically interacting with the yeast and hyphal forms of *Candida albicans* have been identified using the phage display library and their potential cellular targets are being characterized.
- Several novel genes differentially regulated different categories of breast cancers have been identified at IISc, Bangalore. One of the genes found to be differentially expressed in these categories is insulin like growth factor binding protein-2. Also, higher expression of AP-2a, a transcription factor has been found to be involved with better prognosis in breast cancer patients.
- Work continued on characterization and validation of the mangrove genes in transgenic rice systems in abiotic stress tolerance at MSSRF, Chennai. Twenty two transgenic lines

have been generated using genes from *Avicennia mariana*,

- At University of Agricultural Sciences, Bangalore, *in planta* transformation protocol in sunflower, groundnut and rice have been standardized.
- Under the programme on translational research on transgenic rice at University of Calcutta, Kolkata, ferritin gene cloned from soybean and driven by endosperm specific promoter for improvement of iron has been incorporated in to Khitish and Swarna-Sub1 varieties. RNAi mediated silencing of phytic acid is in progress to enhance the bioavailability of iron.
- At Bose Institute, Kolkata, cre-lox mediated antibiotic marker excision phenomenon has been validated in *Allium sativum* expressing transgenic insecticidal tobacco plants. About 130 gene sequences of *Sinapsis abla* induced on infection with *Alternaria brassicola* has been deposited into the database for the first time.
- Several transgenic lines of rice for salinity and drought tolerance using different genes have been generated at ICGB, New Delhi. An expression cassette for five candidate genes involved in ascorbate glutathione cycle has been constructed, transferred to the vector, and is now ready for rice transformation.
- A dual erythrocyte isotope incorporation technique to measure iron absorption has been standardized at St. Johns Medical College and Research Institute, Bangalore.
- A programme on human genetic disorders has continued at Banaras Hindu University, Varanasi. Studies carried out on 156 affected children of jaundice shown that uridine diphosphate glucuronosyl transferase 1 has significant association with the disorder whereas mutations do not show any risk.
- Efforts continued on developing CD40-based immunotherapy against *Leishmania* infection and cancer at NCCS, Pune.
- A programme on development of efficacious vaccine for filariasis and establishing diagnostic platform for infectious diseases has been initiated at Anna University, Chennai. Bioprocess development for large scale production of filarial vaccine candidates has been optimized. Monoclonal antibodies have been produced for the filarial diagnostic protein for the development of antigen based assay kit prototype.
- Several novel biomaterial scaffolds and gels have been prepared for cartilage tissue engineering at SCTIMST, Thiruvananthapuram. Isolation and characterization of progenitor cells from rat bone marrow and their differentiation into hepatocytes have been completed.
- The stem cell facility has been upgraded by adding cGLP lab for culturing patient limbal cells for transplantation at L. V. Prasad Eye Institute, Hyderabad.
- Efforts have been initiated towards identification of candidate genes associated with raised intraocular pressure associated with primary open angle glaucoma.
- A programme on melanocyte-keratinocyte biology has been initiated at NII, New Delhi. Altered cellular state in the vitiliginous region has been noted as compared to the corresponding non-lesional skin of the

same individual. Based on mouse model, novel genes which may have important role in melanin pigmentation have been identified.

- A programme on genetic medicine has been initiated at AIIMS, New Delhi. Technique for detecting fetal RhD status using maternal plasma has been standardized. Mutations have been identified in eight out of 98 patients with steroid resistant nephritic syndrome.

Long-term R&D Projects

It aims to provide long-term R&D support to an outstanding investigator with good publication record. Salient achievements are:

A novel interfering RNA (siRNA) targeting the human papilloma virus-16 enhancer has been synthesized jointly at AIIMS, New Delhi and UDSC, New Delhi. A patent for the sequences of siRNA1 has been filed. One potent siRNA down-regulatory both E6 and E7 oncogene expression have been identified.

At IICB, Kolkata, N-acetyl cystein has been shown to enhance anti-cancer activity of Imatinib in chronic Myeloid Leukemia patients. High level of sialate-o-acetyl transferase activity has been recorded in lymphoblasts of childhood Acute Lymphoblastic Leukemia.

Efforts continued to identify genes for engineering apomeiosis in *Arabidopsis* at CCMB, Hyderabad. It has been shown that the DYAD/SW11 gene of *Arabidopsis* can be altered to give rise to functional apomeiosis. Work has been published in Journal *Nature* and recognized as a landmark in the field.

A total of 356 samples from acute flaccid paralysis patients have been analyzed by RT-PCR for the presence of enteroviruses at IISc., Bangalore. Two isolates have been identified to be recombinant/new type.

Serotypes EV11, EV21, EV33 and EV19 have been found to be prevalent in children suffering from acute diarrhea.

Efforts continued on epigenomics of chromatin and chromatin remodeling during male germ cell differentiation and glioma progression at IISc., Bangalore.

Work on IdeR associated gene regulatory network in mycobacteria has been initiated jointly at CDFD, Hyderabad and LEPRASociety, Hyderabad.

Technology Platforms

The “Technology Platform” term has been accepted as “Grouping of high-tech infrastructure and Human Resource” with a purpose to have “High-level technological resources” as service providers for the users. Some future schemes envisaged include:

- Large scale DNA/RNA Sequencing;
- Transcriptomics and proteomics;
- *In vivo* imaging, cellular imagery and electronic microscopy;
- Animal houses;
- Gene/organisms Banks;
- Chembanks and collections;

- Platforms for Structural biology;
- Drug discovery;
- Metabolomics & Lipidomics;
- Molecular spectrometry;
- Biocomputing.

Technology Platforms set-up during 2008-09

Platform for Translational Research on Transgenic Crops- PTTC at ICRISAT, Hyderabad is planned to “translate transgenic technology and harness its products to meet the needs of agricultural growth”. The objectives of the PTTC are to:

- Develop synergistic links with different research institutes, Universities and industry offering services on tissue culture and transformation, product development, consultancy services, intellectual property advice & management, and guidance on biosafety issues;
- Serve as center of reference to strengthen national, regional & international linkages; collaboration in transgenic research and development; exchange of materials & information; support training & consultation and commercialization of technologies.

Platform for Macromolecular Crystallography: DBT negotiated cost/time based sharing mechanism at BM14 beamline of European Synchrotron Research Facility (ESRF), Grenoble France in partnership with Medical Research council U.K and European Molecular biology Laboratories (EMBL). The facility aims to distribute the beam time to researchers in India

for macromolecular crystal data collection/structure determination. The focus of Indian investigators is on relevant proteins in infectious organisms specifically *M.tuberculosis*, *P. falciparum*, Hepatitis and HIV etc. for exploring their potential for structure-based drug/inhibitor design.

Primate Resource and Research Center and Facility on Small Animals: The Department is setting up a colony of genetically defined non-human primates at the THSTI, Faridabad, in addition to strengthening existing small Animal Facility at the NII, New Delhi. The primate animal platform shall provide services to other DBT institutions as well.

New Research Resources planned:

- Toxicology and allergenicity testing labs;
- Experimental animal facilities;
- Plant genetic resources;
- Genomic/proteomic data bases;
- GMO detection facilities;
- Repositories of genes, vectors;
- Protein purification and characterization;
- Pepsin digestibility facilities;
- Specialized centers for screening/ validation;
- Compositional analysis for GM crop research and services; and
- Gene flow/pollen flow research information/ experimentation.

Research Resources recently made operational:

- Flowcytometer sorter facility at ILS, Bhubneshwar.
- P3 facility at JNU, New Delhi;

- Automatic DNA sequencing and controlled environment growth chamber facility at NIPGR, New Delhi;
- National facility for Microarray Genetics and Cell Imaging at IIT, Kanpur;
- Structural biology of proteins and nucleic acid fragments at University of Madras;
- Host-Pathogen biology signaling events for development of new model system at IISc, Bangalore;
- High-throughput genomic analysis in Human Complex Disorders at JNU, New Delhi;
- Aerosol containment facility for slow growing and fast growing pathogens and microscopy cum flow cytometry unit at NII, New Delhi.

Salient Achievements from existing Research Resources

International Depository Authority (IDA), Institute of Microbial Technology, Chandigarh: The Department jointly with CSIR established an International Depository Authority at the Institute of Microbial Technology, Chandigarh in October, 2002. Besides IDA deposits, cultures for regular patents purposes and safe deposits are maintained in the IDA. MTCC has more than 12000 cultures and database of 38000 records on microbial diversity of India. IDA has more than 200 patent deposits.

GM products toxicology facility at the Shriram Institute for Industrial Research, New Delhi: The facility which has been opened to the public in November, 2006 continues to evaluate GM

products. The facility is expected to produce modules for toxicological evaluation for safety assessment on rabbit and rats, rats & goats/ buffalos, rabbits & guinea, pigs & mice.

Repository for filarial parasites and reagents at the Mahatma Gandhi Institute of Medical Sciences, Sevagram, Maharashtra: The activities of the facility include maintenance of *B. malayi* filarial infection in rodents and isolation & storage of different stages of *B. malayi* parasite; isolation of *W. bancrofti* microfilariae from field samples from different regions and storage; immunoscreening of filarial cDNA libraries to identify, clone and express the genes of diagnostic and prophylactic importance; analysis of gene polymorphism; and development of *in vitro* and *in vivo* anti-filarial drug screening systems. The facility has also filarial parasite bank and filarial Serum Bank. The bancroftian filarial sera of different patient groups are supplied for diagnostic work.

Projects under BUILDER

UoH-DBT Centre for Research and Education in Biology and Biotechnology was funded at the University of Hyderabad has plans for the establishment of 8 state-of-art laboratories; strengthening and modification of labs, air-conditioning and uninterrupted power supply. The facilities to be set-up are: Biological Containment Facility, Animal House, Green House, Culture (plant/ Animal/ Microbial) Facilities.

The expected output from this approach is: Increase in number of M.Sc. students from 58/ annum to 150; Ph.Ds from 26 to 100; Post-docs from 4 to 50; R&D projects from 100 to 150;

“BUILDER” Scheme

Boost to University Interdisciplinary Life science Departments for Education and Research (BUILDER)

During 11th plan, the Department has launched a new scheme known as DBT-University Interdisciplinary School of Life Sciences for Advanced Research and Education (DBT-ISLS) to strengthen Universities for globally competitive emerging bio-economy. The aim is to promote networking of existing life sciences departments of Universities and invigorating interdisciplinary bioscience research. The model would be to upgrade the post-graduate teaching and training laboratories in terms of infrastructure, new faculty, fellowships for students, training programmes and re-grouping research activities. The academia-industry interaction would be promoted taking advantage of the strengths and weaknesses of specific Universities.

Publications from 120 to 250; and about 5 to 10 patents. In addition, about 10 technicians and 50 Ph.Ds with additional skills will be generated. The scheme is fully operation with faculty appointed; equipment in place and laboratories built. Several publications in high impact journals have also been published.

DBT Infrastructure Programme Support for Basic Biological Research at Indian Institute of Science, Bangalore has three components: Pathogen Biology; Bio-molecular Architecture and Interactions; and Biological Signaling Mechanisms involving 49 Faculty Members, 260 Ph.D

students, 20 Post-doctoral fellows and 40 Project Assistants.

New Role for DBT's Autonomous Institutes

A new role is visualized for autonomous institutions of DBT to promote excellence in R&D. Selected institutions will be financially empowered for promoting excellence and translational R & D by supporting 'Research Resource Units' in Universities and sister institutions through extramural funding. The idea is to encourage DBT's institutes to develop efficient outreach programmes, R&D networks and partnership.



A large amount of budget is provided for basic R&D in anticipation of getting technologies for translation. The areas that are given focus for R & D include:

- *Agricultural Biotechnology*
- *Bioresource Development and Utilization*
- *Medical Biotechnology*
- *Stem Cells*
- *Bioengineering & Devices*
- *Human genetics and Genome Analysis*
- *Environmental Biotechnology*
- *Nano-Sciences and Nano-Technology*
- *Energy Bio-Sciences*

Each area has its own priorities set up through respective Task Force(s) and Expert Groups under the overall ambit of the National Biotechnology Development Strategy (NBDS). The modalities for project generation are through:

- *Open submission;*
- *Call for proposals in specific areas at defined intervals/as and when needed ;*
- *Expert Group brain-storming/meetings;*
- *Idea generation workshop;*
- *In-house brain-storming on National priorities.*

The average time for competitive research-grant processing is 6-9 months following a three-tier system. The average funding for an R& D project is between 30-40 lakhs. The strength of the DBT funding is that most of the research leads into high-impact publications, patents & translational technologies.

Agriculture Biotechnology

The focus of R & D in agriculture area is on three main staple crops viz. rice, wheat & maize, followed by pearl millet, groundnut, pigeonpea

and cassava. After success of Biofortification programme in main staple crops, Phase-II programme on pearl millet, groundnut, pigeonpea and cassava for alleviating micronutrient deficiencies is planned to be taken up. In all

genetic manipulations, the objectives are to define the function of the predicted genes, particularly those affecting yield and tolerance to various abiotic & biotic stresses. A project on identification of DNA markers for enhanced protein content and development of Quantitative Trait Loci (QTL) intro-gressed genotypes for high protein content on rice has been recently implemented. Functional genomics of rice for discovery & functional validation of genes and novel genes conferring resistance against biotic stress are getting continued support. India is planning to join “International Wheat Genome Sequencing Consortium (IWGSC)” for physical mapping and sample sequencing of wheat chromosome No. 2AL. A National Plant Gene Repository has been approved for procuring important plant genes, promoters, vectors and Expressed Sequence Tags (ESTs) in the form of DNA clones etc. cloned by our institutions and maintain them for their long term storage and uses.

Some important highlights are:

Crops

Rice

- At DRR, Hyderabad, molecular diversity among aromatic short grain local land races collected from different states local basmati and races from the traditional basmati growing areas was studied using a set of SSR markers linked to genomic loci implicated with grain quality traits;
- At CCMB, Hyderabad, it was seen that *Xanthomonas oryzae* pv. *oryzae* (Xoo) uses a type 3 secretion system (T3S) to suppress rice

innate immune responding bioinformatics tools;

- Gall midge resistant varieties Kavya and Abhaya were utilized as donors for transferring GM resistance into the locally popular varieties of Tamil Nadu. F1s & F2 plants were generated. Studies are in progress to identify superior lines with gall midge resistance.

Wheat

- At CSK HP Agricultural University, Palampur, project is underway on application of molecular cytogenetic approach and chromosome elimination technique for the genetic upgradation of bread wheat and other hill crops for various biotic and abiotic stresses;
- In a project at PAU, Ludhiana on Targeting Induced Local Lesions IN Genome (TILLING) for Novel Cytokinin Dehydrogenase Alleles in Diploid Wheat *Triticum monococcum*, the primers were designed based on the CKX gene sequences of rice, maize and wheat. These will be further used;
- At DWR, Karnal efforts are on for the improvement of biscuit making quality of Indian wheats utilizing molecular approaches.

Pulses

- The cumbersome and time consuming nature of traditional methods for detection of pea wilt pathogen *Fusarium oxysporum* f. sp. *pisi* warrants development of rapid but precise diagnostic assays. Ribosomal DNA regions were used to develop cleaved amplified

polymorphic sequence (CAPS) markers for detection of *F. oxysporum* f. sp. *pisi*.

- In the evaluation, validation and introgression of transgenic chickpea and pigeonpea for resistance to the legume pod borer, efforts are made to develop transgenic plants. Several *Bt* genes have been used for genetic transformation of the crops.

Cotton

- In the development of cotton transgenics with improved fibre strength, attempt has been made to amplify *rsW 1* gene using specific primers designed by Bio-software gene tool. Genetic transformation of cotton parental lines is in progress;
- Towards genetic transformation of Desi cotton, an elite genotype of *Gossypium arboreum* (RG 8) has been chosen for genetic transformation by *Bt-cry1Ac* gene specific to cotton lepidopteran pests. The transgenic nature of the regenerated plants was confirmed by PCR and Southern blotting. The plants obtained are phenotypically normal;

Oilseeds & other crops

- In the project on tagging and mapping of resistance to late leaf spot and rust in Groundnut, two hundred and sixty eight RILs segregating for late leaf spot and rust were used to undertake QTL analysis. Phenotyping of the population was carried out under artificial disease epiphytotics for three seasons. The QTL was found tightly linked to a SSR marker and could be conveniently used in marker assisted breeding for rust resistance in groundnut;

- PAU, Ludhiana is working on molecular characterization and introgression of QPM for maize quality improvement & genetic diversity.

