CENTRE FOR BIOSEPARATION TECHNOLOGY (CBST)

About Us

The Advanced Centre for BioSeparation Technology (CBST) is dedicated to the field of separation sciences and molecular interactions. It has a unique combination of being innovative and highly intellectual with keen interest in translation. This has been built as a policy and scientific culture.

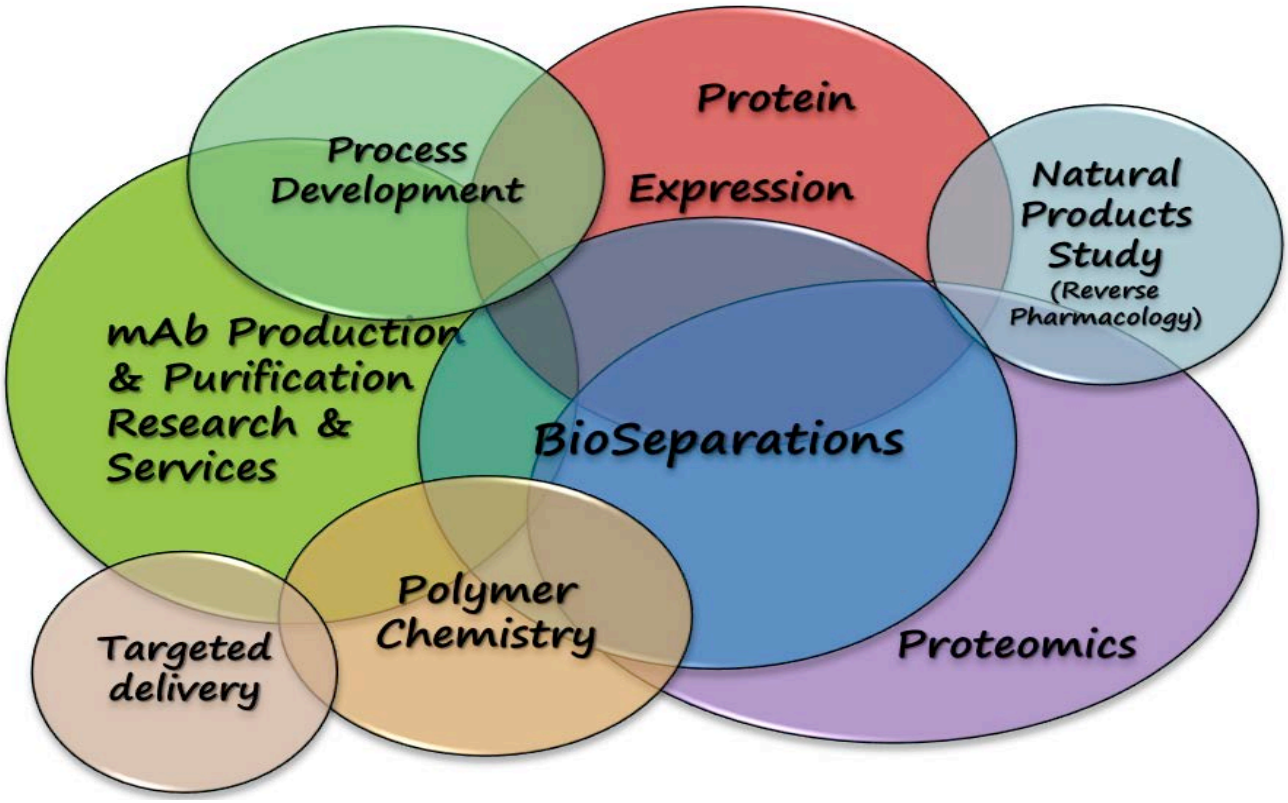
This innovative research with high intellectual input has resulted in development of very original and simplified systems for both analytical and preparative aspects of proteins. These methods are complimentary/competitive to conventional ones in efficiency and are being adopted by the industries both in India and abroad. This has made an important contribution for India both scientific and technological aspects to face the global challenges, resulting in products produced by Indian Industries contributing to its growth. This culture is successfully transferred to youngsters in India, in bringing a paradigm shift in the young researchers shaped at CBST.

