सीएसआईआर–आईआईसीबी
CSIR-IICB
वार्षिक प्रतिवेदन
Annual Report
2010-2011

सीएसआईआर–भारतीय रासायनिक जीवविज्ञान संस्थान
CSIR-Indian Institute of Chemical Biology
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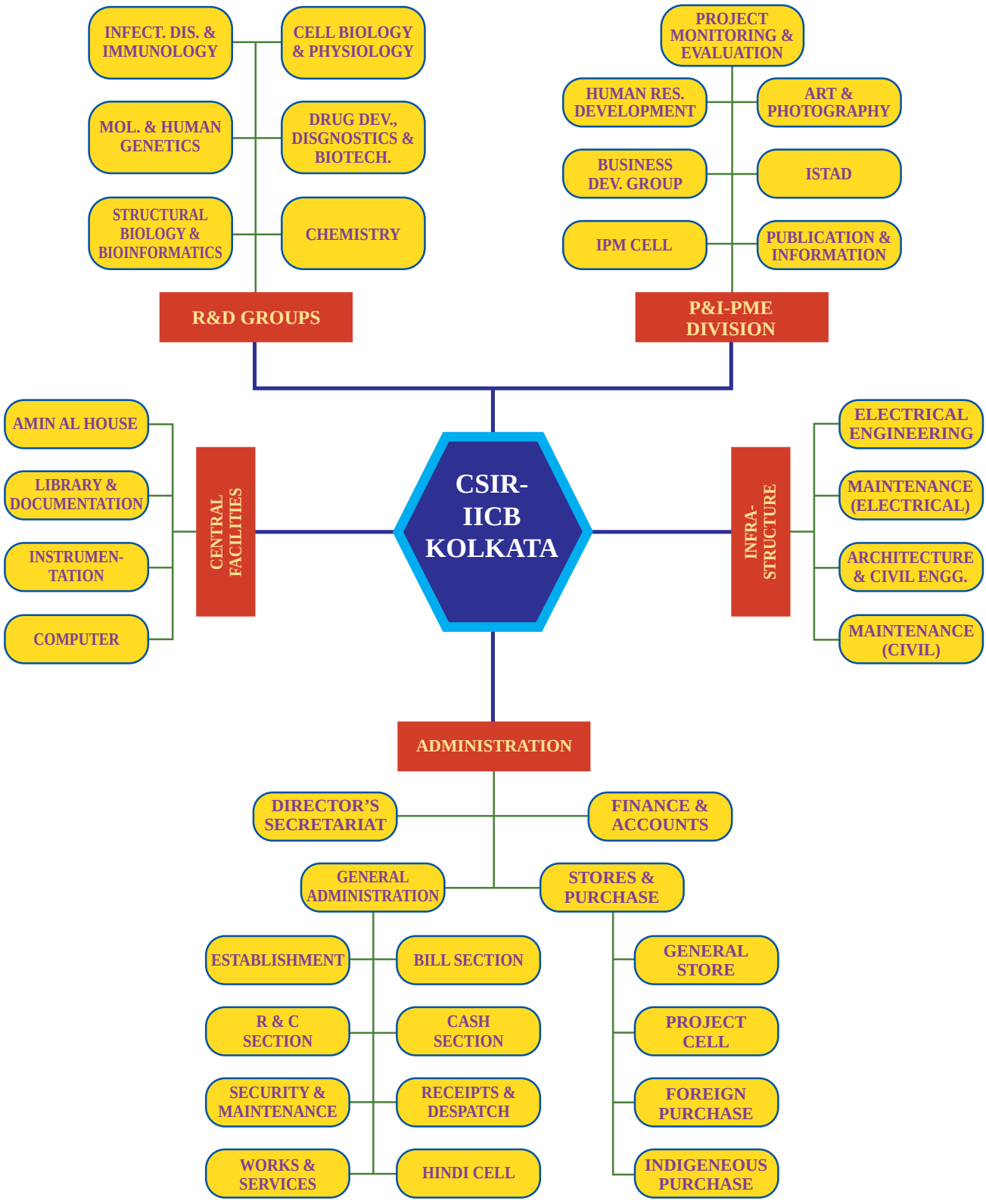
CSIR-
IICB
KOLKATA
R&D GROUPS
INFECT. DIS. & IMMUNOLOGY
CELL BIOLOGY & PHYSIOLOGY
MOL. & HUMAN GENETICS
DRUG DEV., DISGNOSTICS & BIOTECH.
STRUCTURAL BIOLOGY & BIOINFORMATICS
CHEMISTRY
P&I-PME DIVISION
PROJECT MONITORING & EVALUATION
HUMAN RES. DEVELOPMENT
ART & PHOTOGRAPHY
BUSINESS DEV. GROUP
ISTAD
IPM CELL
PUBLICATION & INFORMATION
CENTRAL FACILITIES
AMIN AL HOUSE
LIBRARY & DOCUMENTATION
INSTRUMEN-TATION
COMPUTER
INFRA-STRUCTURE
ELECTRICAL ENGINEERING
MAINTENANCE (ELECTRICAL)
ARCHITECTURE & CIVIL ENGG.
MAINTENANCE (CIVIL)
ADMINISTRATION
DIRECTOR'S SECRETARIAT
FINANCE & ACCOUNTS
GENERAL ADMINISTRATION
STORES & PURCHASE
ESTABLISHMENT
BILL SECTION
R & C SECTION
CASH SECTION
SECURITY & MAINTENANCE
RECEIPTS & DESPATCH
WORKS & SERVICES
HINDI CELL
GENERAL STORE
PROJECT CELL
FOREIGN PURCHASE
INDIGENEOUS PURCHASE