Plant Molecular Biology Programmes

Towards understanding stress response of plants, DSC pursued global analysis of SAP gene family and RLCK gene family in rice unraveling 154 & 379 genes, respectively. Domain analysis and expression profile helped to recognize their role in stress tolerance. Transgenic plants for selected genes have been raised to improve stress tolerance. To understand the mechanisms involved in light-regulated plant development, the genes encoding blue/UV-A sensing photoreceptors were sequenced and characterized from *Brassica napus*. It is observed that *Cry1* plays a predominant role in controlling plant height and anthocyanin accumulation, and *Cry2* positively regulates flowering time and cotyledon/leaf expansion. Wheat transgenics containing *HVA1* have been raised using dihaploid technology and analysis of progeny plants is in progress.

State Agriculture Universities (SAUs) Programme Support for R&D in Agricultural Biotechnology

The Department has provided programme Support to four State Agriculture Universities (SAUs) with an aim to find research based solutions to the local growing crops and also to improve their productivity using modern tools. SAUs getting support are:

- Punjab Agricultural University, Ludhiana
- Tamil Nadu Agricultural University, Coimbatore

- University of Agricultural Sciences, Dharwad,
- GBPA&T, Pantnagar

Salient achievements are:

Punjab Agricultural University, Ludhiana

The PAU programme is focused on four major crops of their region, for (i). Physiology and biochemistry of heat tolerance at different stages of plant growth in wheat and germplasm development; (ii) Biotechnological interventions to enhance water use efficiency in rice; (iii) Molecular mapping and transgenic development for resistance to stem borer, and tolerance to abiotic stresses in maize; and (iv) Biotechnological inventions for resistance to *Phytophthora* and tolerance to salinity in rough lemon.

Tamil Nadu Agricultural University, Coimbatore

TNAU is focused on engineering resistance against viral diseases in hill banana and mungbeen, improving drought resistance in rice and cotton, improving bioavailability of nutrients in poultry maize and policy research. In hill banana toward engineering resistance against banana bunchy top virus, regeneration protocols has been further improved so as to give better quality of the somatic embryos and enhanced multiplication rate.

University of Agricultural Sciences, Dharwad

UAS is focusing on pigeonpea, Chilli and sorghum for developing disease resistant varieties. A repository has been developed with 158 isolates of *Serratia marcescens* showing chitinolytic activity, 467 purified isolates of *Bacillus thuringiensis* and

235 independent *Trichoderma* isolated from native soils. The gene from potent isolates viz., *Serratia chiA*, B.t.cry1A and vip3, T.chitinase and glucanase genes have been isolated and modified for expression in target plants.

GBPA&T, Pantnagar

The program support is focused on (i) Understanding the basic role of MAP kinase cascades in pathogenesis of Alternaria blight in rapeseed mustard; with an objective to develop *de novo* resistance against the disease of one of the major oilseed crops (ii) Molecular breeding of rice for defined aroma with an overall object of developing branded varieties for specific processed foods and (iii) Development of ragi (finger millet) as major nutraceutical crop by identifying appropriate genes and promoters for enhancing nutritional value and requisite stress resistance.

Crop Biofortification programme

Bio-fortification of wheat, rice, maize with enhanced iron and zinc content is being aimed at through conventional and molecular breeding approaches. Some of the projects are:

- Biofortification of wheat for micronutrients through conventional and molecular breeding approaches;
- Development of micronutrient-enriched maize through molecular breeding;
- Rice bio-fortification with enhanced iron and zinc in high yielding non-basmati cultivars through marker assisted breeding and transgenic approaches;

- (iv) Establishment of screening facility for iron and zinc bioavailability using Caco-2 Cell line;

Network Projects

- (i) Virus-resistant rice for India: Diversifying transgenic resistance to popular varieties;
- (ii) Use of Molecular Marker Technology Approach in Wheat Quality Breeding.
- (iii) Development and application of biotechnological tools for millet improvement: The programme has a number of components in R&D mode that are aiming towards:

- Mapping and identification of QTLs for drought and diseases in millets;
- Marker-assisted selection in sorghum;
- Transgenic approach for millet improvement.

- (iv) Biotechnological approaches towards forage crop improvement

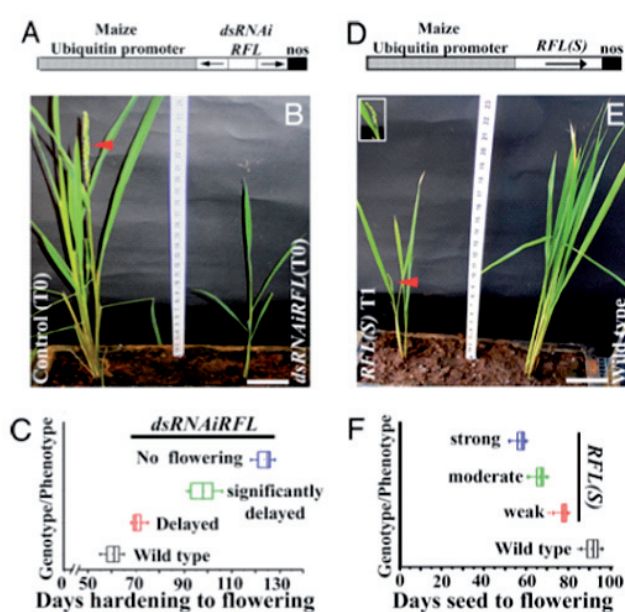
DBT is supporting a new network project to improve forage crops with focus on: Egyptian clover (*berseem*), oats, sorghum and lucerne.

- (v) Development of virus resistant Transgenic Crops: Various projects under the overall ambit of virus resistant transgenic crops include:

- Transgenic Watermelon resistant to Watermelon bud necrosis virus
- Transgenic hill banana resistant to banana bunchy top virus
- Black pepper resistance against viruses

- (vi) Functional genomics on rice

- Gene expression profiling during flower and seed development and functional validation of identified genes;



Phenotypes of RFL(S) and dsRNAiRFL plants.

- Identification and functional analysis of genes related to yield and biotic stress in rice;
- Generation, characterization and use of EMS induced mutants of upland variety Nagina-22 for Functional Genomics in Rice.



Dwarf mutant



High-density panicle mutant



Glyphosate herbicide Resistant Mutant

Indo-US Collaborative Projects in Agricultural Biotechnology

There are three network projects being pursued under this umbrella programme:

- **Development and evaluation of salt and drought tolerant transgenic rice** The ICGEB, New Delhi, DRR, Hyderabad and CSSRI Karnal are working to develop transgenic rice in the background of IR64

through genetic transformation with TPSP gene(s) received from US side.

- **Fruit and shoot borer resistant eggplant** TNAU Coimbatore, UAS Dharwad and IIVR, Varanasi are working on a project to introduce *cry1Ac* gene in important local brinjal varieties through back-crossing with an elite Bt brinjal event, EE1 of Mahyco. The BC_3F_1 plants will be selfed to produce BC_3F_2 generation for multi-location evaluation. The UAS Dharwad advanced all its selected 6 local brinjal varieties to BC_3F_2 stage. Regulatory trial of all the six Bt cultivars was successfully conducted in four locations-two Karnataka and two in Maharashtra. The data, now will be soon submitted to RCGM for regulatory approvals and procedures and large scale trials.

Development and evaluation of transgenic groundnut for resistance to the groundnut stem necrosis disease (GSND) caused by the tobacco streak virus (TSV)

ICRISAT is pursuing a project for engineering resistance to TSV in groundnut by using the TSV coat protein (*TSVcp*) gene. Several putative transgenic events of popular groundnut cultivars have been developed and are being advanced to subsequent generations to study the inheritance pattern and further evaluations.

National Plant Gene Repository

Repository at the NIPGR, New Delhi would serve as a national facility for procuring, storage and distribution of important genes, promoters and ESTs. It would develop a database for all the stocks and other information.

Biofertilisers

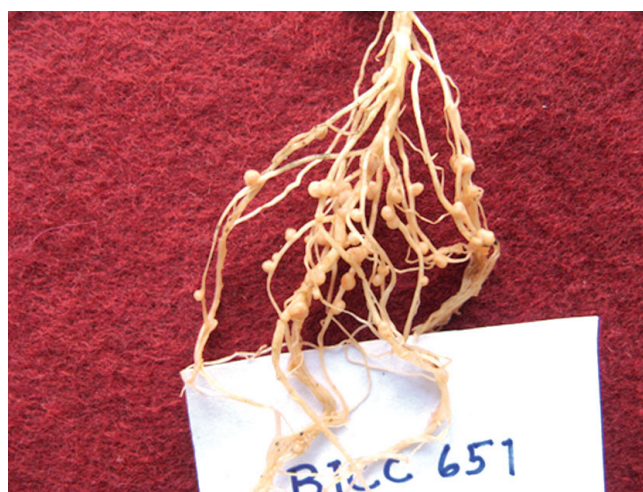
In continuation with the efforts to provide simpler solutions for fertilizers, a biofertilizer programme has been supported by the Department for the last two decades. Salient achievements are:

Due to several reasons, the carrier-based preparations currently in use are now being replaced with “liquid biofertilizers”. The technology for liquid biofertilizers is being developed and tested. In order to have high cell count, longer shelf life, minimum contamination, protection against abiotic stresses as well as convenience in packing, storage and transport, lyophilized diazotrophs are sometimes utilized in the making of liquid biofertilizers using cost-effective eco-friendly locally available material. AMM Murugappa Chettiar Research Centre, Chennai has developed liquid biofertilisers in a medium that could be constituted by the farmers themselves just before application in the field. Field application could be as “single bacterium liquid biofertilizer” or as “consortium biofertilizer” containing diazotroph, P and K solubilizers and PGPR;

For the development of a broad-spectrum next generation biofertilizer for multiple applications, TERI, New Delhi has taken up gradation and refinements of mycorrhiza mass inoculum production technology that was earlier developed by them. In a study conducted jointly by Kashmir University, Srinagar and Thapar University, Patiala, University of Kashmir conducted field surveys at six sites for documentation of ecto-mycorrhizal diversity of Kashmir Himalayas associated with *Pinus* and *Cedrus*; for selecting promising ECM isolates; and evaluate their performance on

improving the growth and survival of these conifers. MCRC, Chennai screened forty two *Methylobacterium sp.* isolates for IAA production, phosphate solubilization and nitrogen fixation. Some promising isolates have been selected.

Bose Institute, Kolkata have been successful in isolating a number of siderophore non-producing and over-producing mutants of the bacterial strain BICC 651 isolated from a root nodule of the host plant *Cicer arietinum*. The strain BICC 651 nodulates *C. arietinum*, and fixes nitrogen very efficiently.



Nodules formed by the strain BICC 651 on roots of *Cicer arietinum*.

North Bengal University, Siliguri selected two rhizobacterial isolates from tea rhizosphere – *B. megaterium* (TRS-4) and *S. marcescens* (TRS-1), which singly or jointly have shown promise as good plant growth promoters when tested against 18-month old seedlings as well as cuttings in sleeves.

Arbuscular mycorrhizal diversity was assessed from forest soil of Uttarakhand at GB Pant University of Agriculture and Technology, Pantnagar and

spores of many species identified and cultured. Strawberry, maize and sugarbeet have been successfully grown resulting into high root biomass and high number of mycorrhizal spores.

Under rhizosphere biotechnology programme, isolation of sulphur reducing and oxidizing bacteria from different rice rhizosphere soil has been undertaken by SRM University, Chennai and a direct method for the extraction of DNA from rice rhizosphere soil sample has been used for PCR mediated diagnostics. Attempts were made by TNAU, Coimbatore to obtain bacterial and fungal isolates capable of oxidizing reduced form of sulphur to sulphate for developing sulphur bacteria formulation to enhance the

productivity and quality of black gram and groundnut.

To overcome the transplant shock leading to seedling mortality, and poor growth of surviving seedlings in Arunachal Pradesh, application of suitable arbuscular mycorrhizal fungi has been undertaken. A consortium of fungal species was found suitable for the better growth of *P. mullesua* seedlings on hill slopes under field conditions. Indigenous soybean rhizobia were isolated from nodules and soil samples collected from farmer's fields by Institute of Agricultural Sciences, BHU, Varanasi. A total of 340 *Bradyrhizobium japonicum* isolates have been maintained. Phage typing of the collected rhizobial isolates is under progress.

“Integrated Nutrient Management Package for Commercially Important Plantation Crops”

A network project involving nine specialized institutions has been launched since February 2008 to standardize package of practices for biofertilizer-based integrated nutrient management of important plantation crops – tea, coffee, cashew nut, rubber, mandarin orange, rosewood, black pepper and cardamom. Under the project comprehensive growth stage specific nutrition management package of practices combining dosages of organic manure, chemical fertilizers and proven strains of biofertilizers are proposed to be developed for each of these crops.

Biopesticides and Crop Management

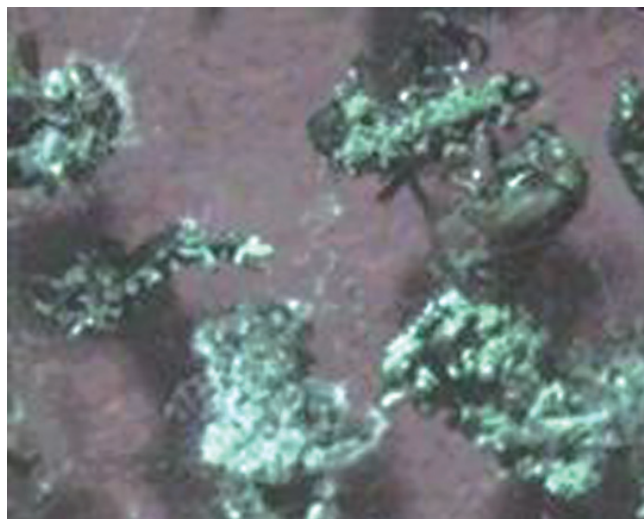
Biopesticides and other natural enemies are environment friendly pest control agents. Pests which are difficult to control by pesticides can be controlled by Biopesticides. A number of research projects has been supported in the area for the control of pests and diseases of economically important crops with a purpose of enhancing the overall agricultural productivity by reducing the loss due to pest infestation. The highlights of some of the ongoing and newly initiated projects are as follows:

Microbial Pesticides and Natural Enemies

- At IHBT, Palampur field survey conducted in Himachal Pradesh on Ginger Rhizome Diseases revealed that the incidence of soft rot is maximum. The pathogenicity of *Pythium*, *Fusarium* and *Meloidogyne* was established;
- In a study supported at IARI, New Delhi antifungal activity of *Bacillus licheniformis* was evaluated against of phytopathogenic fungi and found effective against many species. It was noted that 10% culture filtrate of *B.*

licheniformis suppressed disease in chickpea by 90-93% as compared with the untreated infested soil after 35 days of treatment;

- At IARI, New Delhi, critical lethal temperatures for root-knot nematode, *M. incognita* have been determined *in-vitro* and at varying power and time combinations *in-vivo*. Complete control of the nematode in potato tubers having infestation upto 8mm depth under surface was achieved;
- In the study of natural antagonists for management of potato cyst nematodes, 90 effective fungal and 47 bacterial isolates were screened *in vitro* at TNAU, Coimbatore. *Aspergillus terreus* gr was found to be highly effective in destroying the oil reserves in the eggs of cyst nematode;
- Studies conducted by TERI, New Delhi on the use of arbuscular mycorrhizal fungi in combination with a nematode isolated from Supi soil suppress the root-knot nematode effectively in the field condition. An increase (25.26%) in yield of tomato crop was observed with the treatment;
- One isolate of Entomopathogenic nematode (EPN) developed for temperature tolerance at CICR, Nagpur could infect *H.armigera* larvae at temperature of 40°C. Application of 1 to 2 billion EPN infective juveniles/ ha has been found to be effective dose against *H.armigera* on pigeon pea and cotton;
- At IBRC, Jalandhar, squalene glucose, fructose and sucrose sugar esters have been isolated from wild tomato and tobacco leaves as biorational insecticides. These were found efficacious against mustard aphid *Lipaphis erysimi* and mealy bugs, and moderately active against lepidopterans;
- At MPKV, Rahuri two commercially viable formulations of biopesticides *HaNPV* and *SlNPV* have been developed. The procedure for their culture has been standardized. The formulation tested *in-vitro* and *in-vivo* on capsicum, gerbera and rose crop under poly house and on gram and soyabean in field condition were found effective for control of pest;
- At MU, Imphal the efficacy of the viral pesticide, *Pieris brassicae granulosus virus* (PbGV) was assessed against the larvae of *Pieris brassicae*. The results revealed total mortality under lab and 80 % under field condition;
- At IIHR, Bangalore, it is observed that entomopathogens *Metarhizium anisopliae* and *Verticillium lecanii* caused 67% mortality of mango hoppers *Idioscopus nitidulus* in field conditions.