The Centre for BioSeparation Technology (CBST) was created under the "Intensification of Research in High Priority Areas" programme funded by the **Department of Sciences and Technology (DST**), Government of India.**Prof. M.A. Vijaylakshmi,** having been identified for her expertise in the field of Purification Science and Technology was invited from France to set up the Centre in India with a host structure of her choice to help our country in developing this important area, much required for Industry-Academia in R&D. She chose VIT, Vellore as the host structure to initiate the Centre and, CBST was formed in the year 2005. The centre is projected by DST as a 'National Facility' for research & development.

Monitored by a steering committee composed of eminent scientists and top members of VIT University. The Centre developed to new heights and in May 2009, the Centre went through an independent "Performance Audit" by a committee headed by the President of Indian National Science Academy (ISA) and was recommended for up-gradation to an "Advanced Centre" with continued funding to maintain it's high level potential and expertise research activities.

CBST, along with it's initial facilities, currently features Chromatographic work stations (FPLC, HPLC, and four manual chromatographic workstations), Proteomic workstations such as Mass Spectrometer (QTOF &Triple Quadrapole ESI LC-MS), mammalian cell culture work, monoclonal antibody production, recombinant protein expression (comprising mammalian, yeast, bacteria and lemna expression systems). Renowned for it's world-class innovative research and intensive training, CBST approaches research with multidisciplinary links involving state of the art-technologies focusing mainly on translational aspects.

CBST practices and has a set up of “Approach research with a high level of multidisciplinary links”. CBST is one of the rare Centres where the coexisting relation of Chemistry-Biology is realized and projects are done and made with this cross-talk relationship of different fields of Chemistry & Biology.



The Centre revolves around multidisciplinary themes involving BioSeparation or the ‘Science of Purification’ as its major arm connecting various disciplines. Linked together by Purification Science & Proteomics, the Centres moves the rest of the areas forward in to the area of translational research work paving path to success and development.

Our Collaborators

utc Université de Technologie Compiègne
université de BORDEAUX
C-CAMP
Agilent Technologies
arkray
BIA separations
Biocon
SPAN DIAGNOSTICS Ltd.
PALL Life Sciences
CNU 충남대학교 CHUNGNAM NATIONAL UNIVERSITY
laila Pharma
In Ventures
INTAS Biopharmaceuticals
SHANTHA A SANOFI COMPANY
GNG

Chromatography& Proteomics

Faculty In-Charge: Prof. Vijayalakshmi M.A, E-mail: indviji@yahoo.com

The Separation Science and Technology field is the central axis of the Centre. It is being developed both as a science to understand the molecular recognition and also as a technology to be exploited for (i) Efficient product recovery; (ii) Development of studies on protein-protein, protein-DNA and protein-ligand interactions; and (iii) As an exclusive tool for proteomics approaches.

- Pseudobiospecific chromatogprahy for recovery ofhigh added value plasma proteins and recombinant proteins.
- Affinity traps - upstream and downstream in LC-MS approach: Applications demonstrated include for plasma proteins, PPD for tuberculosis, microbial fermentation broth.
- Chromatographic stationary phase development through ultra high performance technology using connective interaction media (CIM) supports with all possible chemistries.
- BIA platform of excellence setup at CBST (BIA-PEC) with the BIA separations, a multinational company with its HQ in Austria.

Patent:

Purification of Factor VIII from Different

Sources using Monolith-based Pseudo-Bioaffinity Chromatography.

