REGIONAL CENTRE FOR BIOTECHNOLOGY

an Institution of education, training and research

(Established by the Dept. of Biotechnology, Govt of India under the auspices of UNESCO)

Annual Report

2010-2011

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Preamble

During the period under report the Regional Centre for Biotechnology underwent different phases of growth. Starting from the a small component of DBT Cell nurtured by the National Institute of Immunology, New Delhi, today it has started functioning as a real autonomous institute having its own infrastructure, administrative machinery and has established its interim laboratories at 180, Udyog Vihar, Phase-I, Gurgaon during the period.

Regional Centre having the futuristic vision of making biotechnology education, training and research is planned to be within Biotech Science yet broad-based and multi-disciplinary. The proposed research and educational activities of the Centre are focussed to be at the interface of disciplines. Indeed the period under report was mainly devoted to establishing the labs and creating infrastructure for research and education activities. While attempts are being made to establish a wide range of disciplines that include Biomedical Sciences, Bioengineering, Biochemical and Biophysical Sciences, Climate Science, Agriculture and Environment, and Biotechnology Regulatory Affairs, IPR and Policy; a small beginning largely in the area of biomedical sciences has been made with the faculty members recruited during past year.

The structural biology studies of regulatory events in physiological processes focussed on immune recognition in the context of antibody pluripotency and structural and molecular bases in host-pathogen interactions. These studies have led to the elucidation of the structural basis of mimicry of two chemically distinct molecules as seen by the immune system. This shows that plasticity of antigen combining site of the mature antibodies could enable pluripotency even with out any structural correlation of the binding antigens. Structural investigations of proteins implicated in pilus assembly and biofilm formation of different bacteria toward understanding bacterial infections and mode of interactions with host are also being pursued.

The molecular mechanisms associated with cell division and intercellular communications including studies on the spindle assembly checkpoint in metaphase, the terminal mitotic process of cytokinesis as well as analyses of the biogenesis and function of tunnelling nanotubes (TNTs) are being studied. Molecular mechanisms in the ubiquitin mediated signalling in cellular pathways with focuss being on the deubiquitination events are being explored. Molecular mechanisms of infectious and idiopathic inflammation relating to SUMOylation are being studied using S Typhi as a model organism.

Molecular mechanisms of how intravascular hemolysis increases the severity and occurrence of the thrombotic complications in hemolytic disorders; more specifically, how the binding of cell-free hemoglobin to the plasma protein von Willebrand factor makes them hyperreactive to culminate cell adhesion and clot formation is being addressed. On another front, that links more to the translational research, engineering of nonmaterial for biomedical applications is being pursued.

Presently faculty members including the International adjunct faculty member and the Executive Director have begun functioning their laboratories in the interim premises. Recruitment processes is still continuing and we are hoping that we should be able to attract interesting combination of faculty members. We are indeed able to attract very smart fresh PhDs for young investigator programme. We have also started the training of students towards PhD degree. The Young Investigator awardee, the

Research Associates, Junior Research Fellows and Trainees programmes have made a beginning, and during the forthcoming year we should be able to get them grow.

The year started effectively with one personnel. It is gratifying that now most of the administrative and support personnel have been appointed. More than half dozen faculty members, several young investigators and students are now actively working. Administrative and financial processes have been established for institute to function independently.

Dinakar M. Salunke
Executive Director

Mandate of the Centre

Mandate of the Centre is to provide a platform for biotechnology education, training and research at the interface of multiple disciplines. The programmes of the Centre will be designed to create opportunities for students to engage in multi-disciplinary research where they learn biotech science while integrating engineering, medicine and science, to provide solutions for human and animal health, agriculture and environmental technologies.

The mission of the Centre is to create opportunities for multi-disciplinary education, training and research in biotechnology. The vision is to produce human resource tailored to drive innovation in biotechnology, particularly in areas of new opportunities and also to fill talent gap in deficient areas.

The Centre shall be an institution of international importance for biotechnology education, training and research (and shall, in due course, be constituted as an autonomous body under an Act of the Parliament). The Centre will also be regarded as a "Category II Centre" in terms of "the principles and guidelines for the establishment and functioning of UNESCO Institutes and Centres".

The Centre functions with following objectives:

- To produce human resource through education and training in a milieu of research and development for application of biotechnology for sustainable development towards building a strong biotech industry through regional and international co-operation with emphasis on novel interdisciplinary education and training programmes, currently not available in the country.
- To develop research programmes of a global quality through international partnerships.
- To establish technology policy development and information dissemination activities.
- To establish desired infrastructure and technology platforms to support above mentioned activities.
- To enable periodic experimentation in design and implementation of biotechnology education and training and to be a source of new concepts and programmes.
- To create a hub of biotechnology expertise in South Asian Association of Regional Co–operation (SAARC) region, and more generally in the Asian region and to address human resource needs.
- To promote and strengthen South-South & South-North co-operations around issues relevant to biotech education, training, innovation, commercialization and trade; and
- To promote a network of satellite centres in these sub-regions.

Scientific Reports

Structural biology of regulatory events in physiological processes

Principal Investigator: Dinakar M Salunke

Young Investigators: Jasmita Gill
Alka Dwivedi
Ashima Bagaria

Junior Research Fellows: Abha Jain
Anamika Singh

The theme of research is to study the structural aspects of molecular recognition and its applications in analyzing the mechanisms associated with specific regulatory events and in rational molecular design. The specific objectives of the projects are: i) to analyze the structural principles of immune recognition in the context of antibody pluripotency, ii) to determine structural and molecular bases in host-pathogen interactions and iii) to study structural proteomics of food allergens.

In order to comprehend the structural basis of molecular mimicry of two chemically distinct molecules, a peptide and a sugar in humoral immune response which was earlier established (Kaur *et al* (1997) *J Biol Chem* 272:5539; Goel *et al* (2004) *J Immunol* 173:7358), an antibody scFv 2D10 was constructed, expressed in bacterial system and the functional protein was retrieved from the inclusion bodies by refolding. The structures of scFv 2D10, in antigen-free state, bound to peptide and sugar antigen were determined. The three structures were superimposed showing no difference in antibody structure. Further investigations of the scFv and antigen interaction at the molecular level, it was evident that though the binding sites of the sugar and the peptide antigens overlapped substantially, they do seem to bind to the antibody employing mostly unique interactions. Secondly, scFv showed plasticity in antigen binding.

Based on a wide-ranging structural data on antigen recognition, it is evident that specificity of antigen recognition requires being refined from what used to be a situation, which is essentially described in terms of complementarity of shape and charge. It is quite evident from the example above that there is certain level of plasticity associated with the specific antigen recognition by the antibody even without conformational changes. A molecular dynamics approach has been initiated to analyse the core structural properties of the antibody paratopes for antigen recognition and delineate if these properties are linked to the level of antibody maturation. The un-liganded native and antigen-bound crystal structures of 36-65 anti-ars germline antibody were analysed using molecular dynamics simulations. It was observed that the un-liganded antibody displays inherent flexibility in its CDR when compared to antigen-bound native structures even when to the antigen is removed, indicating that while the antigen-combining site is relatively flexible, the antigen locks the conformation in a antigen-specific state.

In the future, crystallographic and molecular dynamics simulations of antigen-antibody recognition as well as broader aspects of host-pathogen interactions will be continued with the ultimate goal to correlate the structural principles with physiological implications. Structural proteomics of plant seed allergens will also be carried out. A pollen allergen from *Oryza sativa* is being studied towards crystallographic analysis and structure-function correlation. Complete processing of the seed proteomes of *Coffea Arabica*, *Solanum melongena*, *Mucuna pruniens*, and *Jatropha curcus*, *Papaver somniferum*,

Carum copticum are being analysed through integrated approaches. Porphyrias, a group of inherited or acquired disorders due to certain aberrations in the heme biosynthetic pathway are also being explored. Molecular pathology of the disease is being explored through understanding the interactions of different porphyrins with carbohydrate binding proteins.

Publications:

1. Lomash S, Nagpal S, Salunke DM. (2010) An antibody as surrogate receptor reveals determinants of activity of an innate immune peptide antibiotic. *J Biol Chem.* 285:35750-35758.

2. Gaur V, Chanana V, Jain A, Salunke DM. (2011) The structure of a haemopexin-foldprotein from cow pea (*Vigna unguiculata*) suggests functional diversity of haemopexins in plants. *Acta Crystallogr* F67:193-200.

3. Tapryal S, Krishnan L, Batra JK, Kaur KJ, Salunke DM. (2010) Cloning, expression and efficient refolding of carbohydrate-peptide mimicry recognizing single chain antibody 2D10. *Protein Expr Purif.* 72:162-168.