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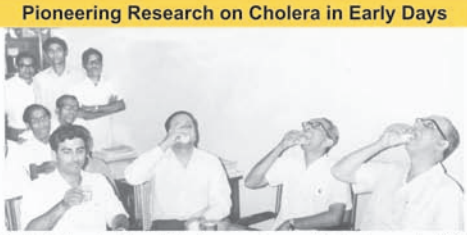
Glorious 75 Years of Indian Institute of Chemical Biology
(CSIR-IICB)

Long before India became an independent republic, a group of biomedical scientists propelled by nationalistic feeling dedicated themselves to the urgent task of tackling problems of tropical disease quite prevalent in our country those days. This simple, selfless motivation led to the foundation of the present day Indian Institute of Chemical Biology (IICB) in 1935 without any support from the Empire. It owed its origin to the inspiration of prominent personalities like Rabindranath Tagore, Acharya Prafulla Chandra Roy, Pandit Jawaharlal Nehru and many others.

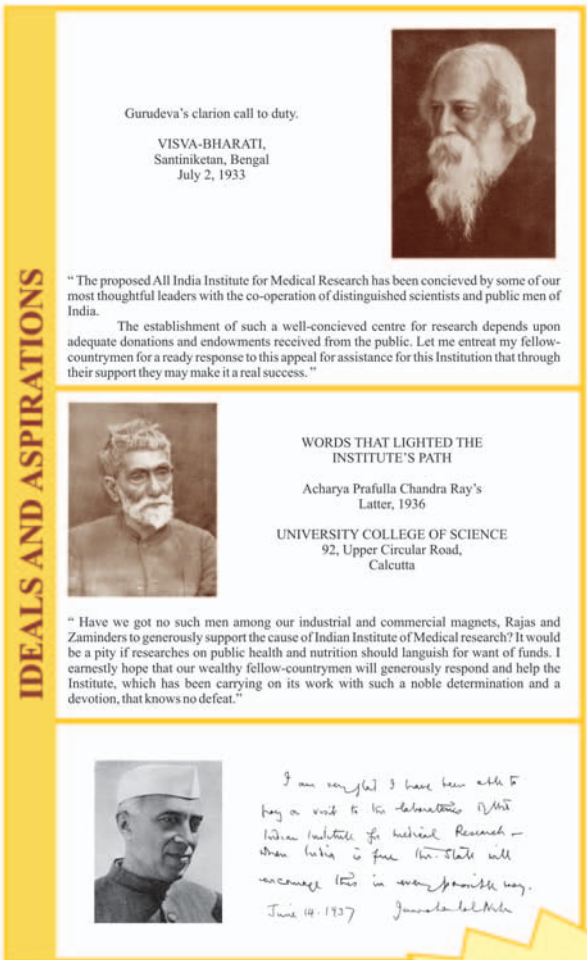
In 60's, the institute gained international recognition when World Health Organization (WHO) identified it as the International Center for Cholera Phage Typing. In late 80's the institute had consolidated its reputation as a National Center for Leishmania research with generous financial support from the United Nations Development Project (UNDP). It continues to hold the internationally recognized title until today.