Inventors: V.N. Janakiraman, R.R. Prasanna,

A.S. Kamalanthan, M.A. Vijayalakshmi

Patent Application No. 5018/CHE/2012; PCT - USA and Europe

Microfluidics devices as affinity based biomolecule separation tools

Faculty In-Charge: Dr. Kali Kishore Reddy TetalaE-mail:kishore.tetala@gmail.com

Microfluidic devices are emerging as potential analytical tools for biomolecule sample pretreatment and screening from complex biological mixtures (serum, milk etc.). They offer several advantages like e.g. requirement of small sample volumes ($10^{-9}$to 10^{-18} L volume), multiplexing of micro channels in a single chip, rapid separation and reliable on-chip analysis.

- Development of a conjoint Immobilized Metal-ion Affinity (IMA) microfluidic device as a pre-fractionation tool for proteomics prior to MS analysis.
- IMA microfluidic system to probe proteins at both molecular and cellular levels.

Highlights of the work:

1. A new polymer material with highly interconnected porous network, hydrophilic and rigid.
2. Polymer material was successfully polymerized within a glass capillary (~ 1 mm inner diameter & 5.5 cm long; 35 µL total volume).
3. A new method to immobilize secondary amine functional ligands (in this case, iminodiacetic acid) on aldehyde functional polymer material was done.

Bioinformatics and chromatography

Faculty In-Charge: Prof. Vijayalakshmi M.AE-mail: indviji@yahoo.com

Pseudobiospecific ligand l-histidine is an inexpensive, highly stable, non-toxic ligand explored successfully over the last twenty years for the purification of immunoglobulins in immobilized histidine ligand affinity chromatography. It is of great interest to know the molecular recognition sites of IgG to immobilized l-histidine.

- We have used an in silico approach to explore the molecular recognition of l-histidine by IgG.
- We have assessed the feasible binding modes of histidine and its moieties at different sites of IgG and considered only those binding conformations which are exhibited via the imidazole ring NH group or any other OH donating group apart from the ones which are terminally conjugated with the support matrix.
- We categorized binding site into two categories; category I: inner binding groove and category II: surface binding groove and observed that the hinge region of IgG has most favourable binding pocket for L-Histidine and histidyl moieties.
- Serine and tyrosine residues on the hinge region make several significant interactions with L-Histidine and histidyl moieties, as hypothesized by Prof. Vijayalakshmi, the Hydrogen bond interactions making it a Hydrophobic interaction chromatography.

Autoimmune Disorder Studies

Faculty In-Charge: Dr. Kamalanathan ASE-Mail: kamalanathan_as@yahoo.com;

Autoimmune diseases are a condition in which the immune system attacks normal, healthy tissues resulting in structural and functional damage to the host. The initiation and perpetuation of diseases is unclear and they are investigated in multi-dimensional approaches.At CBST research are conducted to understand the pathobiology of the autoimmune diseases at molecular and cellular levels. Focus of our research activity is on characterization of the anti-immune antibodies or anti-idiotypic antibodies and understanding of their role(s) in autoimmune pathologies. In the past, we have worked on anti-phospholipid syndrome (APS) antibodies, systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) diseases.

At present we are working on following -

- Rheumatoid arthritis: Understanding the molecular features of the molecules involved in the inflammation or triggered due to inflammation and their consequences.
- Neuro-immunology diseases: Here we are working on the Major Psychoses disorder wherein, study is carried out to understand the dysregulation of the immune system and, if any, connectivity to the autoimmune disorder conditions.
- Inflammatory diseases: Neuro-inflammatory conditions and inflammatory conditions of eyes and their autoimmunity studies are under discussion and preparation for a future project work with associated partners.

High Value added proteins: expression, purification & validation

Faculty In-Charge: Prof. Krishnan VenkataramanE-Mail: bmkrishna1@yahoo.com

Recombinant Therapeutic Proteins:The Centre is developing Recombinant Therapeutic proteins of very high value with a "Gene to Vial" concept. This implies the gene construction, expression, optimization of the expression systems, purification, characterization and product formulation. Three important proteins with high value were chosen. They are anti- TNF α, single chain variable fragment (ScFv), functional Factor VIII and ApoA1.