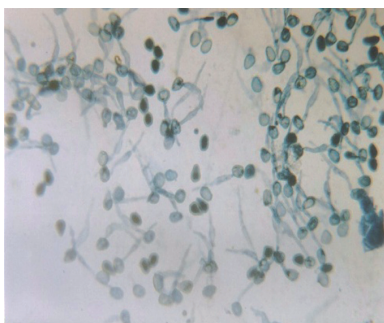


Mongo hopper *Idioscopus nitidulus* infected by *M.anisopliae*

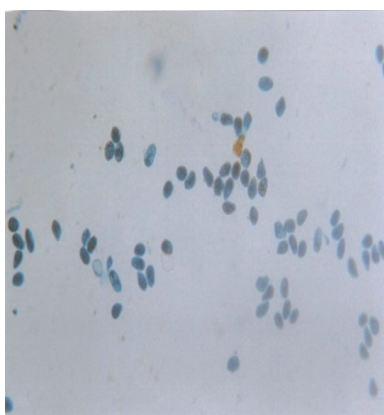
- At Pondicherry University, novel functional genes that encode antifungal metabolites from metagenome of soil microbiota were identified.
- At College of Horticulture, Thrissur, efficacy of bioformulations against rhizome rot, bacterial wilt of ginger and chilli are being evaluated to develop consortia for plant disease management.

Botanical Pesticides

- At KSSRDI Bangalore 25 plant extracts (PE) were screened as biofungicide for the management of leaf rust in mulberry. PE-1 has shown significant reduction in rust severity and withering of foliage over control and also is non-toxic to silkworms.



Control



PE. 1

Urediniospores Response

Pheromones

- In the study of pheromone technology for the control of sugarcane stem borer, AHRE, Chennai has synthesised Z-11 hexadecen-1-ol and intermediate of Z-13 Octadecenyl alcohol at the laboratory scale. Ten different types of indigenous dispensers were prepared and their respective release rates observed;
- Methods for large-scale multiplication and segregation of male & female of *Caryedon serratus* and technique for collection of volatiles by air entrainment have been successfully standardized at IICT, Hyderabad;
- Study was conducted on pomegranate pests at IICT, Hyderabad in collaboration with MPKV, Rahuri. Four pheromone components from *E. materna* and three from *D. isocrates* female have been identified and synthesized successfully at the lab level. Their bioactivity has been confirmed.

Molecular Studies on Biocontrol Agents

- At Pondicherry University, a transgenic *Cry IAc* toxin gene from *B. thuringiensis kurstaki* has been generated and stability of *IAC* toxin gene has been established;
- The diversity of *Acinetobacter* species associated with rhizosphere of wheat has been studied at ARI, Pune in collaboration with University of Pune. Results revealed that *Ac. calcoaceticus* 37 was the most effective that inhibited 75 % of growth of *Fusarium oxysporum in vitro*.

Integrated Management of *Parthenium* through multicentric programme

- At NRCWS, Jabalpur, a large scale demonstration project on management of

parthenium has been completed. The *Zygogramma bicolorata* was successfully mass-reared and its performance was assessed as biocontrol agent;

- Studies conducted at UAS, Bangalore in collaboration with IISc., Bangalore for management of *P. hysterophorus* revealed that calcium alginate pellets of dry leaf extract of *Hyptis suaveolens*, *Cassia uniflora* and *Lantana camara* botanical agents reduces the germination and seedling growth of the *Parthenium*;
- A safe and effective protocol has been developed by the IARI, New Delhi for Parthenium management known as PPPM-2008.

Storage Pests and their Eco-friendly Management

- At NMU, Jalgaon a series of cyclotides produced by members of the *Rubiaceae* and *Violaceae* families were screened and evaluated for the insecticidal properties against *C. chinensis*, and *H. armigera*. The isolated proteins indicated good preservation over a period of 4 to 6 months without much compromise on nutritional aspects;

- At PDBC, Bangalore FAT3 and FAT6 fat oils were screened for their inhibitory effects on growth and sporulation of *T. harzianum*. Phytotoxicity tests with chickpea, tomato and groundnut proved that the formulations were non-toxic to these crop plants;
- Considering the importance of *Trichoderma* spp. in disease management, several isolates of *Trichoderma* were evaluated against soil and seed borne pathogens of pulse crop. Seed dressing formulation Pusa 5 SD showed the highest viable cfu/g for all the isolates of *Trichoderma* upto 25 months of storage at room temperature;
- At IIPR, Kanpur four new entomopathogenic nematodes (EPN) have been isolated belongs to *Oschieus* and *Acrobeliodes* sp. able to kill *Coreya cephalonica* larvae within two days under laboratory conditions. Pulse beetles, *Callosobruchus chinensis* and *C. maculatus* have been found highly susceptible to EPN, *Oschieus amsactae*.

Patents

Several patents have been filed for the mass production technologies and bioformulations:

Strategy Document on Biopesticides

As a sequel to a brainstorming on "Reinvigorating Indian Agriculture through Science & Technology" in July, 2007 to focus and strengthen activities that could deliver tenable results Biopesticides was identified as one of the important areas. A "Strategy Document" has been prepared, analyzing various issues including constraints in their registration and commercialization. The "Strategy Document on Biopesticides" has been approved by Hon'ble Minister. Follows up actions are being taken up with Ministry of Agriculture, Ministry of Commerce & Industry; and Ministry of Environment and Forests.

- A US patent has been granted for Dimer of phenazine-1-carboxylic acid and to the process of preparation thereof. Patents have also been filed for biopesticides development from bacterial symbiont for management of sucking pests of cotton.
- A US patent has already been granted to liquid fermentation mass production technology of *Trichoderma viride*.
- Three bioformulations viz. Biowiltex (*Trichoderma harzianum*), Bionem-x (*Pochonia chlamydoisporia*) and Biocomp-x (*Pseudomonas fluorescens*) have also been granted Indian and USA patents.

Referral Labs

DBT has designated seven “Referral Laboratories” in the country viz., AAU, Jorhat; RRL, Jammu; UAS, Dharwad ; MPKV, Pune; IARI, New Delhi, GBPUAT, Pantnagar and AAI-DU, Allahabad. These centres have been identified as certification labs for Bio-pesticides on the basis of sufficient core competence, infrastructure and assurance parameters under

existing regulatory guidelines. These centres have also been notified by the Ministry of Agriculture by an extra Gazette notification.

Launching of Website on Biopesticides

Initiatives have been taken for developing a comprehensive website for Biopesticide/ Biocontrol programme with a view to disseminate the information generated through the R & D projects as well as other information relevant to this area. The website “Biocontrol Strategies for Eco-Friendly Pest Management in India” was developed and officially launched on 23rd June 2008. Salient achievements from more than 124 completed projects have been covered. The website is being updated, upgraded and maintained by TERI through a DBT supported project. The URL of the developed website is www.dbtbiopesticides.nic.in.

Bioresource Development and Utilization

National Bioresource Development Board (NBDB) focuses on the application of biotechnological and related scientific approaches

Microbial Culture Collection

A Microbial Culture Collection – Biological Research Centre has been established with a plan to hold more than 2,00,000 bacteria and fungi following International Standards; and aiming to attain the status of an International Depository Authority (IDA). The services offered are:

- To collect, maintain and preserve microorganisms as well as other biological materials related to applied biology, microbiology, biotechnology and other areas of research.*
- To supply and exchange cultures of microorganisms*
- To act as a center for the safe deposit of biological material and the deposit of biological material for patent purposes upon request in India and abroad under the National law and the Budapest Treaty.*

for R&D; and development of new products and processes. The thrust is on:

- Bioresource inventorisation and characterization both spatial and non-spatial;
- Prospecting of bioresources for novel genes and genes products, biomolecules and compounds;
- Improvement of economically important bioresources and
- Capacity building including strengthening of infrastructure.

Bioprospecting and Product Development

A public-private “Mission Programme on Microbial Prospecting” for screening of microbes: A mission programme through academia-industry alliance for prospecting of drugs from microbes initiated last year aims at prospecting of microbes of different environmental niches using high-throughput screening for bio-molecules. Nine institutes and NPIL Research and Development Limited (NRDL) are involved in the partnership. About 7,000 isolates per month are being collected by the academia partners and screened for bio-molecules with anti-cancer, anti-diabetes, anti-infective and anti-inflammation activities by NRDL. Till date, more than one lakh bacterial isolates have been isolated and screened. More than two lakhs extracts have been prepared for assays and about 7,000 hits obtained till date.

Characterization and Digitized Inventorization: Indian Bio-resource Information Network (IBIN) portal www.ibin.co.in launched by the Hon'ble Minister in 2006, is providing diverse range of data sets related to bio-resources and biodiversity of India to a wide section of end users. It is now

expanding as a single platform where exponentially growing data and information on bio-resources and biodiversity in various sectors can be brought together in a compatible and accessible format. The following data has been added during the year:

- Plant Data has been updated from 264 MB to 684 MB of information with an added 3500 images for over 1600 species.
- Insects: A total of 314 additional species of pollinators and predators are updated with over 1000 images and information of about 98 MB.
- Translation of HTML files to Hindi, Kannada, Bengali and Telugu languages has been completed for about 100 species each.
- Patent data on plants has been converted to Web-format for loading on to www.ibin.co.in and the IBIN's format has been reworked
- The programmes on mapping and quantitative assessments of geographic distribution and the population status of plant resources of Western Ghats, Eastern Ghats and Eastern Himalayan Regions have made significant achievements.
- A joint initiative of the DBT and the Department of Space to develop a baseline database for important landscapes in India to facilitate prioritization for bioprospecting and conservation studies have been undertaken to cover the entire country in different phases.

Prospecting of genes and molecules for product development: DBT continued its support for programmes in the area of bioprospecting of novel genes, transcription factors, promoters, molecules

etc from different plants, lichens, microbes etc. Several technologies in the area of natural dyes, biopesticides, stress related genes for salinity, nutritional quality have been developed and negotiation with industry are on for technology transfer.

- A technology for the production of 'Bollcure', a biopesticide formulation extracted from Eucalyptus plants and effective against cotton bollworm (*Helicoverpa armigera*) has been developed by TERI, New Delhi. The technology has been transferred to Sri Biotech Laboratories India Pvt. Ltd., Hyderabad and Pasura Biotech Pvt. Ltd., Hyderabad for commercial production.
- A multi-institutional programme for identifying potential molecules from selected plant and lichen sources to develop them as products against cancer and tuberculosis has been initiated at MSSRF, Chennai; Tuberculosis Research Centre, Chennai and Cancer Institute, Chennai.
- Two actinomycete isolates which exhibit broad spectrum antimicrobial activity against various drug resistant bacteria and yeasts have been reported by Guru Nanak Dev University, Amritsar.

DNA Barcoding

DNA bar-coding that provides a "universal key" allowing identification of a species by running unknown DNA sequences through a DNA barcode database is being worked upon on selected species of plants (Orchids-Dendrobium, Bamboos, Rattans, Phyllanthus, Berberis L., Zingibers, and Dalbergia), insects (Butterflies) and Amphibians as case studies.

Resource Specific Programme

The programme focuses on: genetic diversity studies, development of molecular markers, prospecting for Value Added Products, macro and micro-propagation & acclimatization and, capacity building. Following programmes are on:

- **Seabuckthorn:** The cold desert of Ladakh and similar other areas where vegetation is scarce, abound in a 'wonder plant, popular known as the 'Ladakh gold' Seabuckthorn with enormous pharmaceutical, cosmaceutical and neutraceutical potential. The studies are on to exploit the same;
- **Network programme on Honey Bee:** A multi institutional network programme which addresses industrial R&D priorities in the Apiculture sector has been developed with focus on value added products from honey, its by-products, quality improvement, study of genetic diversity, development of molecular markers in Indian bee species and new pheromones/compounds for attracting bees for pollination.
- **Indian Coffee Genome Research Programme (ICGRP):** A multi-institutional network project involving CCRI, CCMB, UAS Bangalore, MKU and CFTRI has been supported for research on coffee genome;
- **Zingiberaceae:** Network Programme launched last year progressed well;
- **Sugarcane Network Programme:** In an ongoing study at SBI, Coimbatore on identification and characterization of differentially expressed genes/proteins involved in sugarcane red rot pathogen interaction,

candidate genes which are potentially involved in red rot resistance have been identified;

- **Network programme on Tea Biotechnology:** Considering the importance of markers assisted breeding and requirement of highly reproducible co-dominant, microsatellite markers in tea, work was initiated at the various collaborative labs for markers development and generation of mapping population of selected important traits.
- **Network Programme on Bamboo:** Field Demonstration and Evaluation of Tissue Culture raised Bamboo species continued and has covered 770 ha with seven species. Genetic Diversity analysis of 56 accessions of three indigenous bamboo species, namely *Bambusa balcooa*, *B. bambos* and *B. tulda* collected from various network research centres under DBT funded Bamboo micromission was carried out. The study shows that there is a need for identification of more diverse genotypes from its natural habitats.

Capacity Building Programme

DNA Clubs: DBT has launched DNA Clubs (DBT's Nature Resource Awareness Clubs) in selected schools in each state. These clubs operate as nuclei for activities and hands-on learning opportunities focused on bioresources, relating these to the school curriculum, wherever appropriate. To guide and manage the activities of DNA Clubs, Regional Resource Agencies (RRAs) have been established at different locations in the country. In all, 23 states and Union territories are participating in this programme and 145 DNA Clubs have been formed so far.

National Geographic Channel: was given the responsibility of conducting School Contact Program for 6th - 9th Standard with the objective to expand and impart awareness on relevance, sustainable utilization, and conservation of bioresources. The Program reached more than 4 lakhs students over 400 schools across the 14 cities.

Rural Bioresource Complex: The Rural Bioresource Complexes continued their activities during the year with a focus on providing new technologies and products to the target beneficiaries.

Plant Biotechnology

The R & D focuses on: Basic Research, Tissue Culture, Molecular Biology of Forestry, Horticulture & Plantation Crops and Solanaceae Genome Initiative.

Basic Research

Under basic research, studies on signal transduction, root development and host-pathogen interactions are continuing. Some highlights are:

- The operation of the Signal transduction machinery in plants under biotic stress is being studied at JNU, New Delhi.
- Salinity sensitive and salinity tolerant cultivars of *Brassica juncea* CUCS52 and *B. nigra* have been identified. Based on expression analysis, *two* genes have been isolated, over-expressed and confirmed transgenic lines obtained. Suitability of these genes as candidates for stress tolerance is being ascertained;

- Study is supported to investigate the organization and carry out expression analysis of selected transcription factors and microRNA genes in mediating the development of leaf and seed at Jamia Hamdard University;
- In a study supported as a network programme at ICGEB, New Delhi, University of Agricultural Sciences & NCBS, Bangalore, 37 desiccation-associated transcription factors have been isolated from *Pennisetum* library. Stress responsive genes have been identified by expression studies and cloned for further validation;
- Calmodulin binding proteins have been purified from sorghum;
- A study at CFTRI, Mysore is aiming to understand the nature and role of food allergens present in egg plant. So far 8 proteins have been identified as allergens in the green long variety of eggplant. The full length gene has been cloned and expression of recombinant polyphenol oxidases in heterologous system is underway;
- In an effort to understand the process of Floral Development, functional analysis of genes and the promoters identified in abscission and senescence is in progress;
- Study has also been supported at IISc, Bangalore to understand floral organ growth and development in *Arabidopsis* as a model system. 40000 EMS mutagenized F2 plants have been screened and ~ 50 mutants with altered organ morphology have been isolated.

Host-Pathogen Interactions

Studies are being supported to understand how a pathogen invading a host establishes itself to cause a disease at molecular level. Following are the developments:

- In a study supported at IISc, Bangalore. Viral movement protein, and capsid protein of a, *Cotton Leaf curl Kokhran virus Dabawal* (CLCukV-Dab) was cloned and over-expressed in *E.coli*. The recombinant proteins were detected by Western analysis using anti-GFP antibodies;
- Studies have also been initiated to identify characterize host proteins from mung bean interacting with Geminiviral replicase;
- Studies on developing diagnostics for detecting viruses infecting stone fruits like plum & cherry have been initiated at IHBT, Palampur;
- Diagnostic tools are also being developed for peach decline disease using molecular approaches at NBRI, Lucknow;
- Bioinformatics tools have been used to identify genes involved in pathogenicity of rice blast fungus *Magnaporthe grisea*;
- A mapping population has been developed using resistant and susceptible chilli lines. SCAR markers are being developed using RNAi technology. Preliminary analysis has been carried out for the eight genes. Detailed analysis is in progress;
- Studies were supported to study stems diseases of important forest tree species like *Ailanthus*

Solanaceae Genome Initiative

Under SOL, an international consortia of ten countries comprising USA, Korea, China, UK, India, Netherlands, France, Japan, Spain and Italy has been made for sequencing of the “Tomato Genomes”. India has been assigned the responsibility for sequencing 12 Mb of euchromatic region of chromosome 5. This task has been taken up by three institutes namely University of Delhi, South Campus (5 Mb region), IARI (5mb) and NIPGR (2 Mb).

excels, *Azadirachta indica*, *Mangifera indica* etc. at MS University, Baroda. Initiation, spreading & penetration mechanism of various fungi and response of above said species is being studied by histological methods. Extraction of secondary metabolites from host and fungal pathogens has been carried out and further work is in progress.