Currenty, IICB is one of the national research establishments with a vibrant academic atmosphere. It has emerged as a major center for biomedical research in the country with an aim to improve human health through basic research.

Pioneering Research on Cholera in Early Days



Worlds first potential oral Cholera vaccine was tried on human in 1967



Major Research Areas :

- Cell Biology & Physiology
- Chemistry
- Molecular & Human Genetics
- Infectious Diseases & Immunology
- Drug Development / Diagnostics & Biotechnology
- Structural Biology & Bioinformatics
- Systems and Synthetic Biology

Vision :

- Carrying out research on chemistry of life
- Training of high quality scientists
- Applying knowledge to generate new technologies that have impact on national health

Achievements :

- Research Publications in High Impact International Journals
- A novel anti-cancer formulation has been patented, out-licensed, currently in phase II clinical trial and has been cited in Nature Reviews Drug Discovery.
- A herbal formulation against prostate hyperplasia has been marketed by East India Pharmaceuticals.
- A DNA vaccine against leishmaniasis is getting ready for clinical trial.
- A bi-herbal anti-asthma formulation has been patented and is currently being prepared for clinical trial.
- Two diagnostic kits for Leishmaniasis and Acute Lymphoblastic Leukemia have been patented and out-licensed.
- Several novel lead molecules against asthma and cancer, isolated from natural sources, are under negotiation with industry for co-development.

An International Symposium on 'Signaling network and Cancer research' is being organised with IACR to mark the 75th Anniversary of CSIR-IICB During February 6 - 9, 2011

INDIAN INSTITUTE OF CHEMICAL BIOLOGY
(A unit of CSIR)
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निदेशक की कलम से
FROM DIRECTOR'S DESK

प्रत्येक वर्ष यह संस्थान पूरे संसार में स्थित हमारे मित्रों, शुभेच्छुओं तथा वैज्ञानिक समुदाय को हमारे अनुसंधान संबंधी क्रियाकलापों की संक्षिप्त जानकारी देने हेतु अपना वार्षिक प्रतिवेदन प्रकाशित करता है, जो अधिकांशत: प्रकाशित कार्यों एवं पेटेंटों पर आधारित होता है। एक बार पुन: मुझे अप्रैल 2010 से मार्च 2011 तक की अवधि के लिए इस संस्थान का वार्षिक प्रतिवेदन प्रस्तुत करते हुए हार्दिक प्रसन्नता हो रही हैं। इस प्रतिवेदन में वैज्ञानिक योगदान के अतिरिक्त हमारी बुनियादी सुविधाओं, बाहरी संस्थाओं से निधि की प्राप्ति, बौद्धिक संपदा तथा वैज्ञानिक प्रबंधन तथा प्रशासन के विभिन्न पहलुओं को शामिल किया गया है।

सीएसआईआर–आईआईसीबी का मूल आधार पिछले 50 वर्षों में वैश्विक स्तर पर जीव विज्ञान के क्षेत्र में किए गए अनवरत तथा अभूतपूर्व अनुसंधान से कदम मिलाते हुए परिष्कृत *स्टेट ऑफ द आर्ट* प्रौद्योगिकी को अपनाकर हमेशा राष्ट्रीय महत्व के रोगों तथा वैश्विक हितों की जैविक समस्याओं पर अनुसंधान कर रहा है। आधुनिक विज्ञान के माध्यम से अर्थक्षम स्वास्थ्य देखभाल में सीएसआईआर–आईआईसीबी की भूमिका को उसकी स्थापना के आरंभिक दिनों से ही अच्छी मान्यता प्राप्त होती रही है। इस संस्थान के अनुसंधान एवं विकास से संबंधित क्रियाकलापों में लगातार उन्नयन का रिकार्ड रहा है और पिछले वर्षों की तरह सीएसआईआर–आईआईसीबी ने विज्ञान की गुणवत्ता में वृद्धि करके समीक्षाधीन अवधि में अपनी प्रगति जारी रखी। हाल ही में संस्थान ने रासायनिक एवं जैविक विज्ञान के नए उत्पन्न हो रहे क्षेत्रों में अनुसंधान के मामले में अपने क्रियाकलापों को तेज करने की योजना बनाई है, जिसमें पद्धति जीवविज्ञान, सिंथेटिक जीवविज्ञान तथा कैंसर जीवविज्ञान में उसकी जोरदार उपस्थिति विशेष रूप से उल्लेखनीय है। इन