- Functional coagulation Factor VIII (FVIII) expression has been done both in CHO and in glycol-engineered strain of Yeast (Pichia pastoris).
- Expression and purification of anti-TNF single chain variable fragments and increasing its avidity using Chemical dimerisation studies.
- Expression of anti TNF- α-ScFv in plants: Spirodela punctate or Lemna with invitro culture, growth & Expression of Lemna.
- Generation of wild type and variants of ApoA1 with studies on protection for Cardiovascular diseases with reduced effect of oxidation.

Diagnostically important proteins:We are also developing recombinant proteins that can be used in the field of Medical Diagnosis to detect diseases which would normally be very difficult to diagnose.

- Truncated HRP 2 against *Plasmodium falciparum* for detection of Malaria.
- Recombinant HRP 3 for detection of *Plasmodium falciparum.*
- Recombinant Brucella porin for detection of Brucellosis in humans and animals.
- Recombinant Salmonella porin for detection of Salmonella in humans and animals.

Patents:

Methods or producing recombinant Factor VIII chains from non-filamentous fungi, their functional reconstitution and applications there of.
Inventors: V.N. Janakiraman, A.R. Sudheer Reddy, P.K. Sateesh Kumar, V. Krishnan, S.C. Nair, A. Srivastava, M.A. Vijayalakshmi. Patent Application No. 3777/CHE/2012; PCT – USA and Europe

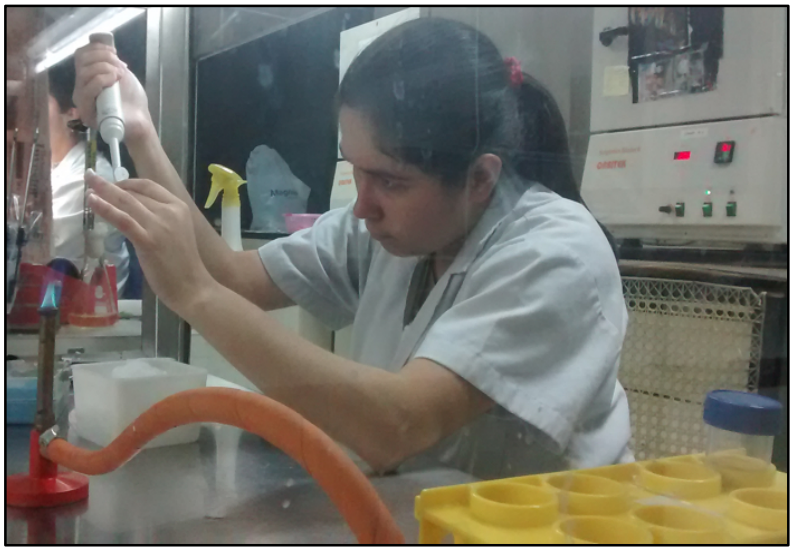
Double mutant coagulation Factor VIII methods and there of.
Inventors: B.C. Joseph, P.K. Satheeshkumar, M.A. Vijayalakshmi.
Indian Patent Application No. 3778/CHE/2012; PCT – USA and Europe

Chemical Dimerization studies: Anti-TNF- α ScFv

Faculty In-Charge: Dr. Sanjit KumarE-Mail: sanjitkrroy@gmail.com

Tumor Necrosis Factor (TNF) is one of the cytokines secreted by macrophages and TH cells in response to infections. Tumor Necrosis Factor (TNF) is secreted by macrophage and T cells in response to infection. TNF -α appeared to be highly potent in pro-inflammatory responses. However, persistent higher concentrations of TNF-α has been associated with human pathology for example, Rheumatoid arthritis, psoriasis, Crohn's disease, Ankylosing spondylitis. In order to treat autoimmune pathogenesis monoclonal antibodies have been proved to be useful. Monoclonal antibodies are produced from a single clone that can bind only to a unique epitope on an antigen. However, use of monoclonal antibodies in an extensive way has been restricted by factors such as; expensive production, longer blood penetration time. To overcome drawbacks of therapeutic monoclonal antibodies, recombinant single chain variable fragments (ScFv) are in demand

- Our objective is to increase avidity of anti-TNF-α ScFv molecule by dimerization.
- This would be achieved by chemical oriented single point site directed mutagenesis.
- Dimerization of two ScFv molecules will be carried out by bifunctional PEG maleimide.