Forestry, Horticulture and Plantation Crops

During the year studies continued in the areas of plant tissue culture; molecular characterization and transformation for desirable traits especially post-harvest. Some highlight are:

- Efforts were made to develop brinjal resistant to root & shoot borer- *H. armigera*. The development of transgenic lines of Pusa hybrid 6 with *cry2Aa* is in progress;
- Citrus yellow mosaic badnavirus (CMBV) has been purified; immunodiagnostic kits developed and DNA dot-blot methods standardized for easy detection of the virus;
- Efforts are on to reduce cold induced sweetening in potato. In this direction two Indian potato cultivars, Kufri Jyoti and Kufri Chisona-1, have been transformed with Nt-Inhh gene construct;

- Multiplication and ex-situ conservation of rhododendron has been taken up at BSI, Shillong.

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

The Department was notified as the Certification Agency for certification of tissue culture plants upto laboratory level as per the Gazette of India Notification dated 10th March 2006 under section 8 of the Seeds Act, 1966. Accordingly, National Certification System for Tissue Culture Raised Plants (NCS-TCP) was established. NCS-TCP is a unique and comprehensive quality management system for tissue culture industry and seeks involvement of all stakeholders i.e. Central and the State government, tissue culture companies, farmers etc.

Under the NCS-TCP, nine Accredited Test Laboratories (ATLs) have been set-up for testing the tissue culture plants on behalf of DBT. The laboratories in public are responsible for both virus indexing and genetic fidelity testing. Two Referral laboratories - Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad for Genetic Fidelity and Advanced Centre of Plant Virology, Indian Agriculture Research Institute (IARI), New Delhi for virus

indexing have been established for developing protocols and providing technical assistance to Accredited Test Laboratories. An Accreditation Unit (AU) has been set-up at Biotech Consortium Limited (BCIL). The Project Management Unit (PMU) at BCIL also assists BT in monitoring the implementation of NCS-TCP and coordinating the various components.

Workshops are being organized alongwith Horticulture Mission, Ministry of Agriculture at State and District levels across the country to create awareness about the NCS-TCP among the stakeholders.

Biotechnology for Medicinal and Aromatic Plants

A programme on biotechnological intervention on Medicinal and Aromatic Plants (MAP) has continued for conservation, characterization, micropropagation, production of high-value metabolites, development of standardized herbal products, isolation and characterization of novel therapeutic agents, genomics and metabolic engineering. A consultation meeting of experts on “Clinical development of promising anti-dengue herbal extracts” was organized at Ranbaxy Research Laboratories, Gurgaon and an action plan has been drawn up. The salient achievements are:

Ex-site Conservation and Characterization

- Morphological, phytochemical and molecular characterization studies have been carried out in different assessments of *Garcinia gummi-gutta*, *Nothapodytes nimmoniana* and *Syzygium cumini* collected from various agro-climatic zones of South India at Arya Vaidya Shala,

Kottakkal. The studies among the different accessions revealed quantitative variations in the fixed oil composition;

- Plants of wintergreen collected from different regions of Sikkim and Darjeeling were analyzed for total oil content in leaf. Plants from Darjeeling have been found to contain highest wintergreen oil;
- AFLP profiles of six species of *Zanthoxylum* revealed considerable genetic diversity at North-East Institute of Science & Technology, Jorhat.

Micropropagation

- Field evaluation of the tissue culture plantlets vis-à-vis open pollinated seedlings of large cardamom planted over an area of 55 ha covering 206 units in Sikkim and Darjeeling districts of West Bengal continued at Regional Research Station, Indian Cardamom Research Institute, Gangtok. TC plantlets started giving satisfactory yield earlier than open pollinated seedlings;
- Multi-location field trials of high yielding cultivars of Patchouli (*Pogostemon cablin*) in



Germplasm of Patchouli with organic mulch maintained at Kamrup, Assam

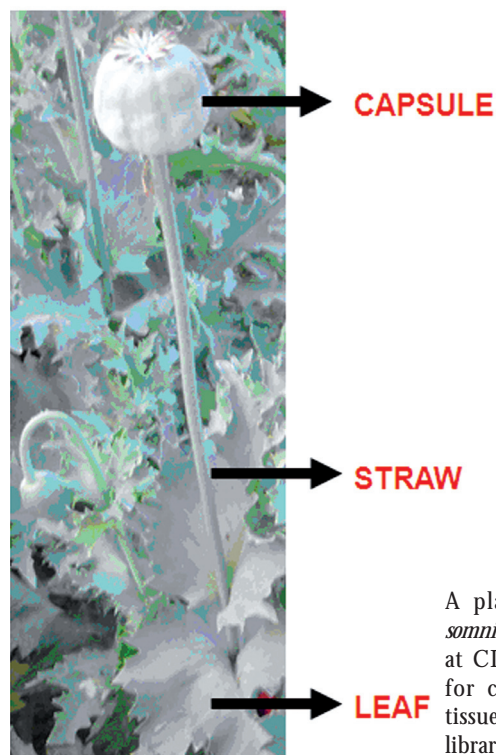
North-East region have been recently initiated at North-Eastern Development Finance Corporation Ltd. (NEDFi), Kamrup.

Herbal Formulation

- Three classes of compounds (OC-1, OC-2 and OC-3) have been isolated from *Oxalis corniculata* having anti-amoebic activities at Bose Institute, Kolkata. Out of these, maximum anti-amoebic activity was found in OC-3 (a novel glycolipid). Further synthesis of the sub-components of this glycolipid led to the identification of the single component that had equivalent amoebicidal effect;
- A network project on development of standardized herbal product for bovine mastitis has continued involving five institutions. Over 1,000 mastitogens from more than 7,500 clinical cases have been isolated. Thirty six extracts from 12 medicinal plants were screened against clinical, standard and drug resistant pathogens;
- Work on developing a herbal formulation utilizing the lead extracts has been initiated. Hydroalcoholic extract of *Cyperus rotundus* significantly reduced hyperlipidemia in rats at C. U. Shah College of Pharmacy, Mumbai;
- Work on development of a standardized herbal product for urolithiasis from *Tribulus terrestris* and *Achyranthus aspera* has been initiated at Jaypee University, Solan. Aquous extract of *A. aspera* has been found to significantly inhibit the calcium oxalate crystal growth in a concentration dependant manner.

Isolation and Characterization of Novel Therapeutic Agents

- Under a joint DBT-Ranbaxy project to identify potential Dengue virus inhibitors from herbal sources, whole cell screening methodology to assay anti-dengue viral activity has been established at ICGEB, New Delhi. A total of 20 plants have been screened as herbal extracts, fractions and pure phytoconstituents for their potential against dengue virus and a few promising herbal extracts identified for further development;
- Chemical profiling of selected plant species from national herbaria for high value metabolites such as galanthamine, warfarin and betuline acid has been carried jointly at UAS, Bangalore and BSI, Kolkata. About 35 plant species for galanthamine and 150 species for warfarin have been screened.



A plant of *Papaver somniferum* maintained at CIMAP, Lucknow for construction of tissue-specific cDNA libraries

Genomics and Metabolic Engineering

- Efforts continued to understand the biosynthesis of santalol, the major constituent of *Santalum album* (sandalwood) oil at Vittal Mallya Scientific Research Foundation, Bangalore.
- Studies continued toward cloning and characterization of regulatory elements of the genes involved in picrosides biosynthesis in *P. kurroa* at Institute of Himalayan Bioresource Technology (IHBT), Palampur.
- A trichome cDNA library of *Artemisia annua* has been constructed at CIMAP, Lucknow. About 250 ESTs have been generated toward establishing an *A. annua* trichome EST bank.
- Around 200 ESTs have been generated from capsule, straw and leaf of *Papaver somniferum* at CIMAP, Lucknow.
- Four genes involved in the biosynthesis pathway of podophyllotoxin in *Podophyllum hexandrum* have been cloned jointly at IHBT, Palampur and National Institute of Plant Genome Research (NIPGR), New Delhi.
- An assay method has been developed for aminotransferase involved in the synthesis of vanillyl amine from vanillin at CFT&RI, Mysore.
- Five putative mucilage genes of *Plantago ovata* (Isabgol) have been cloned and characterized at University of Jammu, Jammu.

Animal Biotechnology

A. Animal Vaccines & Diagnostics

The Department is implementing an “Animal

Vaccines & Diagnostics Programme” since 9th Five Year Plan. Some leads include: Candidate anthrax vaccine; development of recombinant e-toxin and DNA based vaccines against *Clostridium petfringens* and *Leptospira* diagnostic kits. The leads are being consolidated through network programmes for major animal diseases of national relevance and also for import substitution. Development efforts are focused towards:

- A recombinant vaccine for leptospira;
- A multivalent oral vaccine against chicken coccidiosis using local isolates;
- Development of recombinant antigen based diagnostic tools for the detection of avian Mycoplasma infections;
- Production and the evaluation of micro particle (Cationic PLG) coated DNA vaccines for Foot and Mouth Disease;
- Serological and molecular characterization of fowl adenoviruses associated with hydropericardium syndrome in domestic fowl with special reference to development of a suitable cell culture vaccine;
- Development of biofilm based vaccine against mastitis causing staphylococcus aureus and Escherichia coli organisms in bovines;
- Evaluation of immunologic response to a recombinant DNA and recombinant BCG vaccines for the control of Bovine tuberculosis;
- Development of diagnostic(s) and immuno-prophylactic(s) for chicken anaemia virus using recombinant DNA technology;
- Study of transmission of livestock-derived pathogenic mycobacteria and its prevalence among humans;

- Development of RNA replicon-based vaccine vector for enhanced expression and immune responses;
- Development of recombinant E-toxin and DNA based vaccine against *Clostridium perfringens*;
- Attenuation virulence of *Mycobacterium bovis* by disruption of glutamine synthetase gene;
- Development of DNA vaccine against rabies using targeted vectors for veterinary use;
- Production and evaluation of self-replicating DNA vaccine for Foot and Mouth Disease.

B. Animal Production

Biotechnological interventions in the area of animal biotechnology focuses on:

- Development of quality feed;
- Animal reproduction;
- Animal byproducts;
- Genetic characterization of indigenous breeds of livestock

Initiatives were taken to generate defined projects/programmes in the area of reproduction and animal nutrition. During the year, progress of 51 ongoing projects and achievements of 16 completed projects were reviewed. 18 new projects on different aspects of animal production were funded. An initiative has been made to set up a National Institute of Animal Biotechnology. Salient achievements in the area are:

Development of Transgenic Animal and Embryo Transfer Technology

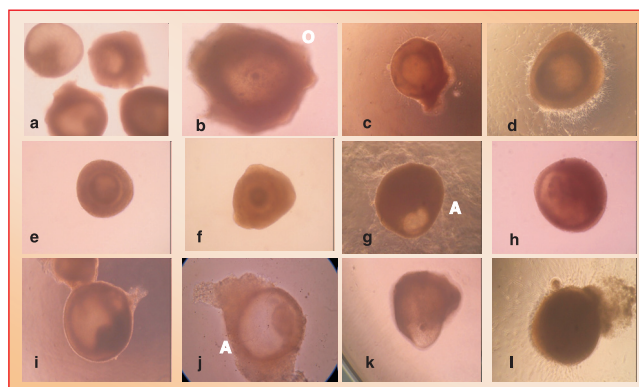
- A comprehensive analysis of the gamete-embryo expression patterns of the Enhanced

Green Fluorescent Protein (EGFP)- transgene during mouse development was done at IISc, Bangalore. The EGFP transgene was successfully expressed in mice with different genetic background by cross breeding approach. These transgenics would be useful to carry out immunological, cancer and stem cell biology experiments.

- Transgenic mice model were developed through a reproducible novel non-terminal technique for inserting genes in spermatogonial cells through *in-vivo* electroporation at NII, New Delhi. Four constructs were developed to confirm the transgenesis and more than 90% of males electroporated with any one of these constructs developed transgenic pups successfully. The method neither required assisted reproductive techniques nor sophisticated laboratory to develop transgenic animal and can be extended to other model.
- Various facets of embryo transfer technology in equines have been standardized.

Animal Reproduction and Related Areas

- A novel collagen gel micro drop method and an efficacious 3D micro environment for the



Photomicrographs of isolated buffalo preantral follicles (Day 0) and after different times and developmental stages in culture

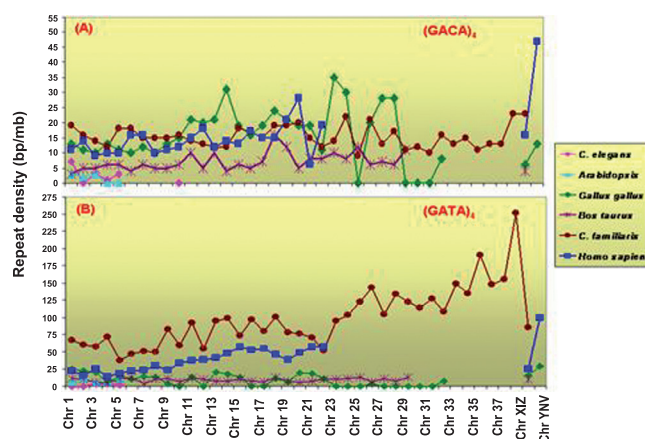
culture of buffalo preantral follicles has been standardized at IVRI, Izatnagar;

- The role of Gonadotropin releasing hormone (GnRH) in the regulation of reproductive processes in buffalo was studied. The study will help in identifying buffaloes with reproductive disorders and GnRH treatment to improve their reproductive status.
- In order to study the gene expression changes in the ovulatory follicles of buffalo, a GnRH-induced ovulation model system for identification of large follicles and induction of luteolysis of the functional corpus luteum was standardized.
- Embryonic stem cells were isolated and cultured from inner cell mass of buffalo blastocysts. These cells formed embryoid bodies in suspension culture and further differentiated into several types of cells including neuron-like and epithelium-like cells in *in-vitro* culture. The expression of transcription based markers viz. *OCT4* and *NANOG* were found to be positive in buffalo embryonic stem cells on fibroblast feeder layers of buffalo, goat and sheep.

Genetic Characterization and Genomics

- Two bacterial artificial chromosome (BAC) genomic libraries of male Murrah buffalo were prepared and characterized at CCMB, Hyderabad. All cattle chromosomes were represented in this comparison indicating that these two libraries represent most of the buffalo genome. These BAC clones would be helpful in whole genome sequencing of buffalo.

- Molecular marker based gene polymorphism status of indigenous cattle breeds (*Bos indicus*) were studied.
- Minisatellite associated sequence amplification technique was standardized for the identification and characterization of novel mRNA transcripts from different somatic tissues, gonads and spermatozoa of water buffalo, *Bubalus bubalis*. The study is a pioneering attempt to explore GACA/GATA tagged transcriptomes in any mammalian species highlighting their tissue stage and species-specific expression profiles without conventional construction and screening of the cDNA library. More than 75% GACA-tagged and all GATA-tagged transcripts were found to be conserved across the species.



Chromosomal distribution of GACA (A) and GATA (B) repeats across the six eukaryotes based on *in-silico* analysis

- Genetic profiling of six sheep breeds viz., Deccani, Muzaffarnagri, Ganjam, Jalauni, Marwari and Sonadi was conducted using 25 neutral (microsatellite) markers. A high level of genetic variation was observed in terms of allele and gene diversity.

- Three different types of markers were used to detect random genomic differences between Red Jungle Fowl and different chicken breeds. The AFLP was found to be most effective technique.
- The iron binding milk protein lactoferrin was purified from colostrum of buffalo, cattle, goat and sheep. Preliminary studies indicated that Buffalo lactoferrin showed greater affinity for iron binding as compared to goat and bovine lactoferrin.
- The expression of the fusion protein gene of Newcastle disease virus was suppressed using siRNA technology. The study confirmed that expression of virus was inhibited in B95 alpha cell line using siRNAs.

Animal Nutrition

- The optimization of solid state fermentation of wheat straw by various species of fungi viz. *Crispellis sp.*, *Pycnoporus cinnabarinus*, *Ganoderma sp* to develop biotech feed for increasing the productivity of animal was carried out in a multicentric project.
- Studies on comparative fibre degradation capacity of various anaerobic fungal isolates indicated the scope for selecting and incorporating superior fibrolytic isolates as direct fed microbial additive for increasing digestibility of fibrous feed in buffaloes.
- *In-vitro* experiments were conducted to study the effect of organic acids and plant extracts on methane reduction, rumen fermentation pattern on dry matter digestibility in buffaloes. The study suggests that fumaric and malic acids had potential

and consistent effect on methane reduction without any negative effect on digestibility. The extracts of garlic and eucalyptus were found to be most potent methane inhibitor.

- Efforts are on to detoxify and utilize the non-conventional oil cakes viz. Jatropha, karanj and neem oil cakes, rich in protein content and good amino acid profile in the feeding of livestock. The anti-nutritional factors of oil cakes were tested and a wide range of variation.