Every year the institute publishes its Annual Report to disseminate a brief account of our research activities, mostly based on published works and patents to our friends, well wishers and scientific communities across the globe. It's my pleasure once again to present the Annual Report of this institute for the period from April 2010 to March 2011. Apart from the scientific contributions, this report also includes critical information about our infrastructure, extramural funding, intellectual property and various aspects of scientific management and administration.

The strength of CSIR-IICB has always been in conducting research on diseases of national importance and biological problems of global interest, employing sophisticated state-of-the-art technology in keeping with the rapid and unprecedented momentum that life science research has gained globally over the last 50 years. The role of CSIR-IICB in 'Affordable healthcare through modern science' is well recognized since its early days. This institute has a steady record of growth in its R&D activities and like preceding years CSIR-IICB continued its progress in the reporting period through enhancing quality of science. Of late, the institute is planning to step up its activities in the emerging areas of chemical and biological research and a special mention may be made about consolidating its presence in Systems Biology, Synthetic Biology and Cancer Biology. The initial thrust

क्षेत्रों में आरंभिक कार्य प्रारंभ हो चुका है और मुझे विश्वास है कि सीएसआईआर–आईआईसीबी में विज्ञान की उच्च गुणवत्ता के आधार पर आने वाले समय में इन क्षेत्रों में और भी सुदृढ़ता आएगी। समीक्षाधीन अवधि के दौरान नई गठित अनुसंधान परिषद ने प्रो.एम विजयन की अध्यक्षता में कार्य करना प्रारंभ कर दिया है और उनके मार्गदर्शन में नए आयाम उद्घाटित हो रहे हैं।

सीएसआईआर–आईआईसीबी की बुनियादी सुविधाएँ लगातार प्रोन्नत हो रही हैं। साल्ट लेक में निर्माणाधीन नया कैंपस अति शीघ्र पूरा हो जाने की आशा है। विद्यमान कैंपस में पशु गृह तथा नया भवन 2014 तक निर्मित हो जाने की उम्मीद है, जबकि नया छात्रावास तथा प्रिंस अनवर शाह रोड में सीएसआईआर की जमीन पर आगत महानुभावों के लिए ट्रांजिट एपार्टमेंट के निर्माण का कार्य 2014 तक पूरा हो जाने की आशा है। निकट भविष्य में कोलकाता के निकटस्थ दक्षिणी क्षेत्र (बरुईपुर) में अनेक पूर्वी आंचलिक प्रयोगशालाओं सहित इनोवेशन कंप्लेक्स के निर्माण की योजना है। सीएसआईआर–आईआईसीबी ने राष्ट्रीय औषधि निर्माण, शिक्षा तथा अनुसंधान संस्थान, कोलकाता (एनआईपीइआर) के दिशादर्शक संस्थान के रूप में कार्य करना जारी रखा।

हमारे संस्थान के छह **शैक्षिक प्रभाग** कुछ बड़े रोगों का अध्ययन करने तथा स्वास्थ्य देखभाल वाले विज्ञान में सुधार करने हेतु आपस में सक्रिय तालमेल के साथ विभिन्न जैविक एवं रासायनिक क्षेत्रों में कार्य कर रहे हैं। हमने अपने देशज एवं प्राकृतिक संसाधनों, जैसे भारत में उत्पन्न होने वाले पौधों से दवाओं का निर्माण करने पर पर्याप्त ध्यान दिया है। संस्थान प्रौद्योगिकी के अंतरण के क्षेत्र में भी काफी अच्छा कार्य कर रहा है। पिरामल लाइफ साइंसेस लिमिटेड एंटी–सीएमएल क्रियाकलाप के द्वारा पौधों से प्राप्त आसव पर द्वितीय चरण के क्लिनिक परीक्षण का कार्य पूरा करने वाला है। प्रोस्टेट हाइपरप्लासिया के लिए प्रोस्टेलिन नामक दवा को अब कोलकाता तथा दिल्ली के बाजारों में बेचा जा रहा है। इसके अतिरिक्त अस्थमा/सीओपीडी के इलाज से संबंधित तीन भिन्न–भिन्न अणु संभावनायुक्त प्रतीत हो रहे हैं और सर्वोच्च प्राथमिकता देकर उन पर कार्य किया जा रहा है। अस्थमारोधी प्रभाव के लिए कोलकाता में *नेशनल एलर्जी अस्थमा ब्रोन्काइटिस इंस्टिट्यूट* के साथ मिलकर पादप उत्पाद का क्लिनिकल परीक्षण करने हेतु बातचीत अंतिम चरण में है।