Monoclonal antibody production

Faculty In-Charge: Dr. Jayaprakash N.S;E-Mail: nsjayaprakash@yahoo.co.in

We target monoclonal antibodies for their applications for diagnostics. CBST has produced and is producing mAbs against various proteins of diagnostic interests. Some of the work includes,

- Monoclonal antibodies highly specific to *Plasmodium falciparum* have been developed.
- Anti Human Serum Albumin monoclonal antibodies (Anti-HSA monoclonal antibodies) for depletion of HSA in proteomic studies.
- Antibodies against porin-protein of *Brucella* sp. and *Salmonella* sp. for specific detection of brucellosis and enteric fever & typhoid, respectively.
- Antibody against chlorinated ApoA1 (HDL) for early detection of Cardio vascular diseases.

Patent:

Monoclonal antibodies against Plasmodium and uses thereof.
Indian Application No: 1137/CHE/2014.
Reena Verma, Jayaprakash N.S, Vijayalakshmi M.A, Krishnan Venkataraman.

Super macroporus Cryogel for monoclonal antibody production

Faculty In-Charge: Dr. Jayaprakash N.S;E-Mail: nsjayaprakash@yahoo.com

CBST is developing a mini-bioreactor module with a new super macro porous cryogel matrix for continuous production of monoclonal antibodies, which produces nine times more antibodies than T-flask batch method. This work was adapted from the initial work of Prof. Ashok Kumar, IIT Kanpur.

Natural Products & Diabetes

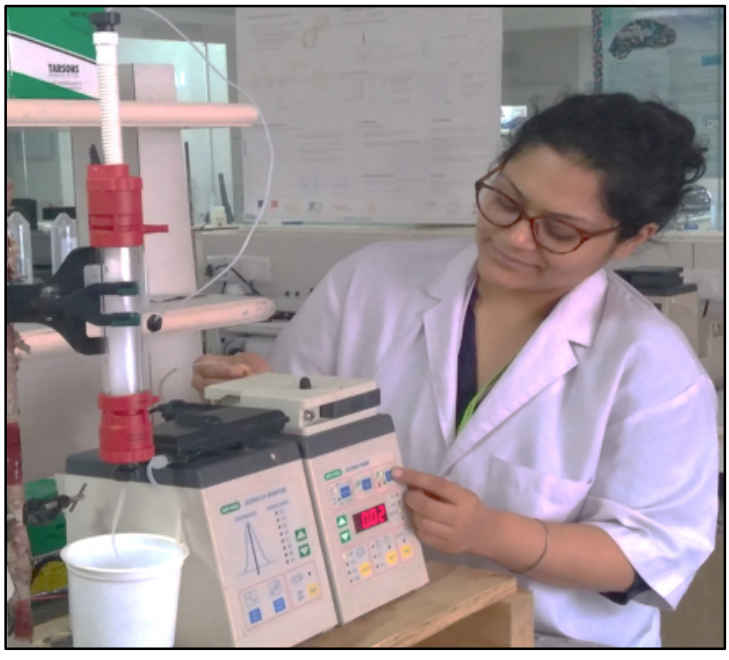
Faculty In-Charge: Dr. Ayesha NoorE-Mail: ayeshanoor17@yahoo.co.in

We are engaged in product development from Natural sources such as indigenous medicinal plants. Main focus is on developing Neutraceuticals with good understanding of the mechanism(s) involved in alleviating the pathology. The Centre has already marked its success in a project using *Aloe vera* as a supplement for alleviating Diabetes.