Mechanisms of cell division and cellular dynamics

Principal Investigator: Sivaram V S Mylavarapu

Young Investigators: Sharmishtha Samantaray

Junior Research Fellows: Sagar Mahalle
Harsh Kumar

Dynamic cellular events are achieved through a tightly regulated interplay of biomolecules, a precise understanding of which is essential to understand human health and combat disease. Molecular mechanisms underlying the basic physiological processes of cell division and intercellular communications are being examined using multi-disciplinary approaches encompassing biochemical, structural, cell biological and high resolution imaging methods. It is hoped extend the relevant studies to stem cells and model organisms collaboratively with a view to understanding the physiological implications of our molecular mechanistic analyses.

Inactivation of the Spindle Assembly Checkpoint

Mammalian cells divide each cell cycle via the process of mitosis with a high degree of fidelity to generate two daughter cells that contain the correct diploid complement of chromosomes. This fidelity is ensured through tight molecular regulation of multiple mitotic stages in the mother cell. Elucidation of the molecular mechanisms of mitotic regulation is imperative to understand the basis for asymmetric stem cell division leading to differentiation, as well as for potential therapeutic intervention in major diseases like cancer and polycystic kidney disease.

The major quality-control mechanism in the metaphase to anaphase cell cycle transition is the Spindle Assembly Checkpoint (SAC), which ensures that sister chromatids of all chromosomes are equally segregated in anaphase. SAC effector proteins are removed (stripped) from kinetochores at the end of metaphase by the pluripotent molecular motor dynein to achieve checkpoint inactivation and facilitate anaphase onset. We had demonstrated that the Light Intermediate Chain 1 (LIC1) subunit of dynein is responsible for this stripping in a phosphoregulated manner. The present focus is on dissecting the molecular mechanism of SAC inactivation along the following lines of investigation: 1) determine the mitotic LIC1 interactome to identify potential collaborators of LIC1, 2) determine the specific role of phosphoregulation of LIC1 and 3) determine the structural basis for LIC1 function.

Potential LIC1-interacting protein candidates have been identified from a genome-wide yeast 2-hybrid screen, which we are validating with a secondary siRNA screen assaying for phenocopy of LIC1 depletion. We have also generated localization and affinity purification (LAP)-tagged cDNA contructs of LIC1 and have expressed them in mammalian cells, to enable us to perform both biochemical affinity purification and microscopic intracellular localization analyses. Both these assays will mutually validate each other as well as the genetic interactions identified in the yeast 2-hybrid screen. We are simultaneously working towards determination of the *de novo* 3D atomic structure of LIC1. These studies will illuminate the molecular mechanism of LIC1-based SAC silencing by dynein.

Role of the membrane trafficking machinery in cytokinesis

Cytokinesis, the physical separation of two daughter cells following telophase, is characterized by a) cleavage furrow ingression between the daughter nuclei, b) narrowing of the intercellular bridge, c) recruitment of specific proteins (e.g. MKLP1, centriolin, BRUCE) to the midbody ring in the bridge, d) traffic of endosomal and secretory vesicles towards the midbody ring, e) severing of the microtubule bundles traversing the bridge and finally f) membrane abscission and daughter cell separation. It is proposed to illuminate the contributions of the membrane trafficking machinery in cytokinesis, an essential but poorly understood process. The target is the Exocyst complex, comprised of eight conserved protein subunits, that tethers secretory vesicles to the plasma membrane, and may regulate SNARE–mediated fusion of the membranes. It was recently shown that several Exocyst subunits are required for completion of cytokinesis; however, lack of knowledge on their specific role in cytokinesis forms the basis of our investigations along the following directions: i) determine which Exocyst subunits help localize the complex to the midbody ring and dissect the domains responsible, ii) identify other proteins that the Exocyst complex collaborates with in cytokinesis and iii) identify the functional significance of Exocyst complex recruitment at the midbody ring.

It is hypothesized that the Exocyst subunit Sec6 is responsible for localizing the whole complex at the midbody ring in cytokinesis. A recombinant localization and affinity purification (LAP)-tagged cDNA expression construct of human Sec6 has been generated. Expression of this cDNA in mammalian cells will enable us to proteomically identify interaction partners using synchronized cells in cytokinesis, as well as to map intracellular localization of Sec6 by high resolution microscopy – both fixed and live. Small RNA-based knockdown of Sec6, which should abrogate interactions, will be used to ascertain interaction specificity of these partners. A battery of rational, structure-guided mutations on the surface of Sec6 to test for their ability to functionally substitute for wild type Sec6 in cytokinesis are being simultaneously generated. Overall, our studies will help elucidate the molecular basis for the requirement of Sec6 in cytokinesis. Similar approaches will be followed for delineating the contributions of other Exocyst subunits in cytokinesis.

Intercellular communication

Tunneling nanotubes (TNTs), recently discovered intercellular conduits important for communication between several cell types and for the propagation of prions, bacteria and viruses, have been implicated in several critical physiological processes in human health and disease. We aim to delineate the molecular mechanisms of biogenesis and function of TNTs in the long term, about which very little is known at present.

Engineering of nanomaterials for biomedical applications

Principal Investigator: Avinash Bajaj
Research Associates: Ashima Singh
Kuppuswamy Panjamurthy

Junior Research Fellows: Sravan Kumar Muppu
Vedagopuram Sreekanth

The challenges in the area of cancer biology, drug discovery, nanomedicine, and biosensors with an interdisciplinary approach using synthetic chemistry, cell biology, and nanotechnology are being addressed. Objectives include i) Exploring the cross-talk between different signalling pathways in cancer, ii) Engineering of nanomaterials for cancer therapy, iii) Engineering of gold nanoparticles/quantum dots for cancer cell detection and differentiation and iv) Exploring the structure-activity relationship of novel kinase and topoisomerase inhibitors.

Cancer Biology: Cancer chemotherapeutic treatments face major challenges of side effects. For example, Tamoxifen though quite effective, can have harmful side effects such as the development of endometrial cancer or acquired tamoxifen resistance. Similarly, Doxorubicin which is one of the most effective anticancer drugs possesses serious effects on the cardiovascular system. The major reason for cardiotoxicity is generation of oxygen-centered free radicals. Betulinic Acid is a naturally occuring pentacyclic triterpenod that exhibits anticancer and antioxidant activities. Combination of Betulinic Acid with Tamoxifen may enhance the cellular toxicity of Tamoxifen as Betulinic Acid shows its anticancer effect by inhibiting the topoisomerase activity whereas Tamoxifen inhibits cell growth via Estrogen receptors. Intial studies using MTT assay showed the combination effect of Tamoxifen and Betulinic Acid in MCF-7 cells. The mechanistic understanding for the anticancer activities is currently being explored. Betulinic acid having antioxidant properties may reduce the Doxorubicin induced generation of reactive oxygen species and cardiotoxicity. It may also enhance the anticancer effect of Doxorubicin due to its anticancer properties via topoisomerase inhibition.

Drug Delivery: Bile acids are endogenous steroidal molecules which undergo entero-hepatic circulation. Conjugation of anticancer drugs to bile acids is anticipated to increase the bioavailability of poorly bio-available drugs and improve tumor targetting. Hence three bile acid-tamoxifen conjugates: Lithocholic acid-Tamoxifen (**LA-Tam**), Deoxycholic acid-Tamoxifen (**DCA-Tam$_2$**), Cholic acid-Tamoxifen (**CA-Tam$_3$**) (Figure 1) possessing 1, 2, 3 tamoxifen molecules respectively using lithocholic acid (**LA**), deoxycholic acid (**DCA**), and cholic acid (**CA**) are synthesized. Currently *in vitro* cellular toxicities of these bile acid-tamoxifen conjugates is being studied. These conjugates will be explored for their oral absorption and bio-distribution properties in rats. For the co-delivery of two drugs, bile acid based dimeric lipids targeting different apoptosis pathways (Figure 1) will be engineered.

Combination therapy: Various cellular signaling pathways regulate cell proliferation, invasion, and metastasis of cancer cells, it is therefore challenging to develop cellular toxicity by cutting down only one of these pathways. Therefore, combination therapy, especially the combination of chemotherapy and gene therapy can be one of the strategies to cut down the multiple cellular pathways for effective

cancer therapy. Lithocholic Acid-Drug-Polyamine conjugates (Figure 1) are being synthesized and will be used for making lipid formulations for delivery of drugs and therapeutic DNA like p53, or silencing siRNA like bcl-2.