Animal Byproducts

- Biomaterial of bovine origin for reconstructive surgery in animals has been developed and its acceptance as surgical material being studied in different phases. Technique for the long term preservation of biomaterial is being standardized.
- Collagen scaffold (3D) of bovine origin was developed for the cardiomyocyte culture of chick embryo. The study confirmed that the collagen from bovine tissue is a suitable candidate for the preparation of a cardiovascular patch which favours cell growth and proliferation.

Aquaculture & Marine Biotechnology

The emphasis continued on the development of new technologies and enhancing the bio-products. During the period, three Task Force meetings were organized to review the progress of 53 ongoing projects and 18 completed projects. 16 new projects were also funded. To find a solution to the White spot syndrome virus (WSSV) problem affecting the Indian shrimp

industry, a brain storming meeting to identify new facets of research. It is proposed to set up an institution on Marine Biotechnology to exploit potential marine resources for pharmaceuticals, nutritional supplements, cosmetics, fine chemicals, agrichemicals and molecular probes. Some achievements of the programme are:

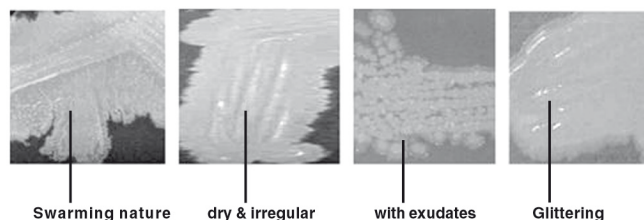
Biomolecules Projects have been supported to detect new compounds and increase the knowledge of selected bio-molecules from various marine organisms and resources, their characterization and potential for industrial exploitation.

- Antibacterial potential of seaweeds were evaluated and the most active marine algal candidate *Asparagopsis taxiformis* was selected for bioassay- guided isolation of active constituents. A large number of secondary bioactive metabolites for potential use as a therapeutic have been isolated.
- The angiogenic factor(s) from the perivitelline fluid (PVF) of Indian horseshoe crab embryos were characterized and the angiogenic activity of various fractions established in developing chick embryos.
- More than 70 neuro-active peptides were isolated and purified from the crude venom of 10 species of Indian cone snails. Their biological activities were analyzed.
- The role of superoxide dismutase (SOD) enzyme in salt tolerance was studied in algae, mangroves and other aquatic plants. Significant enhancement in the activity of Catalase and Superoxide Dismutase was observed in the test plants in response to the salt treatment.

Bioremediation An anaerobic consortium has been developed from marine sediment and biological sludge for the application of wastewater treatment. The consortia degrades organic compounds released from plant material like coconut husks completely. An improved method and device using high rate anaerobic system to separate fats and solids from wastewater of sea food processing industries was also developed and found to be suitable for the treatment of effluents from dairy industries, food processing plants, slaughter houses, etc.

Methods have been standardized to recover the lipids from fish industry waste using fermentation techniques.

A number of marine bacterial species were identified and characterized for their potential as biosurfactant / bioemulsifier producing organism. A marine potent bacterial strain, *Bacillus circulans* was further analyzed for its biosurfactant activities and a yield up to 4-6 g/L of purified bio-surfactant was obtained showing emulsification activity against oils and tannery waste management.



Varied morphology of the isolated marine bacterial species exhibiting biosurfactants activity.

Cell Line Development A multicentric programme on cell line development has been initiated for their possible use *in -vitro* toxicological studies and vaccine development. The primary cell culture of hepato-pancreas from

edible crab, *Scylla serrata*, clownfish and *Etroplus* have been developed. Cell lines have been characterized, designated with different names and deposited in NCCS, Pune. A novel medium has been developed and standardized exclusively for shrimp cell culture.

Diagnostics and Vaccine A multiplex PCR assay has been developed for the detection of *Salmonella* species using various genes viz. *sefA*, *invA* and *fimA*. Efforts are on to develop multiplex PCR for the simultaneous detection of bacterial pathogens *Salmonella*, *Vibrio cholerae* and *E. coli* in fish and fishery products.

For the diagnoses of viral nervous necrosis, a RT-PCR assay was standardized. The diagnostic has helped in selecting viral free broodstock of seabass (*Lates calcarifer*) and mullet (*Mugil cephalus*) for hatcheries and disease free larvae/juveniles for farming.

Various isolates of lytic phages specific to pathogenic strains of *Pseudomonas fluorescens* (PFP1-38) and *Flavobacterium columnare* (FCP1-9) were isolated and characterized. The study suggests that phage specific to pathogens may be a prophylactic and therapeutic candidate to alleviate morbidity and mortality in fish hatchery, aquaria and culture system.

Immunoglobulins of Indian major carps viz. Rohu, Catla and Mrigal were raised against foot and mouth disease vaccine/bovine serum albumin. A sensitive MAb based Enzyme-Linked Immunosorbent Assay has been developed for specific detection of Igs of IMC.

Genetic Characterization Gene expression in

Penaeus monodon and *P.indicus* in relation to microbial infection and environmental stress was carried out in a multicentric project. Analysis of subtraction library generated for *P. monodon* and *P. indicus* infected with white spot syndrome virus and *V. harveyi* has revealed functional categories of proteins.

Microsatellite markers were developed for studying genetic variability in *Penaeus indicus*. These loci will be useful for population genetic analysis of *P. indicus*.

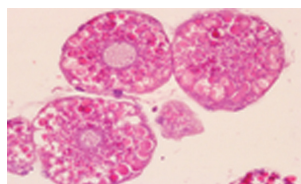
The species specific DNA markers for economically important shellfish species, green mussel and edible oyster have been developed using standard PCR technique with the universal primers.

Genomic analysis of white spot syndrome virus positive shrimp samples were carried out at FCRI, Thoothkudi for the detection and characterization of virulence markers. Preliminary study indicates that the isolates collected from different region belongs to different genotypes.

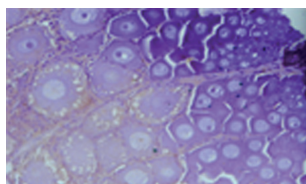
Nutrition The production and growth of cell-bound phytase of yeast, *Pichia anomala* in fed-batch fermentation and cyclic-fed batch fermentation has been standardized. The inclusion of soybean oil in the medium improved oxygen transfer rate and led to a high yeast growth and phytase synthesis.

Reproduction Efforts are on to develop early maturation techniques for commercial brooders of *P. monodon* to improve its reproductive status and availability of seed. The results suggest that presence of vitellogenin in hepatopancreas rather

than ovaries might have crucial role in ovarian maturation and also indicate that hepatopancreas have supplementary role in oocyte maturation.



Hematoxylin and eosin staining in the vitellogenic ovary



Immunolocalization of StAR protein in the vitellogenic ovary

Techniques for captive breeding, rearing and culture of Indian seahorse (*Hippocampus species*) have been developed at National Institute of Oceanography, Goa. Effect of photoperiod on juvenile survival as well as influence of back ground color of rearing tank on the survival of juvenile seahorses is underway.

Regeneration Cellular and molecular mechanisms of regeneration of Zebra fish spinal cord was studied by inducing standardized injury to individuals. The number of proliferating cells increased significantly in response to injury and cells were generated at specific proliferating zones. The study indicates that proliferation and neurogenesis in Zebra fish is associated with regenerative events allowing this species to regenerate the damaged organs. Apoptotic cell

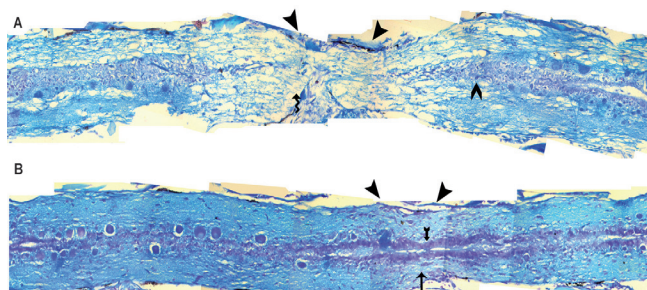


Fig.1. Luxol Fast Blue and Cresyl Violet staining of injured zebrafish spinal cord. A) 3 day regenerated spinal cord shows loss of axonal connections (↓) and disappearance of neuronal cell bodies (↑) at the injury epicentre (▲, ▴). B) The 1 month regenerated spinal cord shows the reconnected axon (↑) fibres and reappearance of neuronal cell bodies (↓) at the epicentre.

death in regenerating zebra fish spinal cord was also confirmed.

Training A training programme in molecular biology for the personnel involved in R&D of aquaculture/marine biology has been initiated. 38 participants were trained at CCMB, Hyderabad for 8 weeks. The trained scientists are being encouraged to initiate R&D work in the area.

Seribiotechnology

Efforts on application of biotechnology for improving the productivity, enhancing the quality of silk, improvement of host-plants, improving the post-harvest processing of silk along with utilization of by-products in sericulture continued during the year. Significant achievements during the year are summarized below:

Development of Better Races of Silkworm for Increased Productivity

A network project was implemented at five institution namely: CDFD, Hyderabad; Seribiotech Research Laboratory, Bangalore; Central Sericultural Research and Training Institute, Mysore; Andhra Pradesh State Sericulture Research and Development Institute, Hindupur and Karnataka State Sericulture Research and Development Institute, Bangalore with an aim to identify the DNA markers for baculovirus resistance in *Bombyx mori*. The project led to identification of silkworm breeds for BmNPV tolerance and susceptibility. DNA polymorphism was observed between the identified breeds and few polymorphic markers have been identified for the potential stocks.

A network project on phylo-geography of tropical tasar (*Antheraea mylitta*) and muga silkworm (*A. assama*) has been continued involving three institutions: SRL, Bangalore; CTR&TI, Ranchi and Central Muga Eri Research and Training Institute (CMER&TI), Jorhat. Most muga silkworm populations of North East region have been found to be genetically homozygous. Muga population of West Garo Hills showed genetic stagnation. Genetic analysis using microsatellites developed from *A. mylitta* showed low polymorphism (39%) among various populations collected from Jharkhand. Lower heterozygosity and high gene flow of wild populations indicated lower level of genetic differentiation with the tasar populations.

With an aim to identify cDNA markers linked to genes controlling cocoon and post-cocoon traits in the mulberry silkworm, the parental silkworm breeds i.e. Pure Mysore, CSR2, their F1s and reciprocal F1s showing contrasting features were reared and the metric data on cocoon weight, shell weight, size deviation, filament length, denier and boiloff loss have been analyzed in three seasons at CSR&TI, Mysore. The EST cDNA clones (five each) pertaining to all the 28 linkage groups have been amplified through transformation of *E. coli* strain. Studies continued on ecogenetic analysis of diapause and reproduction in tropical tasar silkworm (*A. mylitta*) at CTR&TI, Ranchi. Four diapause related proteins have been identified during early and mid-aged pupae in diapausing generation.

Development of Control Measures for Major Disease of Silkworm

Efforts continued on identification, characterization and diagnosis of some important

muga silkworm diseases jointly at Assam Agricultural University, Jorhat and CMER&TI, Jorhat. *Bacillus thuringensis* and *Aeromonas salmonicida* have been found to cause toxicons and septicemia of muga silkworm, respectively. Pathogenecity tests of various fungi elucidates *Baeuveria bassiana*, *Aspergillus* spp. and *Fusarium moniliforme* causing muscandine, aspergillosis and fugorosis diseases, respectively, in muga silkworm.

Improvement of Host Plants

A network project implemented at five institutions namely – Centre for Cellular and Molecular Biology, Hyderabad; CSR&TI, Mysore; KSSR&DI, Bangalore; CSR&TI, Berhampore and Central Sericultural Germplasm Resource Centre, Hosur continued with a view to identify DNA markers associated powdery mildew and pests (tukra and root knot nematode) resistance in mulberry. Two markers have been identified that each appeared to be associated with resistance to tukra and powdery mildew. These may be useful in the breeding programmes of mulberry.

Transgenic mulberry lines with osmotin gene have been raised for drought and salinity tolerance under a collaborative project at UDSC, New Delhi and CSR&TI, Mysore.

Efforts have been initiated for developing mulberry transgenics overexpressing transcription factors to increase drought tolerance and reduced post harvest water loss at University of Agricultural Sciences (UAS), Bangalore.

Efforts continued to identify QTL for root traits and water use efficiency in mulberry jointly at UAS, Bangalore and CSR&TI, Mysore. Putative

markers linked with these traits have been identified. More markers are being added and QTL will be identified by composite interval mapping strategy.

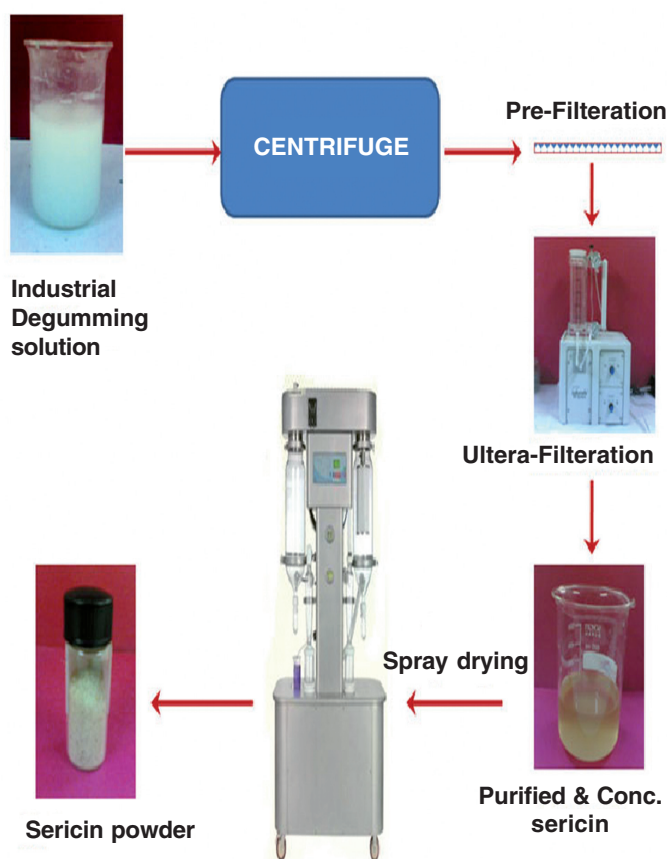
Improving Post-Harvest Processing of Silk

With a view to improve the fabric quality, work on production of microbial dyes and their application on silk and other fibres has been recently initiated under a collaborative project at Bhavan's College, Mumbai and University Institute

of Chemical Technology (UICT), Mumbai. Fifteen microbes have been selected with their abilities to produce pigments within the entire colour spectrum.

Utilization of By-Products

A process for the recovery and production of sericin powder from the waste cocoons and industrial degumming liquor has been developed at laboratory scale at IIT, New Delhi. The application of sericin on various textile materials such as polyester, cotton and its blend has been standardized. The process of recovery of sericin from the waste degumming liquor is planned to be scaled up at plot level in collaboration with an industrial partner.



Process flow-chart of the recovery and production of sericin powder at IIT, New Delhi



Sericin finished polyester garments with moisture absorption and antistatic properties (IIT, New Delhi)

Basic Research in Modern Biology

Programme on basic research, are being supported to increase understanding of fundamental principles and to provide scientific information and theories for the explanation of the nature and the properties of the world around us. However, in the long term, it is the basis for many commercial products and applied research. Projects are being funded under following categories:

- Drug Discover
- Proteomics
- Computer Modelling, Simulation and Optimization
- Molecular Immunology
- Gene Cloning and Biochemical studies
- Plant Molecular Biotechnology
- Nanobiotechnology
- Bioengineering
- Reproductive health

Highlights of the findings have been grouped into following areas:-

Drug Discovery

- Studies at CUSAT, Cochin on hypoxia and brain disorders explained that hypoxia causes an up regulation of epinephrine and those treated with oxygen and epinephrine showed a down regulation in the experimental groups.
- At University of Delhi, Octa hydroquinolin-6 has been modified as double bond isomers and characterized by IR, NMR and mass spectroscopy.

- The complex formation of curcumin with bovine casein micelles (CM) and its use as vehicle for drug delivery to cancer cells have been investigated at IIT Guwahati.