- In-vivo studies performed in streptozotocin induced diabetic rats with the *Aloe vera* extract.
- Extract was validated as per 'AYUSH' (regulatory structure for alternative medicine systems) guidelines.
- Human clinical trial in safety and efficacy evaluation has been carried out in collaboration with Laila Pharmaceuticals, Vijayawada.
- Understanding the molecular mechanisms of regeneration is underway and single molecule identified which is involved in one of the regeneration pathways.

Patent:

Pyrole derivative as hypoglycemic agent.
Application no.: TEMP/E-1/26750/2015-CHE
Prasanna Raja, A.S Kamalanathan, Krishnan Venkataraman and M.A. Vijayalakshmi.



Targeted Drug Delivery

Faculty In-Charge: Dr. Kali Kishore Reddy TetalaE-Mail: kishore.tetala@gmail.com

Polymer chemistry has played an important role in the synthesis, derivation, degradation, application and evaluation of biocompatible and biodegradable polymers, which can be used as drug delivery systems. Many of the pharmacological properties of conventional free drugs can be improved through the use of polymeric drug delivery system.

- Poly (ethylene oxide) [PEO]: non toxic, ion-transporting ability, water solubility, and non recognition by immune system. A potential polymeric delivery system.
- Bouquet structure of PEO with two ends: One holding target agent and the other holding a functional compound at the other extremities.
- Plant based anti cancerous agent: Lupeol, extraction, identification and purification from Aloe vera. Stabilization and targeted delivery of Lupeol using PEO dendrimers.

Patents:

Dendrimers conjugates and methods there of.

Inventors: J. John, Y. Gnanou, V. Kari, M.A. Vijayalakshmi. Indian Patent Application No. 3797/CHE/2012 filed on 13 Sept 2012. PCT (Ref. PCT/IB2013/058534) filed on 13 Sept 2013.National phase application made in USA.

Services Platform

- Mass spectrometry sample analysis: With two different types of Mass Spectrometer available, CBST encourages sample analysis to be performed for VIT residents and outsiders.
  Triple Quadrapole ESI LC-MS & QTOF Faculty In-charge: Dr. V. Sabareesh, Assistant Prof., CBST. Contact No: 9487233686. E-Mail ID: sabareesh6@gmail.com
- BIACORE 3000 SPR: Using Surface Plasmon Resonance, it is possible to calculate the binding affinity such as protein-protein interactions.
  Faculty In-charge: Dr. Jayaprakash NS, Associate Prof., CBST. Contact No: 9486436377. E-Mail ID: nsjayaprakash@yahoo.co.in
- Both monoclonal antibody and polyclonal antibody production in mice and rabbits respectively, are rendered for antibody production with a defined collaboration. We have collaborated with Karnatak University, Dharwad for producing both monoclonal and polyclonal antibodies against fungal lectin protein and now currently a collaborative work between SPAN SARL, France and CBST, India is underway for production of Monoclonal antibodies against a malarial protein.
  Faculty In-charge: Dr. Jayaprakash NS, Associate Prof., CBST. Contact No: 9486436377. E-Mail ID: nsjayaprakash@yahoo.com

- Purification experiments are designed at lab-scale and scale-up advising is also performed.
  Faculty In-charge: Prof. Vijayalakshmi M.A, Director, CBST. Ph: 0416-220-2375/220-2374. E-mail: indviji@yahoo.com
- Molecular biology service platforms are also available at CBST.
  Faculty In-charge: Prof. Krishnan Venkataraman, CBST. Contact No: 9400241204. E-Mail ID: bmkrishna1@yahoo.com

KEY HIGHLIGHTS

Indo-French Collaborative project

CBST, VIT University is the primary member of an Indo-French consortium consisting of one academia & one industry partner from each side, which has been granted a project jointly funded by CEFIPRA & BIRAC. This project, titled "Oxidized HDL-Apo lipoprotein A1 as a risk predictor of cardiovascular disorders and development of novel diagnostics" will work towards development of a novel diagnostic kit that could help in the rapid diagnosis & prognostics of cardiovascular disorders. The other partners in this consortium are GeNext Genomic Pvt Ltd, Nagpur, India, ENSTBB, Université de Bordeaux, France, and Span Diagnostics SARL, Compiègne, France. The basic foundation for this project was based on preliminary work done at CBST, VIT University, which led to the formation of this consortium leading to a project.