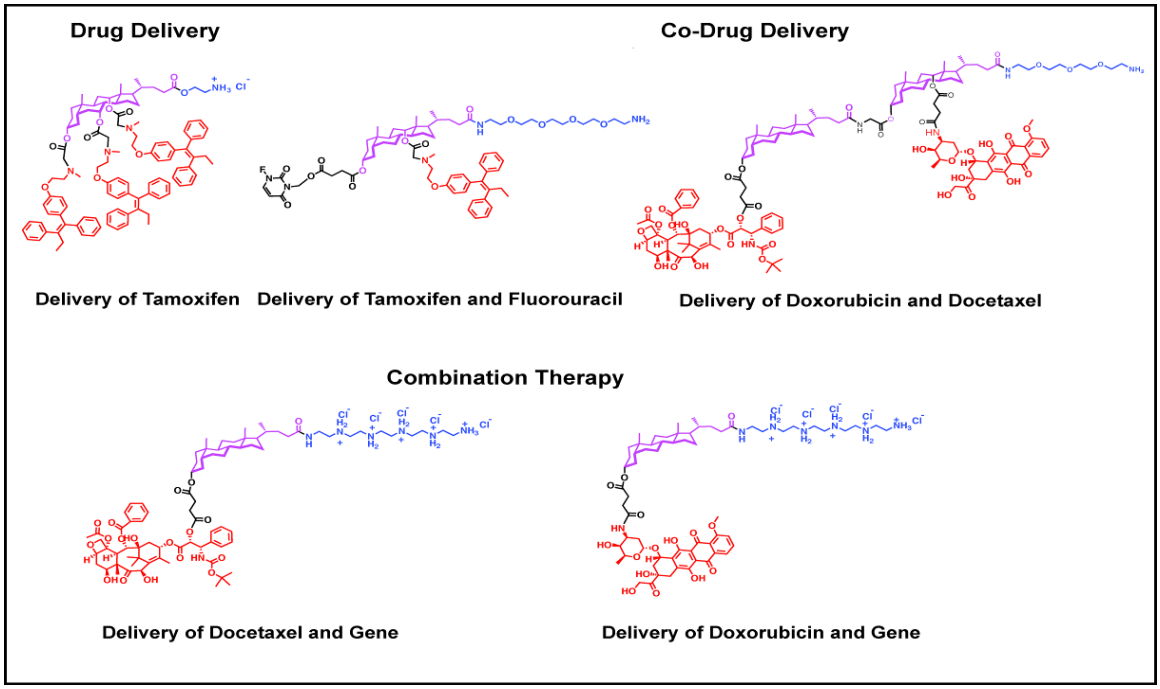


Figure 1. Molecular structures of different molecules for drug delivery, co-drug delivery and combination therapy applications.

In the near future, the interaction between different signaling pathways responsible for cancer growth will be explored. The investigation of different signaling pathways and their interactions would help to explore the engineering of nanomaterials for cancer therapeutic applications. Biodegradable polymer-based nanomaterials will be synthesized that would be able to deliver the drugs and DNA to target cancer cells. For drug discovery aspect different kinase inhibitors as well as some topoisomerase inhibitors are being synthesized and would be investigated for the structure-activity. The differential expression of proteins inside the cancer cells would be used for engineering of nanoparticles and polymers for early cancer detection studies. Small molecule-nanoparticle array based approach would be explored for early cancer cell detection and differentiation.

Publications:

1. Saha, K., Bajaj, A., Duncan B, Rotello VM. (2011) Beauty is Skin Deep: A surface monolayer perspective on nanoparticle interactions with cells and bio-macromolecules. *Small 7*: 1903-1918.

2. Rana, S., Bajaj, A., Rotello, VM. (2011) Monolayer coated gold nanoparticles for delivery applications. *Adv. Drug Del. Rev.* (In Press).

Structural biology of bacterial surface proteins

Principal Investigator: Vengadesan Krishnan

Adherence to host tissues is the first step in the establishment of a bacterial infection. Both Gram-negative and Gram-positive pathogens display a multitude of proteins and protein assemblies (pili or fimbriae) on their cell surfaces for this purpose. Recently, hair-like structures known as pili have been identified with aid of electron microscopy (EM) and genomic analysis in several Gram-positive pathogens. The pili are often utilized for adhesion to host cells, colonization, biofilm formation, etc. The pilus shaft is composed of several small subunits (major pilins) assembled in a head-to-tail manner. In some cases, the minor pilins are decorated along the pilus shaft and also at the tip. Interestingly enzymes called sortases are required in the assembly and anchoring of pili in Gram-positive bacteria.

The fundamental questions like; how are pilins associated in the pilus architecture? How does the pilus assembly take place at bacterial cell surface? Is the pilus assembly mechanism universal among gram-positive bacteria? What are their targets on host cells? How do they interact with targets? How do they involve in biofilm formation? How do the sortases discriminate pilus polymerization and cell wall anchoring? are highling intriquing. These questions are being addressed with the help of X-ray crystallography, biophysical and biochemical techniques. Some of our specific objectives would include i) understanding the pilus architecture and the molecular mechanism of pilus assembly, ii) exploring the role of surface proteins and pili in bacterial pathogenesis, and host cell recognition and biofilm formation at molecular level and iii) integrating structural information with biophysical, biochemical and bioinformatic data for drug design and vaccine development.

New approaches for the prevention and treatment of bacterial infections that do not elicit multi-drug resistance require greater understanding of the infectious process, especially at the molecular level. Bacterial surface proteins and proteinaceous pili extensions play crucial roles in microbial attachment, a critical first step in pathogenesis. Not much is known about the assembly of the pili in Gram-positive bacteria; whereas Gram-negative pili are well investigated. The availability of DNA sequences for many genomes has allowed the *in silico* identification of pilus gene clusters that encodes proteins with sorting signals and sortase genes in several Gram-positive bacteria. The pilus gene cluster encode generally one major pilin that forms the pilus shaft, one minor pilin that play a role in anchoring is deposited at the pilus base in some cases along the pilus shaft, and another minor pilin with an adhesive nature is located at the pilus tip. The pilins are connected covalently (isopeptdie bonds) by pilus-specific sortase, and the assembled pili is then attached covalently to the cell wall by a housekeeping sortase. Autocatalytic intra molecular isopeptide bond, sortase catalyzed inter molecular isopeptide bond and cell wall anchoring are specific to gram-positive bacteria.

These adhesive pilins and pili-related proteins are potential candidates in protein-based vaccine attempts, and understanding their interactions in the assembly and with the host will provide crucial knowledge which will facilitate vaccine design. Our initial focus will be on visualizing the surface proteins including individual pilins, their complex with host cell components, pili-related proteins and enzymes at the atomic level and understanding the pilus assembly mechanism and role of pili in bacterial pathogenesis and biofilm formation. The structural investigations of these proteins and complexes will have a high impact on advancing our understanding of bacterial infections.

Investigating molecular mechanism in the ubiquitin mediated signalling in cellular pathways

Principal Investigator: Tushar Kanti Maiti

Ubiquitination is one of the most important post translational modifications involved in protein quality control in eukaryotes. The main theme of our research is to understand how ubiquitin is involved in different cellular pathways. The ubiquitin mediated signalling cascade is initiated by the formation of isopeptide linkage between target proteins and lysine residue of ubiquitin. In the ubiquitin signalling cascade there are two major events: one is ubiquitination which leads to the conjugation of ubiquitin and second is deubiquitination which leads to the deconjugation of ubiquitin.

The structural basis of ubiquitin recognition of deubiquitinating enzymes DUBs, their involvement in cellular functions, and molecular basis of how these DUBs distinguish between different types of polyubiquitin chains will be exploited. In the context of cellular functions it is also pertinent to investigate how some of these DUBs are involved in disease association (Parkinson disease, Alzheimer, Ataxia, heart disease and cancer) and exploring their plausible therapeutic approaches. In the future, apart from the ubiquitination pathway, structural and mechanistic investigations of other related enzymes in fundamental biochemical processes such as DNA repair, histone modification, and endocytosis of plasma membrane proteins would be explored.

Protein ubiquitination is emerging as one of the most important regulatory posttranslational modifications achieved by a covalent attachment of ubiquitin, a highly conserved 76 residue eukaryotic polypeptide. The destruction of proteins is as important as their synthesis for the maintenance of protein homeostasis in cells. In eukaryotes, the ubiquitin–proteasome system is responsible for most of this protein degradation: the small protein ubiquitin acts as a death warrant, tagging and targeting other proteins to the large proteolytic chamber of the proteasome. Its role in intercellular protein degradation is well established. However, recently it has been demonstrated that ubiquitination has also implicated different cellular events like cell signalling, intracellular trafficking and DNA damage response. The functional diversity of ubiquitin is achieved due to the formation of different polyubiquitin chains, which determines whether it will trigger proteasomal degradation or cell signalling process or DNA damage response. Thus ubiquitination can be thought of as the starting event of a signalling cascade (ubiquitin signalling) that is eventually terminated by the hydrolytic removal of the ubiquitin tag by deubiquitinating enzymes (DUBs).