Proteomics

- Study done at BHU, Varanasi envisaged that Hsp60C protein in *Drosophila melanogaster* is essential for female gametogenesis. The depletion of Hsp60D on polyQ-based neurodegeneration has potential clinical applications in mammalian systems.
- At Delhi University, peptide nucleic acids (PNA) analogues having improved permeability and hybridization potency has been designed and developed successfully.
- The mechanism of induction of apoptosis by tumour suppression p53 protein studied at CCMB Hyderabad. It is observed that p53 plays an important role in mediating response to DNA damage and other stresses resulting in either growth arrest or apoptosis.
- At ICGB, New Delhi the role of chemokines RANTES and IP-10 have been investigated in regulating protective immune responses from *tuberculosis*. Pathway specific microarray analysis showed that many Th 1 promoting the chemokines and chemokine receptors.
- Accurate biochemical marker for differential diagnosis of liver disease has been established at WBUT, Kolkata. Hepatitis B can be diagnosed by slight elevation of alpha glycoprotein (AGP) and alaphafeto-protein (AFP) where as Hepatitis cirrhosis by high elevation of AGP and AFP. Similarly the Hepatitis B Cirrhosis can be diagnosed by high branching in both AFP and AGP in

patients sera whereas alcoholic liver cirrhosis by highest level of AFP in patients' sera.

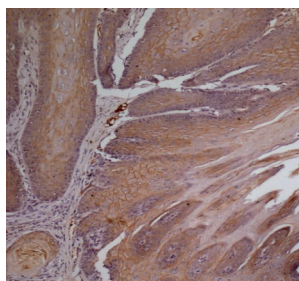
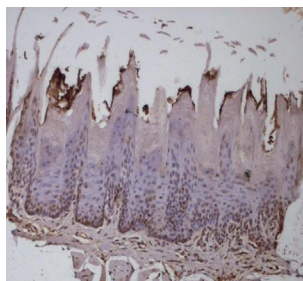
- At IISc., Bangalore scientists have determined of crystal structures of pyridoxal 52 - phosphate dependent enzyme called serine hydroxymethyl-transferase. This is the first enzyme structure from a mesophilic organism that has been determined and serve as a basis for the design of drug.
- Studies at NII, New Delhi indicate that phosphorylation of BLM can play an important role in regulating the function of the helicase. Further studies are on.

Computer Modelling, Simulation and Optimization

- Study conducted on bioinformatic analysis of putative histidine kinases Rv0600c and Rv0601c at IIT, Kharagpur revealed that HK1 has an ATP binding domain while HK2 is a unique HPt-mono domain protein.

Molecular Immunology

- All the stages including dysplasia, papiloma and carcinomas of Lingual carcinogenesis have been studied on treated dorsal rat tongue



IHC staining of Beta 4 integrin in lingual tumors of rat showing elevated levels in 200 days treated rat tongue in comparison to untreated tongue.

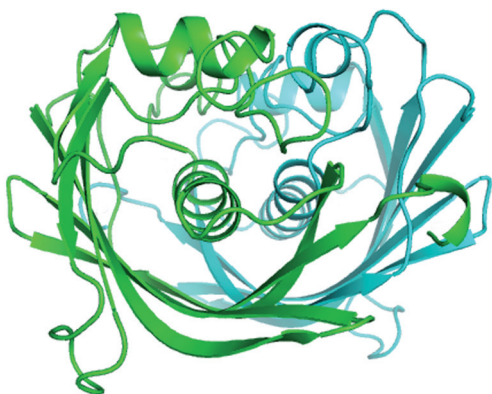
and human leucoplakia /submucous fibrosis samples. The changes observed in experimental model can be extrapolated to human system which is indicative of the utility of model.

- Two single nucleotide polymorphisms SNP's have been analyzed at NCCS, Pune. The protein that binds to the 5'UTR of insulin by RNA affinity have been identified and characterized.
- Studies conducted at IISc, Bangalore on immunomodulatory activity revealed that glycodeclin is a galactose-binding lectin and this characteristic of Glycodeclin A is responsible for its apoptogenic function. The study links the lectin activity of GdA to its biological function.
- Studies conducted on molecular regulators of platelet apoptosis at BHU, Varanasi revealed loss in mitochondrial transmembrane potential in stored platelets indicative of mitochondrial permeability transition leading to apoptosis. The nano silver significantly impaired platelet functions in a dose-dependent manner and led to apoptosis-like changes which has with possibility of anti-platelet therapeutic applications.

Gene Cloning and Biochemical studies

- Scientist at IIT, Madras, Chennai have cloned the cytosolic regions of the G protein couple receptor into expression vectors to understand the role in physiology and medicine.
- At IISc., Bangalore α -hydroxyacyl-Acyl Carrier Protein Dehydratase (FabZ), proteins

structure has been determined and the inactive dimeric forms of the enzyme established. The enzyme-inhibitor interactions are being examined with a view to design better inhibitors which could be potential antimalarials.



Crystal structure of the dimeric form of FabZ of *P. falciparum*.

- At University of Delhi, *Leishmania* ortholog of the DNA replication protein ORC1 has been cloned and overexpressed in *E.coli*. Findings indicated that, contrary to what is widely believed to be the case in humans, *Leishmania* ORC1 remains in the cell's nucleus cell of the cell cycle. This is the first report in any of the disease causing trypanosomatids attempting to identify novel *Leishmania* proteins involved in DNA replication.
- At IISc., Bangalore scientists have identified the Dufour's gland as the likely source of queen pheromone. It has been confirmed that the Dufour's gland is the source of the queen pheromone in *R. marginata*.

Plant Molecular Biotechnology

- At NRCPB, New Delhi, a 1147bp gene has been identified as promoter sequence from

Arbidopsis thaliana cv. columbia using a reporter gene b-glucuronidase. This could be used in bioengineering the trichome machinery for generation of biomolecules of economic importance. The efficacy of the promoter was evaluated in a Tomato (var. Pusa Ruby) and found capable of driving trichome specific expression.

- Studies on plant salinity tolerance conducted at ICGB, New Delhi demonstrated that rice plants transformed with a pea DNA helicase gene grow normally under high salt condition. Results indicate the potential for improving stress tolerance in crop plants.

Nano-biotechnology

- At IIT, Bombay, nano-composite bone graft materials and materials for maxillofacial and orthopaedic use have been developed. Results have indicated a good correlation between the oxygen-deficient nanofraction in the bhasma and its *in-vitro* ROS scavenging activity.
- A biomimetic process to produce nanocomposite hydrogel scaffolds has been developed at NML, Jamshedpur. Due to uniform distribution of nanosized hydroxyapatite particles (100 nm) and their ordered integration on hydrogel surface this approach is likely to make useful to produce bioactive scaffolds suitable for cartilage repair and low load bearing bones.
- Magnetic nanospheres of about 200 nm have been developed at IIT, Kharagpur. Further, super paramagnetic nanoparticle *N*-methyl-*O* carboxymethylchitosan (NMOCMCS) with highly positive surface, charge for protein

drug delivery has also been developed *In vitro* studies showed that the NMOCMCS/Fe₃O₄ nanoparticles have good biocompatibility.

Bioengineering

- Electron microscopic studies are being conducted at JNU, New Delhi on HpDnaB and N-terminal deleted mutant D2-HpDnaB. The study indicates that the linker region between the N- and C-terminus is essential for hexameric conformation and its function.
- In a collaborative study at CDRI, Lucknow, three dimensional solution structures of MtPth have been determined and deposited with Protein Data Bank under the PDB ID 2JRC.
- At TIFR, Mumbai ¹⁵N-edited-NOESY HSQC, ¹³C edited-NOESY HSQC and ¹³C edited (aromatic)-NOESY HSQC spectra were recorded on 800MHz NMR spectrometer for getting the NOE-based distance constraints for structural calculations. Further analysis of protein backbone dynamics, has shown that most of the protein backbone was rigid and was associated with the substrate peptidal-tRNA .

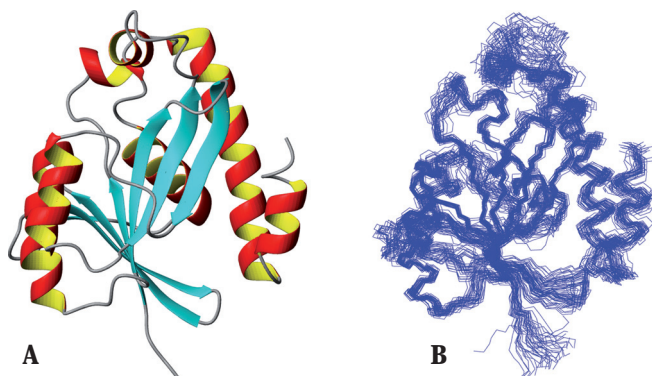


Fig.3. (A) Ribbon representation of the solution structure with lowest target function of an ensemble of 40 NMR structures. (B) Superimposition of backbone traces of MtPth for 40 lowest target function structures. PDB ID- 2JRC.

- Novel Hydroxyapatite (Hap)-Mullite composite has been densified successfully by pressureless sintering and without any sintering additives at IIT, Kanpur.

Reproductive health

In the study of follicular fluid and embryo development, 486 samples of ovarian follicular fluid taken from 114 women undergone *in vitro* fertilization (IVF) were analysed at IIT Kharagpur. Results revealed that higher levels of reactive oxygen species (ROS), lipid peroxidation (LPO) and total antioxidants capacity (TAC) directly affect oocyte and embryo quality which can be correlated with successful pregnancy.

Medical Biotechnology

Medical Biotechnology research and application activities have expanded exponentially during later part of the 10th plan and continuing during 11th plan period. There is paradigm shift towards translation of research leads and consolidation of open ended R&D projects into distinct programs, Centers of Excellence and Public-private partnership. The newer programs also include setting up distinct Diagnostics and Vaccine Research Facilities, developing clinical trial sites, clinical trials of various lead compounds, validation facilities for Diagnostics as well as certain Technology Policy Units. The cluster approach towards establishing newer institutions along with academic centers is also being explored and gradually implemented with novel management structures.

The programmes of Medical Biotechnology are grouped into:

- Vaccines & Diagnostics
- Infectious Disease Biology
- Chronic Disease Biology

Vaccine Development

The Department initiated a programme to develop vaccines through National Jai Vigyan Mission. Candidate vaccines for Rotavirus, Cholera, Typhoid, Rabies, animal, human (DNA based), Anthrax, Malaria, Dengue, Tuberculosis and Japanese Encephalitis Virus emerged. Some of these are into pre-clinical or clinical trial stages. Salient achievements are:

Rotavirus: The rotaviral diarrhoea projects resulted into the development of two candidate vaccines 116E and I321. The vaccine candidate 116E completed phase-II human clinical trials successfully. A double blind placebo controlled dose escalating phase Ib/IIa trial has been initiated by SAS, New Delhi to evaluate the safety and Immunogenicity of a live attenuated rotavirus vaccine manufactured by M/s Bharat Biotech International Limited, Hyderabad under GMP conditions, in healthy non malnourished infants 8-20 weeks of age. The vaccine induced immune response was reported in ~90% of recipients. Site preparation for Phase-III clinical trial is going on. The same is prepared to be undertaken in mid 2009.

Cholera: An oral, live, recombinant, non-residual cholera candidate vaccine has been developed using novel methods of strain isolation and genetic manipulations and clinically tested. Based on encouraging results, the candidate VA1.4 is now being cGMP manufacture for large scale trials. The formulation for the vaccine has been worked

out and batch data on stability is being collected for regulatory purposes. Site preparation is going on parallelly.

Malaria: The efforts at ICGB, New Delhi in collaboration with National Institutes of Health, USA resulted into candidate vaccine for of *P.falciparum* and *P. vivax*. The recombinant candidate antigens have been produced under GLP conditions at a pilot scale (10L fermentation scale). Methods for production of PvRII have been scaled up to 50L and 100L under cGMP conditions by M/s Bharat Biotech International Limited, Hyderabad. Three batches of vaccine to initiate preclinical and clinical trials have been provided. A field trial site has been prepared at Malaria Research Centre, Rourkela, to evaluate the candidate malaria vaccines. Clinical development plan to initiate phase I & II clinical trials are being worked out in consultation with international partners.

Japanese Encephalitis: While the work on tissue culture based vaccine (Indian strain adapted to Vero cells) transferred to M/s. Panacea Biotech has progressed towards establishing tools and techniques for Phase I clinical trials, a new approach using Adeno based vectors as a backbone for JE DNA vaccine has shown encouraging results. Partnership is being sought for further development.

Dengue Vaccine: Under the project “Experimental tetravalent dengue vaccine: accelerated development” implemented at ICGB, New Delhi, developed a novel tetravalent chimeric protein. Efforts are being made to continue animal studies in AGK0129 mice strain for the development of tetravalent dengue vaccine.

Tuberculosis: Several candidates for tuberculosis vaccines have been developed under the Jai Vigyan Mission program. Currently partnership is being sought for taking them further for developing product development and clinical development plans.

Pneumococcal: Project on “Evaluation of streptococcus pneumoniae derived proteins for development of protein based pneumococcal vaccine” implemented at NII, New Delhi identified pneumococcal vaccine candidates and the study was further extended to continue with additional objectives to establish proof of concept in animals with few protein based candidate vaccines.

Vaccine Grand Challenge Programme: Approvals have been obtained to initiate Vaccine Grand Challenge Programme with an objective to accelerate development of candidate vaccines for which earlier leads are available; and to take them through pre-clinical and clinical studies development and commercialization.

Delivery System: Under the project “Immunological evaluation of polymer particle-based delivery system for carbohydrate and protein antigens” implemented at NII, New Delhi, polymer particle entrapping Vi polysaccharide antigen of *S. typhi* were prepared using PLA polymers in microparticles (2-8 µm) and nanoparticles sizes were prepared. Immunization was carried out in BalbC mice to evaluate the immunogenicity of the particle entrapped polysaccharides. Single dose of intramuscular immunization of polymer entrapped Vi was able to induce long lasting antibody titers.

Indo-US Workshop on Low-Cost Diagnostic and Therapeutic Technologies: Indo-US

workshop on “Low-Cost and Therapeutic Medical Technologies” was organized at the Centre for DNA Fingerprinting and Diagnostics (CDFD) on behalf of Department and National Institute of Biomedical Imaging and Bioengineering (NIBIB), U.S.A. in November 2008 at Hyderabad. Five sessions focused on various areas such as Cancer Screening; Cardiovascular Diseases; Digestive Diseases; Diabetes and Liver Disease; Maternal/Newborn/Infant Health and Trauma and Injury. The discussion was on development of low-cost biomedical imaging technologies; low-cost, point-of-care diagnostic technologies for disease areas of greatest need; telehealth, health-related information technologies, and telecommunications and neonatal health technologies for small and mid-size hospitals. Few areas have been identified as priority for the community health improvement. It was decided to develop joint proposals in the identified focused areas amongst academic institutes, clinicians and industries of both the countries.

Immuno-modulator / Adjuvant Research: The clinical trials using *Mycobacterium w* (now known as *Mycobacterium indicus pranii*) as an adjunct to chemotherapy in Category II of the pulmonary tuberculosis at seven centers i.e. AIIMS, New Delhi; LRS Institute of TB & Respiratory Diseases, New Delhi; Central JALMA Institute for Leprosy and other Mycobacterial Diseases, Agra; SMS Medical College, Jaipur; N.H.L. Municipal Medical College, Ahmedabad; Bhagwan Mahavir Medical College, Hyderabad and Tuberculosis Research Centre, Chennai. Recruitment has been completed and 3rd Interim Analysis carried out recently. The results are promising. An independent CRO is now collecting and compiling data for filing with USFDA.

Infectious Disease Biology: The Task Force has emphasis on development of new interdisciplinary infectious disease platforms to address important issues relating to specific pathogen biology aspects relevant to the country, keeping in view of disease burden, mortality and morbidity. Two meetings were held during the year, 48 new R&D projects were considered and also reviewed progress of the ongoing projects. A total of 28 new R&D projects have been implemented in the areas of HIV/AIDS, hepatitis, chikungunya, respiratory diseases, diagnostics drug development etc. Significant achievements of ongoing R&D programmes are summarized below:

Viral diseases

- Genetic variations among diverse primary viral isolates have been studied by carrying out functional analysis of the NF- κ B polymorphism in the terminal repeat of HIV-I subtype-C which could contribute to global dissemination of this important viral subtype.
- It has been observed that replacement of QGD motif of Tat-C with RGD motif of Tat-B led to increased apoptosis suggesting that RGD motif alone contributes substantially to Tat-C mediated apoptosis which helps to understand the molecular basis of pathogenesis of HIV.
- Studies on molecular basis of CTL dysfunction in HIV infection have provided important leads for devising an immunotherapeutic strategy to control HIV replication or boost existing strategies.
- A Lentiviral (HIV-2, Indian Isolate) gene transfer vector has been developed at ACTREC, Mumbai which can be used in

creating mammalian cell lines, adapted to serum free media for producing therapeutically important recombinant glycoproteins.

- Strategies for small interfering RNAs (siRNAs) for inhibition of Hepatitis
- E virus (HEV) replication and transcription have been successfully developed.
- Recombinant S protein derivatives of SARS associated Coronavirus (SARS-CoV) & highly specific mAbs against S protein have been generated and RT-PCR for the N gene has been standardized for its detection using *in-vitro* transcribed RNA transcripts as template for diagnosis purpose.