CBST's spinoff awarded Biotechnology Ignition Grant (BIG) from BIRAC, Govt. of India

CBST's project on purifying coagulation factor VIII from various sources was patented with PCT (PCT/IB2013/058449) with the objective of making affordable haemophilia treatment available to India. This attracted the attention of a few investors, who came forward to license this work for further industrial development. Subsequently, the student Mr. Vignesh Janakiraman, who worked on the project created a start-up (Regd. Office at Ahmadabad, Gujarat), and was awarded the Biotechnology Ignition Grant (BIG) from the Biotechnology Industry Research Assistance Council (BIRAC), A Govt. of India Enterprise. This company has signed a developmental license agreement with CBST to work towards realizing the first prototype, under the scientific mentorship of Prof. Vijayalakshmi.

CEFIPRA-funded project on psychosis disorders

Dr. Kamalanathan of CBST, VIT University is part of a collaborative project titled "Immunogenetic and Immuno-phentoype characterization of Major Psychosis: Characterization of Antibodies from Major Psychosis patients sera", focusing on the study of antibodies in psychosis disorders like Schizophrenia and Bipolar Disorders. This CEFIPRA-funded research project is a collaborative project with Dr. Ryad Tamouza, Hôpital St Louis, Paris, France and Dr. V.S. Negi, JIPEMER, Pondicherry.

CBST – KAUST Project

CBST in collaboration with KAUST (King Abdullah University of Science and Technology, Saudi Arabia) is involved in the study of a PEO Polymer based drug delivery system. This project is done under collaborative effort between Prof. M.A. Vijayalakshmi (CBST), Dr. Kali Kishore Reddy Tetala (CBST) and Prof. Yves Gnanou (KAUST).

Inter-institutional collaborative projects

- Department of Science & Technology project entitled 'Engineering of beta-glucosidases for improved yield of glycoconjugates' in collaboration with IIT Delhi

- Production of anti TNF-α using different expression systems for cost effectiveness. Collaboration with M.S. University of Baroda. Project under the DBT Programme Support on Improved Production and Processing of Therapeutic Proteins.

- Cost effective production of recombinant human coagulation factor VIII (F-VIII). Collaboration with Christian Medical College (CMC), Vellore. Project under the DBT Programme Support on Improved Production and Processing of Therapeutic Proteins

- Bio-TIFAC, Govt. of India, New Delhi. Development of novel process in isolating standardized extract of *Aloe vera* and its application for diabetes control. Bioprocess and Bioproducts Programme

- PALL Life Sciences, Europe. Study and evaluation of new chromatographic supports

- IIT Kanpur. Development of cryogel based bioreactor for monoclonal antibody production

- Dharwad University, Dharwad. Production of polyclonal and monoclonal antibodies Jiwaji University, Gwalior. Production of monoclonal and polyclonal antibodies to Mycobacterium antigens

- KanchiKamakoti CHILDS Trust Hospital, Chennai

- Central Institute of Brackishwater Aquaculture, Chennai

- National Institute for Research in Tuberculosis, Chennai.

Faculty

Prof. M. A. Vijayalakshmi , Ph.D., D.Sc (France)
Founder Director

Dr. Krishnan. V
Professor & Director

Dr. Jayaprakash. N. S
Associate Professor

Dr. Ayesha Noor
Assistant Professor (Sr)

Dr. Kamalanathan. A. S
Assistant Professor (Sr)

Dr. Priyankar Sen
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