The important role of DUBs is the maintenance of free ubiquitin pool in cells. Like other posttranslational modifications, ubiquitination is reversible. Human genome analysis has revealed almost 100 DUBs, which provide different functionalities and specificities. Most of the DUBs functions are not well understood yet. These enzymes are classified into five distinct structurally unrelated families like Ubiquitin specific proteases (USP), Ovarian Tumor (OTU), Ubiquitin C-terminal Hydrolases (UCH), Josephin domain DUBs and JAMM/MPN+ DUBs. All DUBs except JAMMs are cysteine proteases, where as JAMMs are Zinc metalloproteases. Our approach studying DUBs is based on the combined application chemical biology, biochemical and biophysical methods.

Understanding the molecular mechanisms of infectious and idiopathic inflammation

Principal Investigator: Chittur V Srikanth

Bacterial pathogen *Salmonella enterica* serovar Typhimurium is one of the most frequent causes of acute gastroenteritis in humans. It is noteworthy that the disease is highly prevalent in developing countries like India, and children under the age of 5 are most susceptible. During infection, using several effector proteins, *Salmonella* manipulates host cells to allow its own replication and its ability to induce inflammation. Functional attributes and mechanism of action of several of these effectors are still unknown. The focus of our research will be to investigate the molecular mechanistic details of infectious and idiopathic inflammation.

Acute gastroenteritis caused by *Salmonella* induced enteritis is a significant public health problem. The disease manifestation results in massive neutrophil infiltration at the site of infection. Remarkably this is a phenotype also seen in several forms of autoimmune disorders of the gut. Several molecular markers of acute inflammatory state (such as biogenesis of neutrophil-chemoattractant hepoxilin-A3, modulation of multidrug resistant proteins) are also shared between these diseases.

Pathways of the gastrointestinal inflammatory conditions to unearth other unidentified mechanisms that are akin or dissimilar in these states of inflammation is being probed. In these studies our main objectives will be to: (1) identify novel bacterial virulence proteins and their mechanisms which mediate inflammatory pathways, (2) identify the host molecular pathways that get affected during infections (such as SUMOylation alteration), and (3) test if the identified pathways are also operational during states of auto-immune disorders. Thus, this study may lead to the discovery of novel biochemical pathways that could potentially advance the development of therapeutic approaches to treatment of intestinal inflammation.

The ability of *Salmonella* to actively invade the host epithelial cells is an important aspect of virulence. The process depends on the concerted action of a cohort of bacterial proteins, a key component of which is a specialized secretory apparatus, a type three secretion system (TTSS). The TTSS works like a molecular syringe and mediates the translocation of the bacterial factors called effectors into the host epithelium. These virulence factors then attack the host-cell machinery and mediate invasion and infection. Our recent finding describing bacterial effector processing by host caspase-3 enzyme opens up potentially interesting areas of research. One of the future goals will be to probe these mechanisms in greater detail. Herewith using state of the art tools of molecular biology, novel bacterial effectors that might undergo caspase-3 dependent activation, and the mechanism and significance of activation in effector function. will be examined

One of the host-cellular mechanisms that pathogens target is post-translational modifications (PTMs) of proteins. Besides phosphorylation and ubiquitilation for which many examples of modulation by pathogens exist, a PTM called SUMOylation has recently been demonstrated to be targeted. Ensuing work has revealed that the intracellular bacterial pathogen *L. monocytogens* modulate host SUMOylation. Preliminary data from our recent experiments suggest that *Salmoenlla* also alters host SUMOylation machinery, a phenomenon that is otherwise unknown in the field. In light of these evidences, modulation of host SUMOylation could play a pivotal role in *Salmonella* invasion and inflammation.

In future role of SUMOylation in inflammation using *Salmonella* model would be elucidated. Specifically, 3 sub-areas are: (i) Investigate the mechanism employed by the pathogen to alter host-SUMOylation pathway using modern tools of molecular microbiology and genetics. These mechanisms will also be tested in a mouse-model of *Salmonella* enteritis. (ii) Use a multi pronged strategy (involving mass-spectrometric, yeast-2-hybrid protein-protein interation assays etc.) to identify proteins that suffer SUMOylation alteration during *Salmonella* infection. The significance of such an alteration in the progression of inflammation will also be analyzed. (iii) Explore similarities/differences between SUMOylation pathways operational during induced inflammation in comparison to idiopathic inflammation in animal model and biopsy samples from patients suffering from these diseases.

Pathophysiology of Hemolysis and Thrombosis

Principal Investigator: Prasenjit Guchhait

Intravascular hemolysis releases excessive extracellular hemoglobin (ECHb) in plasma, causing many vascular dysfunctions in patients of all kinds of hemolytic disorders including sickle cell disease, thalassemia, paroxysmal nocturnal hemoglobinuria, hereditary spherocytosis and stomatocytosis, microangiopathic hemolytic anemia, pyruvate kinase deficiency, ABO mismatch transfusion reaction, paroxysmal cold hemoglobinuria, severe idiopathic autoimmune hemolytic anemia, infection induced anemia, malaria and mechanical or chemical induced anemia. These patients commonly experience some clinical complications related to blood vessels occlusion, thrombosis, ischemia, strokes or infarctions, that occur due to unusual cell adhesion to the vessel wall. Investigations suggest that the occurrence and the severity of the above complication in these disorders have the close correlations with different states of intravascular hemolysis in patients.

Molecular mechanisms of the hemolysis mediated thrombosis and vascular occlusion in hemolytic conditions is being explored. It has been shown that ECHb crucially regulates the activity of the plasma glycoprotein von Willebrand factor (VWF) that normally serves the hemostatic functions to stop bleeding in injured vessels, and also causes thrombosis to block blood flow in diseased vessels. Our goal is to identify the details of ECHb interactions with VWF and other molecules that propagate thrombosis or vessel occlusion in hemolytic conditions, using *in vitro* and *ex vivo* experiments. To understand clearly the molecular interactions between ECHb and VWF, details of their binding kinetics, stoichiometry and precise binding sites using the recombinant polypeptides of VWF and Hb will be studied. The mechanism for ECHb mediated activation of VWF; and role of hyper-reactive VWF in thrombosis will also be exploited.

Based on the above observations studies in patients as well as in mice will be exteneded such as: i) Determining the correlations between hemolysis and thrombosis in patients with all hemolytic disorders; and ii) identify the biomarkers associated with the hemolysis mediated crisis events such as thrombosis, vessel occlusion, strokes, ischemia and infarctions in hemolytic disorders. Furthermore, genetic markers such as SNIPs associated with the above clinical conditions in hemolytic patients would be explored.

To translate our molecular and genomic findings on diseases to clinical practice, anti-thrombotic and anti-adhesive therapeutics will be developed and tested *in vivo* in mice models of intravascular hemolysis (such as $ThCD59^{RBC}$ mice) or hemolytic disorders (such as sickle cell anemia, Thalassemia etc.).

Significant collaborations will be developed with other laboratories/clinics/ hospitals to investigate more about the debilitating hemolytic disorders such as thalassemia, sickle cell anemia and malaria that are very common in India. Collaborations would help us to pursue the basic, clinical and translational researches on thrombotic and cardiovascular disorders that cause maximum death in India and around the world.

Profiles of Faculty Members joining during 2010-2011

Sivaram V S Mylavarapu
Assistant Professor

Postdoc: **University of Massachusetts Medical School, Worcester, USA**
PhD 2001: **National Institute of Immunology, New Delhi, India**

Research Interests:

We are interested in illuminating the basic molecular mechanisms of mitosis and its underlying impact on important biological processes. We will focus initially on events controlling the metaphase to anaphase cell cycle transition. We will also study late events in mitosis that ensure completion of cell division. Another interest of ours is to explore the biology of novel modes of intercellular communication. We will later collaboratively extend the relevant studies to stem cells and model organisms with a view to understanding the physiological implications of our molecular mechanistic analyses. In the future, we will collaboratively study cell division mechanisms and intercellular communication in stem cells using model organisms for cellular regeneration. Our approach to answering these questions will be multi-pronged, equally involving biochemical, biophysical, structural biology, cell biology and high resolution optical microscopy approaches.