Bacterial diseases

- Polymerase chain reaction (PCR) to amplify the specific regions of *M. pneumoniae* P 1 gene, *C. pneumoniae* Pst-1 region, *L. pneumophila* MIP gene, has been standardized. Also the standardization of Real-Time PCR for diagnosis of *M. pneumoniae*, *L. pneumophila* and *C. pneumoniae* and development of multiplex Real-Time PCR for diagnosis of *M. pneumoniae*, *L. pneumophila* and *C. pneumoniae* has been accomplished.
- Studies on *S. typhi* virulence polysaccharide Vi in host-pathogen interaction suggest that Vi can bring about inhibition of T cell activation.
- In the study of programmed cell death in pathogenic bacteria towards evaluating the potential for developing novel antibodies to control infectious diseases, the recombinant toxin/antitoxin was expressed (in BL21 (DE3) cells) and purified.

- Diagnostics for five pathotypes (STEC, EPEC, EAEC, ETEC, and DAEC) of diarrhoeogenic *E. coli* as well as for *Salmonella* and Rotavirus in man and animals have been established.
- Reagents for easy visualization of PCR products for the prototype kit developed for detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* have been developed and validation studies are underway.
- Studies on effect of zinc in newborns with serious bacterial infection indicate positive correlation of serum zinc concentrations with the total lymphocytes and CD4/CD8 which may be affected by changing zinc concentrations, further studies are in progress.
- Studies to explore mechanism of drug non-responsiveness to SbV in field isolates of *Leishmania donovani* demonstrated a good correlation between clinical response, sbIII insensitivity of promastigotes and sb V refractory response of parasite in animal model. It was also established that IC50 of SbIII can be used as a marker for antimony resistance. The role of intracellular thiols in antimony resistance in clinical isolates has been established. Also, the role of both MDR and MRP efflux pumps in clinical resistance to antimony in field isolates of *L. donovani*, has also been shown.
- Surface modified liposomal system for developing and characterizing carrier mediated non invasive/conventional DNA was performed which could be successfully prepared and used as immunoadjuvants for genetic immunization. It also enhanced humoral as well as cellular immune response, but further extensive work is essential to prove the efficacy and safety of the liposomal carrier systems before they can be accepted clinically as alternative vaccine delivery system(s).
- About 50 Scientific publications have been made and 4 patent applications have been filed.

Parasitic diseases

- Studies on the role of Eh29 (29kDa protein) of *E. histolytica* in survival and pathogenicity provides important target for rational drug design towards treatment of amoebic liver abscess.
- Effect of gene silencing on the modulation of cell signaling mechanisms during early phase of *L. donovani* using siRNA indicate that CCR5 and TLR2 participate during early events of visceral leishmaniasis. CCR5 specific siRNA holds a great promise to restrict parasite entry and its entry in macrophages and could play a major role as an immuno-therapeutic target for the prevention of visceral leishmaniasis.
- A recombinant leishmania antigen-rF14 has been found to be a potential candidate for vaccine as it provided partial protection when used along with MPL or incorporated into PLGA microparticles.

DBT-ICMR Collaborative Effort

Collaboration between DBT and ICMR initiated during 2007 to promote research in the HIV/AIDS and Microbicides area involving investigators from academia and research laboratories to design HIV antigens/antibodies/drugs/microbicides. Currently 18 projects are operational. The programme is monitored by an Expert Committee. Salient achievements are:

HIV/AIDS

- Towards designing and characterizing stable folded fragments/derivatives of HIV env for use as immunogens, an improved and longer bridging sheet peptide analog has been designed and synthesized. Also, a monomeric well folded version of domain D1 of human CD4 has been designed.
- A total of 15 HIV-1 strains and their co-receptor usages have been identified and isolated to carry out neutralization epitope mapping in HIV-1 envelope of Indian origin. It was observed that serum of a chronically infected ART naïve patient conferred broad neutralization of diverse heterologous envelopes.
- A study has been initiated to determine genetic variations in the AIDS modifying genes and compares genetic differences, correlation with viral load, circulatory chemokines and AIDS progression in infected individuals & unrelated healthy individuals.
- A novel luciferase based simple and quick assay system has been developed for evaluating the inhibitory potential of anti-Tat agents /drugs that interfere directly with the Tat-TAR interactions.
- Study indicates the possibility of involvement of spermatozoa in sexual transmission of HIV. Human Mannose Receptor (hMR) was found to be localized on human sperm and vaginal epithelial cells, thereby indicating the possible association of hMR with risk of sexual transmission of HIV.
- Studies indicate that CD40 and CD40L mediated signaling down regulates ERK mediated pathway during HIV infection.
- Virtual knowledge and resource center for reagents, protocols and technology in the context of HIV/AIDS research has been established at NARI, Pune.

Microbicides

- Six nucleoside reverse transcriptase inhibitors (NRTIs), 3 non-nucleoside reverse transcriptase inhibitors (NNRTIs) and 8 integrase inhibitors have been synthesized for developing antiviral compounds as inhibitors of HIV replication.
- A protein having antibacterial activities has been identified from the hemolymph/hemocytes of Indian mud crab, *Scylla serrata* which has been expressed in *E.coli* and purified to its homogeneity by HPLC. Nisin from *Lactococcus lactis* or its combination with Carrageenan (NisCar gel) showed activity against several standard strains, multidrug resistant pathogens and clinical isolates.
- Towards *in vitro* testing of potential microbicides, a national facility (BSL-3 Level) has been established at NII, New Delhi. MTT Cell Cytotoxicity assay to analyze the cytotoxicity of different plant extracts has been standardized.
- Phase I Clinical trial studies on safety, acceptability, side effects and vaginal sensitivity of daily intravaginal application of 'BASANT' polyhedral gel as a vaginal microbicides for 14 consecutive days in sexually active HIV-uninfected women have been initiated.
- Eight Scientific papers have been published and one patent application has been filed.

Chronic Disease Biology (CDB)

Chronic Diseases Biology area has emerged as an important area over the years. Funding to the tune of Rs. 3000.00 Lakhs annually is provided to the projects covering: Cancer, Neurosciences, Cardiac Diseases, Reproductive Biology, Diabetes etc. Most projects currently are investigator generated with no strategic focus on any of the areas. A new Task Force has been constituted for three years who are contemplating a “Ten Years Perspective” to: define areas of strategic research for each chronic disease; modalities to generate strategic projects; newer modalities for funding; new systems of appraisal; defined monitoring and management structures on following crucial areas:

- Cancer;
- Neurosciences;
- Reproductive Biology;
- Cardiac Diseases;
- Metabolic Disorders including Diabetes;
- Autoimmune Diseases including Joint diseases.

Salient achievements are as follows:

Cancer: There are about 120 on-going projects on cancer covering various aspects such as:

Biomarkers for early diagnosis, prognosis and drug response; drug-target identification; novel drugs; genetic pattern in different cancers etc.

Curcumin Trials: Clinical trials using curcumin in different cancers have been initiated. Each site has already recruited 50% of the patients. The programme is being reviewed regularly by the CROs and an apex group;

Human Papilloma Virus Vaccine: The network programme on the development of vaccine candidates for Human Papilloma Virus has resulted into establishment of tools and techniques. Private partnership is being sought;

Cell based immunotherapy: Development and clinical evaluation of Dendritic cells (D.C.) vaccine derived from autonomous mononuclear cells from peripheral blood of patients and primed with whole cell lysates from tumours of individual patients for the immunization has shown safety. The programme is being expanded as focused activity.

Cancer Immunotherapy: Approaches for identifying new targets for cancer therapy are going on.

Chemical genomics based programme on cancer drug development: A major effort on new drug design using chemical genomics is under preparation.

Neurosciences

There are about 30 on-going R&D projects in the area of neurosciences, including projects on neuronal aging, cognitive malfunctioning in normal and diseased conditions, neuro-genetic disorders, neuronal modeling etc. A multi-center project on “Dementia” is under development.

Stem Cell Research

In continuity with the priority areas identified and categorized, both basic and clinical researches is being promoted by the Department. The programmes have been identified and implemented on various aspects of both embryonic

and adult stem cells such as limbal, haematopoietic, embryonic, pancreatic, neural, cardiac stem cells; generation of human embryonic stem cell lines; use of banana lectins for stem cell preservation; haematopoietic stem cells (HSC) for haplo-identical etc.

During the year, 12 new projects have been sanctioned. The projects include: protein profiling of human ovarian tumour stem cells; differentiation of human fetal pancreatic progenitor cells for potential use in cell replacement therapy for type-1 diabetes; establishment of propagable cell lines from pancreas and adipose tissue of embryo and adult WNIN obese rats, *In-vitro* differentiation of hESC and MSC into cardiomyocytes, characterization of cultivated oral mucosal epithelial cells and its application for reconstructing the ocular surface in patients with severe ocular surface disease; MSCs therapy in diabetic induced mice skin wounds etc.

Embryonic Stem Cells

Four human embryonic stem cell lines (hESC) have been generated at JNC SAR, Bangalore and NIRH, Mumbai. Out of these, two hESC lines are from discarded grade III blastocysts. The cell lines have been deposited in UK Stem Cell Bank and NCCS, Pune.

Three hESC lines have been generated on human fibroblast feeder layers and in near xeno-free environment for the first time in the country at NIRRH, Mumbai. The cells have been cryopreserved at various passages and studies initiated for lineage specific differentiation. These cell lines have also been deposited at NCCS, Pune and available for the researchers in the country.

Stable ES cell lines over expressing *asrij*, a novel stem cell marker with potential role in cardiovascular development has been generated. Pathways that are likely to be affected by *Asrij* over expression have been identified. Role of *asrij* in endothelial cells during angiogenesis has been identified. At IISc, Bangalore, the immortalized breast stem cell lines with the potential to continuously initiate mammospheres has been successfully generated. Stem-cell based breast cancer model system has also been developed.

At NCCS, Pune, five neural stem cell lines from adult human brain tissue that are enriched with neural stem cells have been developed.

Adult Stem Cells

Projects have been implemented on *in-vitro* differentiation of mesenchymal stem cells into neuron-progenitor cells; generation of human autologous ESCs by somatic cell nuclear transfer (SCNT) and parthenogenesis; functional assessment of adult human pancreatic islets following autologous transplantation; differential proteomics of human corneal stem cells versus corneal epithelial cells; unraveling the role of microRNAs in self renewal and tumorigenicity of brain tumor stem cells derived from neuroepithelial tumors of the central nervous system; development of assays for toxicity testing and drug discovery using cardiomyocytes differentiated from hESCs.

In the project supported at NCCS, Pune on harnessing the potential of multipotent adult stem cells, promising results have been obtained. A patent has been filed. Mesenchymal-like cells isolated from umbilical cord have been found to

be the best candidate for islet generation due to their quicker multipotent differentiation and higher yield of ILCs. The placental mesenchymal stem cells (PMSCs) grown in 2D vs. 3D conditions in terms of their expression profiles for various cell surface molecules (e.g. integrins), both at protein and RNA levels have been characterized. The hematopoietic stem progenitor cells (HSPCs) cultured in 3D conditions found to have enhanced engraftment potential as compared to those of 2D.

At LVPEI, Hyderabad, continuous limbal cultures in the laboratory and clinical transplantation has been successfully completed to overcome the limitation of low cell yield from cultures grown on human amniotic membrane. In another study, the limbal stromal cells showed striking resemblance to bone marrow derived mesenchymal stem cells.

At IIT, Chennai, a simple and rapid method for the isolation of cardiomyocytes from neonatal mice heart and their maintenance in primary cultures that consistently yielded long-term cardiomyocyte cultures in their laboratory has been established. In one of the studies, endothelial cells have been isolated from human umbilical vein and confirmed with Immuno-cytochemistry. MSCs have been isolated from umbilical cord matrix and characterized.

Human Trial

In the phase-I clinical study on acute myocardial infarction using autologous bone marrow mononuclear cells implemented at five hospitals in the country, about 30% recruitment has been

completed by all the Centres. A CRO has been engaged for proper monitoring of this study at each site.

All the five sites have initiated the recruitment of patients under phase-I clinical study on acute ischemic stroke. The procedure to initiate recruitment of patients under critical limb ischemia has been completed and ethical clearances from all the centres obtained. The selection of CRO is under process.

India is participating in the Stem Cell Network on Asia Pacific" (SNAP), a conglomerate of seven countries. The participation would include training of young scientists, researchers and students, exchange of scientists between the member countries and also to organize workshops & conferences.

Stem Cell Guidelines

The guidelines for stem cell research in the country finalized jointly by the DBT and ICMR have been submitted to the Ministry of Health and Family Welfare. A National Apex Committee for Stem Cell Research and Therapy (NAC-SCRT) is being constituted jointly by the DBT and ICMR as per this guideline.

CMC-DBT Centre for Stem Cell Research

CMC-DBT Centre for Stem Cell Research is functional at CMC, Vellore as a translational unit of the "Institute for Stem Cell Science and Regenerative Medicine" being established at Bangalore to carry out both basic and translational stem cell research.

Bioengineering

Bioengineering programme is to improve the quality of the nation's health by increasing biological knowledge and facilitating the development of novel devices and drugs and integrates physical, chemical, mathematical, and computational sciences and engineering principles to study biology, medicine, behaviour, and health. It advances fundamental concepts; creates knowledge from the molecular to the organ systems levels; and develops innovative biologics, materials, processes, implants, devices, and informatics approaches.

During the period, the department sanctioned 30 projects across various disciplines. On-going projects resulted in publication of research papers in high impact journals. Significant achievements are:

Tissue Engineering

Scientists at CMC, Vellore studied the efficacy of cultured autologous chondrocyte transplantation in the treatment of physal injury in goats. They have established a model for physal arrest in the upper medial tibia using autologous chondrocytes harvested from the iliac crests of the animals.

Scientist at SCTIMST, Trivandrum fabricated porous, biodegradable and non-cytotoxic tubular scaffolds of 2mm, 3mm, 4mm and 6 mm diameter and 8 cm length for construction of tissue-engineered small diameter vascular graft. All physico-chemical properties were found to be matching with that of the native blood vessel. Confocal microscopic analysis of the scaffold shows integration of endothelial cells into the scaffold

pores and deposition of collagen by cells on the scaffold. In order to address the potential early bacterial contamination of the construct during *in vitro tissue* engineering, scaffolds were incorporated with silver nano particles. The scaffold containing silver nano particles showed good antimicrobial effect as demonstrated by the zone of inhibition assay using *E.coli* and *S. aureus* microbial cultures.

Scientist at SCTIMST, Trivandrum bioengineered the cell sheet for corneal Tissue Engineering Limbal stem cell deficiency (LSCD). A polymeric formulation based on N- Isopropylacrylamide (NIPAAm) was co-polymerized with derivatives of methacrylate and subsequently coated on to the surface of Tissue culture polystyrene culture dishes. For ocular surface regeneration, Limbal Stem Cell Deficiency was created in rabbit models. Two transplantation experiments were successfully completed in rabbit with bioengineered limbal cell sheet.

Biomedical Sensor

Scientist at IIT, Mumbai studied co-immobilization in nanoengineered biopolymeric carriers as biosensors. The development of zero order release systems capable of delivering immunomodulating agents for successful performance of implantable "Smart-Tattoo" glucose sensors is under development. The results have shown that nanoengineered alginate microspheres show promise as release systems to improve biocompatibility and prolong lifetime of implantable "Smart-Tattoo" glucose sensors.

A study on 'Development of DNA biosensor for detection of *Neisseria gonorrhoeae* in clinical samples' was undertaken at the NPL, New Delhi

in collaboration with the AIIMS, New Delhi. They carried out immobilization of DNA onto electrochemically prepared polyaniline and polyaniline-carbon nanotubes. The studies carried out on clinical samples indicated that this electrode can detect presence of *N. gonorrhoeae* from culture and culture positive swab sample of patients. Those results also revealed that the electrode can distinguish presence of *N. gonorrhoeae* from other species like *N. meningitidis* and *E.coli*.

Studies at UDSC, New Delhi demonstrated DNA sequence detection for medical diagnostic using water soluble Cationic Conjugated polymers and PNA probes. The large difference between the emission intensities for complementary and non complementary ssDNA validates the technique for detection of the DNA sequence where it has been possible to take advantage of the optical amplification of the conjugated polymers to detect DNA hybridization.

Scientist at IIT, Delhi carried out studies for the development of low cost biosensor for rapid detection of pathogenic bacteria.

Implants

Scientist at SCTIMST, Thiruvananthapuram studied development and evaluation of surface modified, hydrogel coated medium & large diameter vascular graft.

Coating optimized to have a uniform surface coating on vascular graft. Hydrogel coating formulations are being developed that will provide adequate gelation time for uniform coating on the graft.

Scientist at NIPER, Punjab synthesized the modified biodegradable polymeric scaffolds for

soft tissues repair. Biomimetic porous scaffold of PLGA and PCL were prepared and evaluated for their degradation, cell attachment and cell growth (MG 63 cell line) using long term studies for 28 days.

Scientist at SCTIMST, Thiruvananthapuram studied use of novel biodegradable polymeric materials as functionally active cardiac implant. The studies on the interaction of cardiac cardiomyocyte cells with the present candidate hydrogel test material revealed appreciable cellular growth. Studies reveal that the present scaffold materials are more promising material for tissue engineering of cardiac tissue.

Scientist at IIT Guwahati, studied Electrospun nanofiber scaffolds for hepatic tissue engineering. In the initial phase of experiments, preparation of Chitosan-PEO nanofibers with the newly installed Electrospinning setup was performed. Subsequently, human hepato carcinoma cell line was cultured on the Chitosan-PEO nanofibers. The nanofibers were later functionalized with CDI linker chemistry. The cross linking of horse radish peroxidase on to the nanofibers was studied successfully.

In a search for novel biomaterials, IIT Guwahati found that fibroin from muga silkworm an excellent biomaterial with a potential for application in tissue engineering. The scaffold compatibility with blood and four different cell lines was also studied in great detail. Angiogenesis properties of the scaffolds established the ability of the scaffold to promote neo-vascularization.

Scientist at Amrita NANO Biomedical Engineering Institute, Cochin developed highly adherent nanostructures on Titanium surfaces

using hydrothermal processing. This is a novel processing technique using temperature and pressure and is also inexpensive and suitable for mass production. The protein adsorption studies revealed that the surface modified nanostructures on titanium adsorbed more proteins and are capable of promoting cell adhesion/attachment.

Biomaterials

Scientist at IIT, Chennai is studying production and biodegradation of curdlan as stent material. Fermentation and downstream process for producing curdlan using ATCC 31750 strain at a yield of 40 g/L was established. The process is being scaled up.

Scientist at IIT-Kanpur developed hybrid polymer-ceramic biocomposites using the tailored processing conditions on compression moulding machine. In vitro biocompatibility tests with L929 mouse fibroblast cells revealed good cell adhesion, cell-cell interaction and cellular bridge formation. Results indicate good cyto-compatibility of the newly developed biocomposite materials.

Medical Devices

Scientist at IIT Kharagpur studied “Biomechanical Analysis and Design of Orthopaedic Implants” and came up with development and application of adaptive bone remodelling algorithm to predict the long term behaviour of the implanted bone structures.

Scientist at IIT, Chennai studied “Design and Development of a Calibration-free Pulse Oximeter”. Theoretical derivations have been formulated to obtain three methods of computation of oxygen saturation. The first design of the analog front end of the circuit has been finalized and is in the PCB fabrication stage.

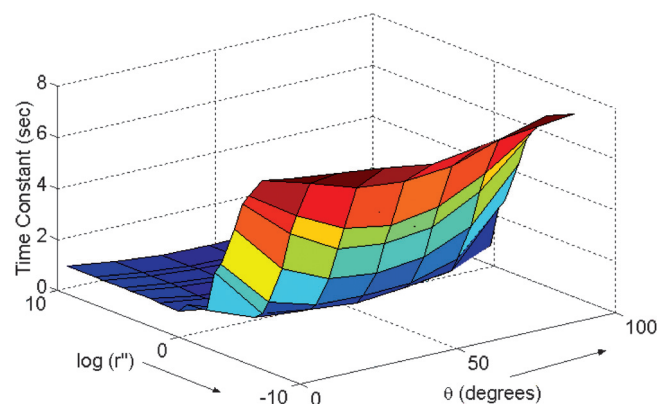
Scientist at Shriram Institute for Industrial Research, Delhi studied “Development of technology for manufacture of low cost diapers for new born infants”. Samples have been prepared for trial run at AIIMS.

Scientist at Christian Medical College, Vellore worked for making an implantable device to acquire and transmit one or two channels EMG. The implantable device will be placed subcutaneously and hermetically sealed. The radio link has been developed and EMG can be streamed to a PC connected to the external device.

Scientists at Central Mechanical Engineering Research Institute, Durgapur are developing Autonomous Intelligent Robotic Wheel Chair with specialized sensor technology & navigation algorithms

Bio-Instruments

Scientist at IIT, Kharagpur studied rapid DNA hybridization in microfluidic channels and established that electroosmotic flow in



Variation in time for attaining saturation in DNA Hybridization in a microchannel with patterned walls in presence of electric fields in vertical (y) and lateral (x) directions (In the figure r'' denotes the ratio of field strengths in vertical and lateral directions and θ is the angle of the pattern)

microchannels can be used as an extremely efficient means of transport and subsequent hybridization of incoming oligonucleotides. The hybridization time could be also lowered by simple modifications of the channel wall and the flow conditions.

A series of glucose specific molecularly imprinted polymer formulations were synthesized and characterized at SCTIMST, Trivandrum for monitoring the degree of binding of glucose onto the polymers. The data suggests that one could shape molecularly imprinted polymers for the selective detection of glucose from various media.

Scientist at NPL, New Delhi demonstrated on-line approach to non-contact IR sensor technique for estimation of sugars and its by-products. The use of mid infrared spectroscopy was explored as a tool to detect sugars and organic acid in packed fruit juices.

Scientist at KMC Life Science Centre, Manipal developed and standardized Raman tweezers, which allows the simultaneous trapping and recording of Raman spectra of single living cells under physiological conditions.

Stanford-India Biodesign Programme

The Department has taken new initiative to promote medical technology innovation in India in collaboration with the Stanford University, USA. "Stanford-India Biodesign (SIB) programme has been formulated as a collaborative venture of DBT, Indo-US S&T Forum and Stanford University, USA. The focus of the programme is on development of implants and medical devices. Identification of opportunities is done by

observation of patients by an interdisciplinary team and to select at least one new technology for designing and developing as a prototype.

The first SIB Centre in India has been established jointly at AIIMS and IIT, Delhi. The fellows of the Centre have been trained in the design innovation process by providing hands-on training at the Stanford University, USA for a period of seven months. The team has joined the SIB Centre at AIIMS and IIT, Delhi to start designing process and identifying clinical needs/challenges in India. They have identified more than 300 clinical needs and selected five of them to develop prototypes. The team has developed five preliminary prototypes under SIB programme.

Human Genetics & Genome Analysis

The Human Genetics & Genome Analysis programme was initiated in 1990-91 with an objective to identify, map and characterize genes associated with genetics disorders prevalent in India. It was planned to exploit the knowledge created by available human, microbial and parasitic genomic sequences to develop molecular medicine tools for better management of diseases and disorders. So far, twenty one genetic diagnosis cum counseling units have been established to provide patient services to the affected families for common genetic disorders. A large number tribal families have benefited from these units.

The programme was enlarged post-Human Genome Project focussing on technology development, computational analysis of genome sequences and disease-based sequencing analysis, making use of the established infrastructure at various institutions across. Major sequencing

projects were undertaken. The existing Bioinformatics network was strengthened by creating Genome Mirror Sites. Projects were initiated in the post-genome era based on the use of HGP data available in public domain. Salient achievements are:

- The programme on Sickle Cell Disease (SCD) in Chhattisgarh with special reference to morbidity pattern carried out by the Pt. J.N.M. Medical College, Raipur, collected patient's samples and provided diagnostic and counseling services to ~500 affected families. Counseling was done amongst the tribal community for prevention of the disease.
- The multi institutional project implemented at the V.S.S. Medical College, Burla; IGH, Rourkela and ILS, Bhubaneswar, Orissa, studied morbidity pattern in sickle cell disease in Western Orissa and its correlation with genetic factors, fetal hemoglobin concentration and other factors like malaria. The analysis showed that there are 2 cases of SCD associated with HbE and HbD, DNA sequencing was done in clinical cases and cases were confirmed for HbS mutations, HbE mutation & unclassified silent mutation.
- Studies carried out on the identification of Novel Gene(s) for Familial Parkinson's Disease at DUSC, New Delhi recruited 15 well-characterized multi-generation Parkinson's Disease families including both affected and unaffected members for linkage analysis. Whole genome scan using was carried out. Putative disease causing genes are being analysed using bioinformatic tools.
- A multi-centric project on "Development of Pharmacogenomics SNP database for critical

candidate genes involved in drug response for Schizophrenia" has been implemented at IGIB, AIIMS, New Delhi & NCBS, NIMHANS, Bangalore. Patient samples have been collected along with matched control and phenotype/genotype studies are on.

- In the studies carried out on "Molecular Genetics and Endophenotypes in psychoses" implemented at NIMHANS, Bangalore, protocols have been standardized for recording EEG and ERP. The results indicate that in the resting eyes closed state, the EEG of schizophrenia probands differ from unaffected sibling and healthy controls on all the absolute power bands. Siblings of index probands also differed from controls in several parameters. The data is being further analysed.
- In a study initiated on pathogen host interaction in Human Mycotic Keratitis at the AMRF & MKU, Madurai, 700 control tear samples and 250 fungal keratitis culture positive tear samples have been collected and being analyzed for *Fusarium* and *Aspergillus*

Post Genome Era Research

POST-HGP, projects on Microbial-functional, structural & comparative pharmacogenomics; Computational Genomics, Clinical proteomics and RNAi. have been initiated. DNA Micro-array facilities have been established at NBRC, Manesar and CDFD, Hyderabad to carry out studies on neurological and infectious diseases. The whole genome sequencing of *Mycobacterium w* was completed with a sequencing efficiency of 83.93% and total sequence coverage of 5.71 Mb. at DUSC, New Delhi and CDFD Hyderabad.

India's participation in the International Cancer Genome Consortium (ICGC)

The International Cancer Genome Consortium (ICGC) has been launched in November, 2008 with commitments of eight countries i.e. India, Australia, Canada, China, France, Japan, Spain and United Kingdom with the support eleven funding organizations to generate comprehensive, high-resolution analyses of genomic changes for eight forms of cancer. ICGC is based on the International Cancer Genome Atlas programme implemented by National Cancer Institute, USA. It will help to coordinate current and future large-scale projects to understand the genomic changes involved in cancer. This genomic information will accelerate efforts to develop better ways of diagnosing, treating and preventing many types of cancer.

Each organization will be coordinating studies of at least one specific type or subtype of cancer, with each project expected to involve specimens from approximately 500 patients. ICGC projects will use common standards of data collection and analysis as proposed in the ICGC Goals, Structure, Policies and Guidelines released in April 2008. Over the next decade, additional nations and organizations are expected to join the ICGC so that up to 50 types of cancer will be thoroughly studied.

Environmental Biotechnology

The goal of environmental biotechnology is to provide cost-effective and quality monitoring technologies, eco-restoration of degraded habitats, conversion of toxic recalcitrant chemicals into harmless by-products, bioremediation of polluted

sites/degraded ecosystems, technologies for the treatment of wastes, production of value-added products from waste/biomass, control of biological invasion through biotechnological interventions, greener process technologies, and effective *ex-situ* conservation strategies. The thrust areas are Bioremediation, Biodegradation of Xenobiotics, Biodegradable plastics/Biopolymers, Biosensors/Bioindicators, Industrial Waste Treatment, Biodiversity Conservation and Bio-energy from Waste. Salient achievements are:

- A comprehensive National Action Plan on Climate change: using "Mitigation technologies" has been prepared and pre/concept proposals invited. Out of 234 concept proposals received, 44 have been screened-in for submission of full proposals.
- A network program of twelve projects has been funded in the area of Biopolymers/Biodegradable plastics ;
- Eleven projects on Environmental Metagenomics to explore the polluted sites for value added products have been funded.

A New Model for Programme generation has been adopted: Six subject-area based scientists have been identified as co-ordinating officers to receive pre/concept proposals and screen/examine them with the help of Expert Committee constituted by DBT, in already identified thrust areas.

Partnership program with the industry: Pilot plant for the production of Oil Zapper has been established at TERI, Gual Pahari at a cost of Rs. 5.8 crores jointly by a group of Petroleum oil companies, DBT and TERI, New Delhi.

List of Technologies Transferred

Four technologies have been demonstrated/transferred/ commercialized

- (i) *Poultry waste treatment with biogas production developed by ANGRAU and IICT, Hyderabad*
- (ii) *Odour (Sulphurous odorants) removal from the Pulp and Paper Industries developed by NEERI, Nagpur*
- (iii) *Oil Zapper – Bioremediation of polluted sites by Petroleum Industries/Installations using Oil Zapper technology developed by TERI, New Delhi successfully transferred to a group of Petroleum Companies (ONGC, IOC, HP and BP)*
- (iv) *Pulp and Paper mill waste treatment technology developed by IGIB, Delhi.*

Legislation/Policies developed: Guidelines for bioremediation of oil contaminated sites, oil contaminated water, oily sludge pits, crude oil sludge and oil contaminated drill cuttings etc. have been prepared and sent to the Ministry of Environment & Forests for approval.

CLIMATE CHANGE

Carbon Sequestration

• **Using Plants/Trees:** A study showed that natural forest of Tadoba Andhari Tiger Reserve (TATR) has highest carbon, followed by afforested and agricultural site. Soil organic carbon accumulated in reclaimed land showed nearly 60% of forest carbon content in 20 years as compared to 100 years of natural forest. The results help the industries to get CDM activity for afforestation of degraded lands as suggested by the guidelines of the United Nations Framework Convention on Climate Change (UNFCCC).

• **Using Microorganisms:** In a study on carbon represented by micro-organisms, the most significant achievement has been the successful

conversion of CO₂ into calcium carbonate using Carbonic anhydrase (CA) from indigenous bacterial isolates (*Micrococcus lylae*, *Micrococcus luteus* 2, and *Pseudomonas fragi*). The time taken for precipitation with crude enzyme of the three isolates was determined approximately 18.6 seconds whereas with pure Bovine CA the reported time is 15 seconds. Proof of concept has been established for carbonation reaction. Feasibility studies on laboratory scale bioreactor for CO₂ sequestration through immobilized carbonic anhydrase enzyme/organism is being carried out.

Bioremediation

Pseudomonas sp. Strain Chl D, one of the five strains isolated by enrichment on chlorpyrifos, has dual ability to produce rhamnolipid based biosurfactant and to degrade chlorpyrifos. This strain, under optimized conditions, was shown to degrade 91% of chlorpyrifos (0.1 g/L) in 7 days.

Ceratophyllum demersum, *H. verticillata*, *Nicotiana tabacum* and *V. faba* have been found to be significant bioaccumulator of heavy metals (Cd,

Pb, Ni) and metalloid (As). Tobacco plants have been transformed with PC synthase. The transgenic plants showed 3.5, 4 and 8 fold bioaccumulation upon exposure to 50, 5 and 100 μ M Cadmium, Arsenite (As^{III}) and arsenate (As^{V}) exposure as compare to wild type with no phytotoxicity.

Biodegradable plastics/Biopolymers

The waste biological sludge generated at wastewater treatment plant is characterized and successfully used for the production of PHB. In an aim to select indigenous PHA producing bacterial strains from crude oil contaminated sites, it was noted that 42 strains out of 262 showed PHA accumulation, out of which 6 strains were novel. One species gave 56% of PHA accumulation on dry weigh basis and PHA quality was medium chain length polymer which is desirable.

Biosensors/Bioindicators

A study aimed at the development of a single tube multiplex PCR method to detect and differentiate five most important diarrhea causing pathogens; *E. histolytica*, *G. lamblia*, *Salmonella spp.*, Hepatitis A and E virus directly from the drinking water. The triplex PCR assay for the detection of *E. histolytica*, *G. lamblia*, and *Salmonella spp* achieved sensitivity and specificity of 100%.

Industrial Waste Treatment

A process for bench scale biological deodorization of emissions generated from pulp and paper industries has been developed and techniques for

monitoring of sulphurous odorant standardized. Five potential cultures for degradation of main odorant Dimethyl Sulphide (DMS) present in pulp and paper emission isolated with good performance.

Two marine derived besidiomycetous and ascomycetous fungi have been isolated for decolorization and detoxification of textile effluents. Microbial induced corrosion causes huge economical losses to the oil and gas sector. For this purpose, biocides from natural sources were screened to determine their effect upon a biofilm generating bacterial consortium. Two fungal strains identified as *Cryptococcus albidus* and *Emmericella nidulans* have been tested for removal of colour and lignin and process parameters are optimized. *Cryptococcus albidus* produced maximum laccase. The result of a study indicated an increase of 1.5 fold production of ethanol. The method was tested in 15 liter sequential bioreactor in which sugar cane baggase was initially degraded by fungus and subsequently fermented by yeast for production of ethanol for scale up of the method for production of bioethanol.

Biodiversity Conservation

The programme essentially targets on delisting the selected threatened species from the red-listed category by reintroducing them in sufficient numbers to their natural habitat. A systematic, multi-institutional attempt towards the recovery of a critically endangered tree species of fresh water swamps of the Western Ghats has been initiated. *Semecarpus kathalekanesis* has been prioritized as 'sink population' for setting up Forest Gene Bank. Over 6000 plants have been