Selected Publications:

1. Mylavarapu V S Sivaram*, Thomas L Wadzinski*, Sambra D Redick, Tapas Manna and Stephen J Doxsey (2009). Dynein Light Intermediate Chain 1 is required for progress through the Spindle Assembly Checkpoint. EMBO Journal, 28(7), 902-14. (*equal contribution)
2. Mylavarapu V S Sivaram, Melonnie Furgason, Daniel N Brewer and Mary Munson (2006). The structure of the Exocyst subunit sec6p reveals a conserved architecture with diverse roles. Nature Structural and Molecular Biology, 13 (6), 555-56.
3. Mylavarapu V S Sivaram, Jennifer A Saporita, Melonnie L M Furgason, Angela J Boettcher, and Mary Munson (2005). Dimerization of the Exocyst protein Sec6 and its interaction with the t-SNARE Sec9. Biochemistry, 44 (16), 6302-11.
4. Mylavarapu V S Sivaram, R Sudha, and R P Roy (2001). A role for the alpha 113 (GH1) amino acid residue in the polymerization of sickle hemoglobin. Journal of Biological Chemistry, 276 (21), 18209-15.

Avinash Bajaj
Assistant Professor
Ramanujan Fellow 2010

Postdoc: **University of Massachusetts, Amherst, USA**
PhD 2008: **Indian Institute of Science, Bangalore, India**

Research Interests:

Our research group is working in the area of Bio-nanotechnology, especially cancer nanotechnology, biosensing, and cellular engineering applications. Research projects include the synthesis of biologically active organic/inorganic nanomaterials especially polymers, nanoparticles, carbon nanotubes, liposomes for bio-sensing, cellular imaging, drug delivery, and gene therapy applications to target different signaling pathways responsible for cancer and other diseases. Targeted Delivery of drugs and genes faces the major challenges in vivo, therefore we have the strong interests to develop targeted drug/gene delivery vehicles, and to explore the cellular and molecular barriers for in vivo delivery applications. In biosensing applications, the detection of cancer cells, and detection of bacteria/pathogens in food and water are the major challenges. We are developing biomaterials for early detection of cancer cells and pathogens. Novel biocompatible biomaterials would als o be designed for biomedical applications like cell imaging and cellular engineering for future tissue engineering applications.

Selected Publications:

1. C. Subramani,* Avinash Bajaj,* O. R. Miranda and V. M. Rotello Anti-Protein Fouling Properties of Gold Nanoparticles on Surfaces. Adv. Mater. 2010, 22, 5420-5423. (* equal contribution)
2. Avinash Bajaj, Oscar Miranda, Ik-bum Kim, Ronnie L. Phillips, D. Joseph Jerry, Uwe H. F. Bunz, and Vincent M. Rotello, Patterned array based detection of normal/cancerous/metastatic cells using nanoparticle-polymer supramolecular complexes, Proc. Nat. Acad. Sci. USA 2009, 106, 10912-10916.
3. Avinash Bajaj, O. R. Miranda, I. B. Kim, R. L. Phillips, D. J. Jerry, U. H. F. Bunz, and V. M. Rotello, Array based sensing of mammalian cell types using conjugated polymers. J. Am. Chem. Soc. 2010; 132, 1018-1022.
4. Avinash Bajaj, Paturu Kondiah and Santanu Bhattacharya, Design, synthesis and in vitro gene transfection properties of novel cholesterol based gemini lipids and their serum compatibility: A structure-activity investigation, J. Med. Chem. 2007, 50, 2432-2442.
5. Avinash Bajaj, Paturu Kondaiah and Santanu Bhattacharya, Effect of the nature of spacer on gene transfer efficacies of thiocholesterol derived gemini lipids in different cell lines: A structure-activity investigation, J. Med. Chem. 2008, 51, 2533-2540.

Vengadesan Krishnan
Assistant Professor

Postdoc: **University of Alabama at Birmingham, Birmingham, Alabama, USA**
PhD 2005: **University of Madras, Chennai, India**

Research Interests:

Adhesion to host tissue is the key step for bacterial pathogenesis, and both Gram-positive and Gram-negative bacteria often use multitude of proteins and pili also known as adhesins that are associated with their cell walls for adhesion. The structural biology of Gram-positive cell surface adhesins is an emerging field of research, whereas Gram-negative pilus assembly and anchoring have been extensively investigated. Recently, the presence of gene clusters encoding putative pili has been identified in several Gram-positive pathogens. The adhesive Gram-positive pili are assembled using two or more distinct proteins (pilins), and their assembly and anchoring are catalyzed by enzymes called sortases. These pilins share certain features with MSCRAMMs (microbial surface components recognizing adhesive matrix molecules) of Gram-positive pathogens but the targets for these recently discovered pili are not yet clearly defined.

Our primary research interest is on visualizing the individual pilin components and sortases of important Gram-positive pathogens at the atomic level. We use crystallographic, spectroscopic, biophysical, biochemical and computational approach to study the structure function relationships of these bacterial surface proteins and enzymes that are responsible for microbial pathogenecity. Understanding the host-pathogen interaction, pili assembly mechanism, and the role of pili in bacterial pathogenesis and biofilm formation are long term objectives of our research.

Selected Publications:

1. Vengadesan, Krishnan, Ma, Xin, Dwivedi, Prabhat, Ton-That, Hung, and Narayana, V.L Sthanam. (2010). Model for GBS pilus assembly: The crystal structure of the major pilin GBS80 of Streptococcus agalactiae 35 kDa C-terminal fragment. Journal of Molecular Biology, 407, 731-743.
2. Vengadesan Krishnan, Karthe Ponnuraj, Yuanyuan Xu, Kevin Macon, John E. Volanakis and Sthanam V.L. Narayana. (2009). The Crystal Structure of Cobra Venom Factor, a Cofactor for C3- and C5-Convertase CVFBb. Structure, 17, 611-619.
3. Vengadesan Krishnan, Andrew H. Gaspar, Naiqing Ye, Anjali Mandlik Hung Ton-That, and Narayana, S.V.L. (2007). An IgG-like Domain in the Minor Pilin GBS52 of Streptococcus agalactiae Mediates Lung Epithelial Cell Adhesion. Structure, 15, 893-903.
4. Vengadesan Krishnan, Yuanyuan Xu, Kevin Macon, John E. Volanakis and Narayana, S.V.L. (2007). The Crystal Structure of C2a, the Catalytic Fragment of Classical Pathway C3- and C5-convertase of Human Complement. Journal of Molecular Biology, 367(1), 224-233.
5. Vengadesan, K. and Gautham, N. (2003). Enhanced sampling of the molecular potential energy surface using mutually orthogonal Latin squares: Application to peptide structures. Biophysical Journal 84, 2897-2906.

Tushar K Maiti
Assistant Professor

Postdoc: **Nagoya Institute of Technology, Nagoya, Japan**
Purdue University, West Lafayette, Indiana, USA
Weizmann Institute of Science, Rehovot, Israel
PhD 2005: **Indian Institute of Technology, Kharagpur, India**

Research Interests:

A wide variety of biological processes are controlled by the reversible, post-translational modification of proteins which is a covalent attachment of ubiquitin, a highly conserved 76-residue polypeptide. Protein ubiquitination controls many intracellular processes, including cell cycle progression, transcriptional activation, and signal transduction. Like protein phosphorylation, protein ubiquitination is a dynamic and reversible process, involving enzymes that add ubiquitin (ubiquitin conjugating enzymes) and enzymes that remove ubiquitin (deubiquitinating enzymes).

The main focus of our laboratory is to understand the functional role of deubiquitinating enzymes (DUBs) in different cellular pathways. The human genome reveals more than one hundred of DUBs, suggesting their involvement in a wide variety of biochemical pathways. Abnormalities in their functions cause different diseases like lung and breast cancers, Parkinson disease, Alzheimer and heart diseases. Our approach to study DUBs is based on the synthesis of small molecule probes, different biophysical techniques, X-ray crystallography and mass spectrometric based proteomic approach. In addition to DUBs, we are also studying structural and mechanistic investigations of other related enzymes that are thought to be involved in fundamental biochemical processes such as DNA repair, histone modification, and endocytosis of plasma membrane proteins.

Selected Publications:

1. Boudreaux D*, Maiti TK*, Davies, CW and Das C (2010) Ubiquitin vinyl methyl ester binding orients the misaligned active site of the ubiquitin hydrolase UCHL1 into productive conformation Proc. Natl. Acad. Sci. USA. 107, 9117-9122. (*Equal contribution)
2. Maiti TK, Engelhard M and Sheves M (2009) Retinal-Protein interactions in Halorhodopsin from Natronomonas pharaonis: Binding and Retinal thermal Isomerization catalysis. J. Mol. Biol. 394, 472-484.
3. Maiti TK, De S, Dasgupta S and Pathak T.(2006) 3'-N-Alkylamino-3'-deoxy-ara-uridines: a new class of potential inhibitors of ribonuclease A and angiogenin. Bioorg. Med. Chem. 14, 1221-1228.

Chittur Srikanth
Assistant Professor

Postdoc: **Massachusetts General Hospital, Harvard Medical School, Boston, USA**
University of Massachusetts Medical School, Worcester, USA
PhD 2005: **Institute of Microbial Technology, Chandigarh, India**

Research Interests:

Research in my lab is broadly directed at understanding the key events that cause inflammation during infection and autoimmune disorders. Uncontrolled inflammation contributes to the pathogenesis of inflammatory diseases as well as the development of cancers. We use Salmonella in cell culture and mouse system with the key objective to understand molecular mechanism underlying the observed inflammation.

The gram negative, facultative intracellular bacterial pathogen Salmonella is one of the most frequent causes of acute gastroenteritis in humans. The disease results from a complex cascade of interactions between the pathogenic bacterium, the host intestinal epithelium, the commensal microbiota and the immune system of the host. The disease manifestation is characterized histologically by massive infiltration of neutrophils (PMN), a phenotype also observed in some of the chronic recurrent inflammatory disorders with unknown etiology such as Crohn's disease (CD) and ulcerative colitis (UC). Our recent paradigm shifting discovery, demonstrating host-caspase-3 mediated processing of Salmonella virulence proteins, has opened several new exciting avenues in biology of infectious diseases. Using state of the art tools of microbiology, molecular biology and fluorescent-imaging we envisage to carry out host-pathogen interaction studies. The ultimate goal is not only to combat bacterial pathogenesis but also find therapeutic solutions to auto-immune disorders.

Selected Publications:

1. Srikanth CV, Wall, DM, Ana Maldonado-Contreras, Shi, H, Zhou, D, Demma, Z., Mumy, KL and McCormick BA. Salmonella pathogenesis and processing of secreted effectors by caspase- 3 Science, 2010; 330;390-393.
2. Johnson EE, Srikanth CV, Sandgren A, Harrington L, Trebica E, Wang L, Borregaard N,Murray M, Cherayil BJ Siderocalin inhibits the intracellular replication of Mycobacterium tuberculosis inmacrophges. FEMS Immunolo Med Microbiol. 2010; 58(1): 138-45.
3. Kumar CM, Khare G, Srikanth CV, Tyagi AK, Sardesai AA, Mande SC. Facilated oligomerization of Mycobacterial GroEL: Evidence for Phosphorylation-mediated oligomerization J Bacteriol. 2009; 191(21):6525-38.
4. Kaur J, Srikanth CV and Bachhawat AK. Differential roles played by the native cysteine residues of the yeast glutathione transporter, Hgt1p. Manuscript accepted for publication in FEMS Yeast Res. 2009; 9(6): 849-66.
5. Harrington L, Srikanth CV, Antony R, Rhee SJ, Mellor AL, Shi HN, Cherayil BJ. Deficiencyof indoleamine 2,3-dioxygenase enhances commensal-induced antibody responses and protects against Citrobacter rodentium-induced colitis. Infect Immun. 2008 Jul;76(7):3045-53.

Prasenjit Guchhait
Associate Professor

Assistant Professor:	**Dept of Medicine, Baylor College of Medicine, Houston, USA**
Instructor:	**Dept of Medicine, Baylor College of Medicine, Houston, USA**
Postdoc:	**Dept of Medicine, Baylor College of Medicine, Houston, USA**
PhD 1998:	**Banaras Hindu University, Varanasi, India**

Research Interests:

Our research investigation is focused on understanding the molecular mechanisms associated with the complex pathophysiology of diseases such as the sickle cell disease (SCD) and Beta-thalassemia (beta-Thal). We have recently shown a new mechanism whereby plasma extracellular hemoglobin (ECHb) leads to a prothrombotic state by increasing adhesive activity of von Willebrand factor (VWF), which plays a role in hemostatic functions. Molecular observation shows that ECHb binding to the protease cleavage site on VWF inhibits its proteolysis by ADAMTS13. We have shown that ultralarge (UL) forms of VWF, which are not adequately cleaved by ADAMTS13 (a metalloprotease) due to the inhibitory effect of ECHb, play a major role in propagating cell adhesion and vascular occlusion in patients. Therefore, the accumulation of UL and hyperactive VWF multimers in plasma and on the vascular endothelium initiates and propagates cell adhesion to the vessel wall and development of crisis events such as thrombosis, myocardial infarctions, vascular occlusion and strokes in patients with both diseases. Our research also shows that other mechanisms are also involved in the complex pathophysiology of intravascular clot formation and vascular occlusion in patients with SCD. We have shown that exposure of sulfatide, a membrane lipid, increases the adhesiveness of sickled-red blood cells (RBC) and activated platelets to the vessel wall. This mechanism is associated with the development of clot formation, vascular occlusion and strokes in SCD.
We are focusing on basic research to explore the complex mechanisms of the pathogenesis of debilitating complications such as thrombosis, cardiovascular and stroke disorders in patients under different disease conditions; and also on clinical and translational research.

Selected Publications:

1. Zhou Z, Thiagarajan P, Udden MA, Lopez JA, Guchhait P*. 2011. Membrane sulfatide plays a crucial role in the sickle erythrocytes adhesion to matrix and endothelial ligands. Thrombosis Haemostasis.105:1046-52.
2. Zhou Z, Behymer M, Guchhait P*. 2011. Role of extracellular hemoglobin in thrombosis and vascular occlusion in patients with sickle cell anemia. Anemia. 2011:918916.
3. Zhou Z, Guchhait P*. 2010. Extracellular Hemoglobin regulation of von Willebrand factor activity. US Hematology Vol 3(1).
4. Zhou Z, Han H, Cruz MA, Jose JA, Dong JF, Guchhait P*. 2009. Hemoglobin blocks von Willebrand factor proteolysis by ADAMTS-13: a mechanism associated with sickle cell disease. Thrombosis Haemostasis 101 (6): 1070-77.
5. Guchhait P*, Shrimpton C, Honke K, Rumbaut R, Lopez JA, Thiagarajan P. 2008. Effects of an anti-sulfatide single-chain antibody probe on platelet function. Thrombosis Haemostasis 99(3):552-57.

Falguni K Sen
International Adjunct Faculty, RCB
Chair, Management Systems Area
Director, Global Healthcare Innovation Management Center
Fordham University
1790 Broadway, #1121, New York, NY 10023

Ph.D. (1983) in Management Science from Northwestern University, Evanston, Illinois

Academic Experience:

Faculty member (1986 – present), Fordham University, Graduate School of Business, New York, N.Y. 10023

Fellow (1985-1986), Center for Technology and Strategy, Dept. of Management, Drexel University, Philadelphia, PA 19104

Faculty Member (1983-1985; 1973-1977), Centre for Energy, Environment and Technology, Administrative Staff College of India, Hyderabad, India

Research interests:

Our research interests include the studies on transformation in the global pharmaceutical industry; knowledge management and transfers in drug discovery partnerships, outsourcing of clinical trials to developing countries: an issue of building ethical capacity. We also have interests of studying value added outsourcing - an issue of control, subsidiary autonomy in medical devices industry - a study of Ireland, technology entrepreneurship in globally networked organizations, and technology transfer and global strategies - Ireland and India .

Selected Publications:

1. Sen, F. (2009). Drug Discovery and Development--Business opportunities in India. New Delhi, India: ORF-FICCI.
2. Sen, Falguni, "Virtual Corporation", in IEBH Handbook of Information Technology in Business, Edited by Milan Zeleny, International Thompson Business Press, London, 1999.
3. Egelhoff, W., Falguni Sen and C.S. Haklisch, "Technical Alliances in the Semiconductor Industry: Predictors of Performance", Jurnal Manajemen Prasetiya, Vol. 3(5), Nov. 1995.

Scientific Activities and Achievements

Seminars delivered by visiting scientists at RCB

Date & Time	Speaker	Title
Aug 24, 2011 11:00am	Partha P. Bera, PhD NASA Ames Research Center	Application of Quantum Mechanics in Atmospheric Chemistry, and Radiation Chemistry of Biomolecules
Aug 18, 2011 03:00pm	Pallavi Kshetrapal, PhD Harvard Medical School Boston MA USA	Deciphering the Molecular Interplay of Cell Proliferation using Drosophila
Aug 16, 2011 11:00am	A Abdul Ajees, PhD Florida International University, Miami, FL 33199.	The 1.4 Angstrom crystal structure of the ArsD arsenic metallochaperone and docking studies provide insights into its interaction with the ArsA ATPase
July 11, 2011 11:00am	Tulika P Srivastava, PhD Laboratory for Metasystems Research Quantitative Biology Centre RIKEN, Yokohama, Japan	Systems Biology of Genomes and Metagenomes: From Simple to Complex
June 28, 2011 2:30pm	Gagan Chouhan, PhD The Scripps Research Institute La Jolla, California 92037 USA	Enzyme and Transition-Metal Catalysis in Organic Synthesis From Hetercycles to Macrocycles
June 07, 2011 11:00am	Akash Gulyani, PhD Department of Pharmacology University of North Carolina, Chapel Hill	Imaging protein activity in living cells: Src kinases at the leading edge
June 01, 2011 3:00pm	Ramakrishna Vadrevu, PhD Department of Biological Sciences BITS-Pilani (Hyderabad), India	Folding and Mis-folding of a 29kDa TIM Barrel Protein: Free Energy Landscape Perspective from NMR Spectroscopy
April 22, 2011 11:00am	Subhrajit Biswas, PhD Department of Medicine Vanderbilt University Medical Center Nashville TN 37232	Alteration of metabolic pathways driven by pro-apoptotic Bax and Bak in early thymopoiesis initiates the stage specific T-cell Leukemia

April 7, 2011 12:00 Noon	Shilpee Dutt, PhD ACTREC, Mumbai	Where do lymphomas meet leukemias? a look at the underlying aberrant DNA damage response and p53 pathway activation!
March 14, 2011 11:00am	Rashmi Mishra, PhD Kai Simons Lab, Max Planck Institute Dresden, Germany	Uncovering The Secrets Behind Cellular Polarization: Different Systems, Common Platform
March 14, 2011 9:00am	Prasenjit Guchhait, PhD Assistant Professor Baylor College of Medicine Houston Texas - 77030, USA.	A new mechanism of hemolysis - induced thrombosis and vascular occlusion in Sickle Cell Disease and Thalassemia-beta; and development of anti-thrombotic therapeutics
March 09, 2011 10:30am	Luciano A G Lucas, PhD Director of Sales and Scientific Applications Europe-Middle East-India Bitplane AG	An Interactive Session on IMARIS
March 08, 2011 11:00am	Tirumala Kumar Chowdary, PhD Department of Molecular Microbiology Tufts University School of Medicine Boston, USA	Herpesvirus fusion machinery - a new paradigm in viral entry
March 03, 2011 9:00am	Vengadesan Krishnan, PhD Center for Biophysical Sciences and Engineering University of Alabama at Birmingham, USA.	Structural Biology of Gram-positive Bacterial Adhesins
March 01, 2011 2:30pm	Sharmistha Sarkar, PhD Department of Medical Oncology Dana-Farber Cancer Institute Harvard University Boston, USA	Initiating Events During Colon and Ovarian Cancers

March 01, 2011 12:00 noon	Kunal Rai, PhD Dana-Farber Cancer Institute Harvard University Boston, USA	DNA Demethylation during Zebrafish Development and Colon Cancer
Feb 28, 2011 11:00am	Purusharth Rajyaguru, PhD Dept of Molecular and Cellular Biology University of Arizona Tucson AZ, USA	mRNP Transition
Feb 25, 2011 11:00am	Vivek Rai, PhD Department of Medicine, New York University Medical Center, New York, NY-10016, USA	The RAGE axis: Novel Structural insights and key regulations in cardiovascular complication and tumorigenesis
Feb 23, 2011 10:00am	Krishnamohan Atmakuri, PhD Department of Immunology and Infectious Diseases Harvard School of Public Health Boston, USA	Investigating the Virulence Determinants of Mycobacterium tuberculosis
Feb 18, 2011 11:00am	Adesh Saini, PhD Laboratory of Gene Regulation and Development, Eunice K Shriver NICHHD, NIH Bethesda MD, USA	Tails of EIF1A Promotes Ribosomal Scanning and AUG Selection: Unveiling Tale of Tails
Feb 15, 2011 11:00am	Atul S. Deshpande, PhD School of Dental Medicine, University of Pittsburgh, Pittsburgh, US	Calcium phosphate nanoparticle with tailored properties for targeted drug delivery and bone tissue repair
Feb 10, 2011 11:00am	Chittur Srikanth, PhD Department of Microbiologyand Immunology University of Massachusetts Medical School Worcester MA, USA	Novel role for Caspase-3 in Salmonella effector processing: a twist in the tale
Feb 03, 2011 2:00pm	Tushar Kanti Maiti, PhD Deptt. of Frontier Materials, Nagoya Institute of Technology, Nagoya, Japan	Structural Basis of Ubiquitin C-terminal Hydrolases' Function

Feb 03, 2011 11:00am	Rachna Chaba, PhD Department of Microbiology and Immunology University of California San Francisco San Francisco CA, USA	Design of Stress Signaling Pathways in Bacteria
Jan 27, 2011 11:00am	Beena Krishnan, PhD Department of Biochemistry & Molecular Biology University of Massachusetts, Amherst, USA	Unraveling the mechanisms of folding and function of Serpins: In vitro and in vivo
Jan 25, 2011 11:00am	Koyeli Mapa, MD/PhD Institute of Genomics and Integrative Biology Delhi, India	Conformational Dynamics of Molecular Chaperones
Jan 12, 2011 11:00am	Ritesh Tandon, PhD Department of Microbiology and Immunology Emory School of Medicine/ Emory Vaccine Center Atlanta GA, USA	Viral tegument proteins and host factors in human cytomegalovirus maturation
Jan 5, 2011 11:00am	Murali Krishna Ghatkesar, PhD University of Virginia Charlottesville, VA, USA.	Real-Time Label-Free Biosensing with Nanomechanical Microcantilevers
Dec 24, 2010 11:00am	Saurabh Chattopadhyay, PhD Department of Molecular Genetics Lerner Research Institute Cleveland Ohio, USA	A New Pathway for Cellular Antiviral Response
Dec 23, 2010 3:00pm	Ramars Amanchy, PhD Department of Cancer & cell Biology University of Cincinnati Cincinnati, USA	Probing protein kinase signaling using proteomic approaches

Dec 3, 2010 11:00am	Biman B Mandal, PhD Department of Biomedical Engneering, Tufts University, Medford Massachusetts, USA	Silk Matrix Based Tissue Engineering
Nov 30, 2010 11:00am	Mahak Sharma, PhD Brigham and Women's Hospital, Harvard Medical School, USA	Multiple Roles of an Arf-like Small G-Protein, Arl8b, at the Lysosomes
Nov 24, 2010 11:00am	Narottam Acharya, PhD University of Texas Medical Branch, Galveston Texas, USA	Molecular Dissections of DNA replication and Trans-lesion DNA synthesis in Eukaryotes
Nov 11, 2010 11:00am	Vikas Goel, PhD Fred Hutchinson Cancer Center Seattle Washington, USA	Modeling Human Pancreas Adenocarcinoma: Treatment Progression by Real Time Imaging
Oct 5, 2010 3:00pm	Srikanta Goswami, PhD University of Wisconsin-Madison, USA	Non - coding RNAs & RNA Binding Proteins: Implication of their Individual & Mutual roles in Regulation of Gene Expression

Lectures delivered / Conferences attended/ Visits abroad

Dr. Dinakar M Salunke

1. Delivered an invited lecture entitled "Specificity of antigen recognition: new paradigms" at the Indo-US Symposium on Modern Trends in Macromolecular Structures, IIT, Mumbai, Feb 21-24, 2011.
2. Delivered an invited lecture entitled " Revisiting the tenets of specificity and recognition in the immune system'' Indian Institute of Science Education and Research, Pune Sept 11-12, 2011
3. Delivered a lecture entitled "Structural biology of immune recognition" at Molecular Reproduction Development and Genetics, IISc. Bangalore August 16-17, 2011
4. Annual day lecture entitled "New paradigms in antigen recognition" at National Brain Research Centre, Manesar Sept 23, 2011.
5. Participated in the bilateral B2B Summit & Bio partnering North America event as part of the Indian delegation during Jan 20-26, 2010 at Vancour, Canada.
6. Visited European Bioinformatics Institute, EMBL as part of the Department of Biotechnology scientific delegation led by Secretary, DBT during Oct 12-15, 2010
7. Participated and chaired a micro-symposium on 'Structural Biology of the Immune System' at the 22nd meeting of the IUCr during August 22-27, 2011 at Madrid, Spain.

Dr. Avinash Bajaj

1. Participated in Macro 2010 Frontiers of Polymers & Advanced Materials, 15-17 Dec. 2010, at New Delhi, India.
2. Participated in 30th Annual Convention of Indian Association for Cancer Research & International Sympsium on "Signaling Network and Cancer" from 6-9 Feb.2011, at Kolkata, India.
3. Presented in Interactive Meeting/Workshop on Nanobiotechnology 28th Feb- 1st March, 2011 at Kochi, India

Membership of professional/ Academic bodies/ Editorial Boards

1. Member, Governing Body, National Institute of Plant Genome Research 2011-
2. Governing Body, Translational Health Science & technology Institute, Faridabad, 2011-
3. Member, Scientific Advisory Committee, Bose Institute, Kolkata 2010-
4. Scientific Advisory Committee, National Brain Research Institute, Manesar, 2011-
5. Scientific Advisory Committee, Centre for DNA Fingerprinting and Diagnostics, Hyderabad, 2006-10
6. Member, Task Force on Interdisciplinary Programme of Life Sciences (IPLS), Dept of Biotechnology, Govt. of India 2010-
7. Member, PAC for Biochemistry, Biophysics, Microbiology and Molecular Biology, Dept of Science & Technology, Govt. of India, 2007-
8. Member, Task Force on Basic Research in Modern Biology, Dept. of Biotechnology, Govt. of India, 2000-2010
9. Editorial Board, Proceedings of the Indian National Science Academy 2006- todate
10. Editorial Board, Resonance - A Science Education Journal 2006- todate
11. Editorial Board, Indian Science Abstracts, 2009-2010

Publications:

1. Lomash S, Nagpal S, Salunke DM. (2010) An antibody as surrogate receptor reveals determinants of activity of an innate immune peptide antibiotic. *J Biol Chem.* 285:35750-35758.

2. Gaur V, Chanana V, Jain A, Salunke DM. (2011) The structure of a haemopexin-foldprotein from cow pea (*Vigna unguiculata*) suggests functional diversity of haemopexins in plants. *Acta Crystallogr* F67:193-200.

3. Tapryal S, Krishnan L, Batra JK, Kaur KJ, Salunke DM. (2010) Cloning, expression and efficient refolding of carbohydrate-peptide mimicry recognizing single chain antibody 2D10. *Protein Expr Purif.* 72:162-168.

4. Saha, K., Bajaj, A., Duncan B, Rotello VM. (2011) Beauty is Skin Deep: A surface monolayer perspective on nanoparticle interactions with cells and bio-macromolecules. *Small 7*: 1903-1918.

5. Rana, S., Bajaj, A., Rotello, VM. (2011) Monolayer coated gold nanoparticles for delivery applications. *Adv. Drug Del. Rev.* (In Press).

Distinctions, Honours and Awards

1. Dr. Dinakar M. Salunke is awarded with gold Medal for excellence in Biological Sciences & Technology for the year 2010, instituted by the Council of Scientific & Industrial Research (CSIR) in the memory of Prof G N Ramachandran, for his outstanding contributions in understanding of the generation of antibody diversity and for elucidating diverse facets of molecular mimicry in the context of humoral immune response.

2. Dr. Avinash Bajaj is awarded with Ramanujan Fellowship-2010 by Department of Science and Technology (DST) for five years.

Infrastructure development

Interim Laboratories in NCR, Gurgaon

During the period under report the Interim Laboratories at 180, Udyog Vihar, Phase I, Gurgaon (NCR) and research activities were started. General lab furnishings like lab benches, faculty cabins, library, administrative offices, seminar room, cold rooms, and cell culture rooms were structured. Lab areas were furnished with deep freezers, -20 ^{o}C freezers, 4 ^{o}C freezers, liquid nitrogen containers, and other common equipments like real-time PCR machine, gradient PCR machines, gel dryers, speed vac machines, lyophilizer, high-speed centrifuge (floor model) and table-top centrifuges (large and small) for running biology/biochemistry labs. Central Instrumentation facility is created with dynamic light scattering instrument, FT-IR spectrometer, UV spectrophotometer (analytical), UV spectrophotometers (smaller), fluorescence spectrophotometer, fluorescence plate reader, isothermal titration calorimeter and differential scanning calorimeter. Microscopy facility is structured with high-resolution imaging confocal microscope, fluorescence microscope, atomic force microscope and imaging analysis capabilities (Imaris suite and workstation, Leica offline software analysis package). Modern chemical facilities are created using fume hoods, rotary evaporators, flash chromatography system, HPLC and GPC systems. Structural biology facilities are fashioned using X-ray diffractometer (sealed tube generator), detector image plate, robotic crystal-tray setting apparatus (Mosquito), vibration-free crystal incubators and data processing computational facility, mass spectrometer, protein sequencer, surface plasmon resonance analyzer, chemiluminescence and multiplexing CCD imager, FPLC systems, Probe sonicator, and microfluidizer.

Permanent Campus of the NCR-BSC Project at Faridabad

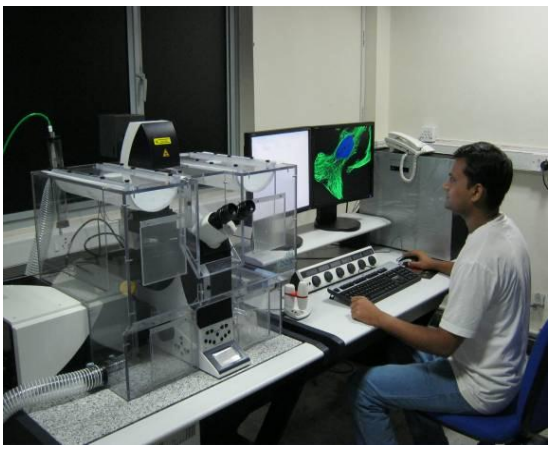
The permanent campus of the Centre is coming up in a big unique NCR Biotech Science Cluster (BSC) being set-up by the Department of Biotechnology (DBT), Government of India in the NCR at Faridabad (Haryana). The other participating constituent partners of the Cluster are: Translational Health Science Technology Institute (THSTI), National Institute of Immunology (NII), and National Institute of Plant Genomic Research (NIPGR). The development is jointly driven by a fundamental commitment to bring together diverse institutional structures into a synergistic cluster with high value resources and infrastructure, co-ordinated development and optimisation of societal benefits with an intent and purpose for laying down foundation for the rules and bye-laws of the cluster for, inter-alia, research and innovation Inclusion of a number of other related Centres to be co-located at the Cluster is at conceptual stage.

The construction work has begun in full force and is being managed by Engineers India Ltd (EIL) as a Project Management Consultancy (PMC). The construction contract has been awarded to Odeon Constructions Pvt Ltd. Excavation work is in progress. 9434 cu.m of excavation has been completed against scheduled of 9350 cu.m (total scope is 34942 cum) PCC work, too, is in progress. 30 cu.m of PCC has been completed (total scope is 3390 cu.m). RCC work is yet to start. Setting up of batching plant has been completed & calibration is under progress. Actual progress is in pace with the scheduled Progress. Site lay out for all of the buildings viz. RCB, THSTI, Primate Research, Small Animal Facility and Library building has been completed.

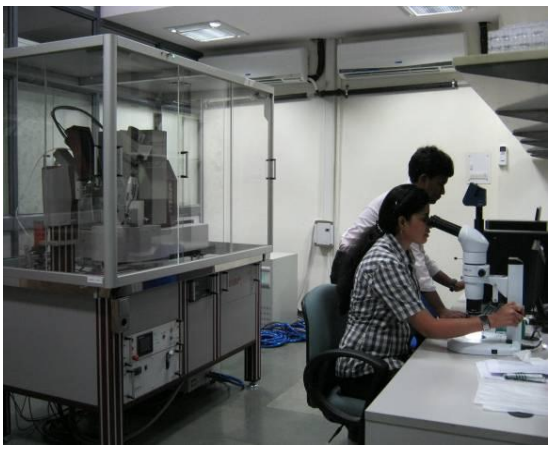
Construction actvities in progress at Faridabad Project site

Functionality of the Labs at the Interim Facilities

A Research Laboratory



Confocal Microscope



X-Ray Diffraction

Institutional Information

Committees of Regional Centre for Biotechnology

Board of Governors

1. Prof. M.K.Bhan,
   Secretary, Department of Biotechnology,
   Ministry of Science and Technology,
   Govt. of India
   New Delhi

2. Sh. Armoogum Parsuramen,
   Director & UNESCO representative to Bhutan,
   India, Maldives and Sri Lanka
   (UNESCO Office, New Delhi)

3. Prof. Akhilesh K. Tyagi,
   Director,
   National Institute of Plant and Genome Research,
   New Delhi

Programme Advisory Committee

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Dr. Avinash Bajaj	Assistant Professor
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