रसायन प्रभाग के विद्यमान अनुसंधान क्रियाकलाप सिंथेटिक एवं प्राकृतिक रसायन के विभिन्न पहलुओं की दिशा में चल

in these areas has already begun and I hope with time to come, these areas will further strengthen the basis of high quality of science in CSIR-IICB. During the reporting period the newly constituted Research Council started functioning under the Chairmanship of Prof. M. Vijayan, offering a new dimension in guidance.

CSIR-IICB Infrastructure continues to be upgraded. The new campus at Salt Lake is likely to be completed shortly. Animal house and the new building in the existing campus are expected to be complete by 2014, whereas a new hostel and Transit Apartments for visiting dignitaries are planned to be built in the CSIR land in Prince Anwar Shah Road by 2014. An innovation complex involving several Eastern zonal laboratories is planned in the Southern fringe of Kolkata (at Baruipur) in the near future. CSIR-IICB is continuing to function as the mentor institute for National Institute of Pharmaceutical Education and Research (NIPER), Kolkata.

The six **Academic divisions** in our institute are working in different biological and chemical areas with active collaboration among them to study some major diseases and improve healthcare sciences. We have paid substantial attention in developing drugs from our indigenous and natural resources, like native Indian plants. The institute is doing well in terms of technology transfer. Piramal Life Sciences Ltd. is about to finish Phase II clinical trial on a plant extract with anti-CML activity. Prostalyn, a drug for benign prostate hyperplasia, is now being marketed in Kolkata and Delhi. In addition, three different molecules related to treatment of asthma/COPD looks promising and are currently being pursued with top priority. Negotiation is in final stage for clinical trial of an herbal product with **National Allergy Asthma Bronchitis Institute** in Kolkata for anti-asthmatic effect.

The current research activities of the **Chemistry Division** are oriented on various aspects of synthetic and natural product chemistry viz. synthesis of novel nucleoside & nucleotides, chiral heterocycles, benz-annulated medium size

रहे हैं, जैसे नए न्यूक्लियोसाइड एवं न्यूक्लियोटाइड के संश्लेषण, चाइरल हिटेरोसाइकल, बेंज–एनुलेटेड मध्यम आकार के रिंग, हिटेरोसाइकलिक रसायन का सिंथेटिक अध्ययन, प्राकृतिक उत्पाद के नए सिंथेटिक रूट (इनेनटियोसेलेक्टिव सिंथेसिस), एंटी–लिसमानिया यौगिकों का संश्लेषण, बैक्टिरियल कोशिका सतह एंटीजेन का अध्ययन, पादप पोलिसैकेराइड एवं नियोग्लाइकोप्रोटीन, जैवसक्रिय सबस्टैंस के लिए चिकित्सीय पौधों की रासायनिक जाँच तथा न्यूक्लिक अम्ल एवं प्राकृतिक उत्पादों के बाइंडिंग गुणों का अध्ययन। इस प्रभाग ने हरित रसायन के साथ उन्हें अपनाया है ताकि अधिकाधिक पर्यावरण की दृष्टि से उपयोगी उत्पाद एवं प्रक्रिया निर्मित हो सके। प्राकृतिक उत्पाद रसायन में विशेषज्ञता ने अनेक सहयोगात्मक औद्योगिक अनुसंधान कार्यक्रमों का ध्यान आकर्षित किया है जिसके फलस्वरूप अनेक बड़े औषधि निर्माण उद्योगों के साथ सार्थक संबंध स्थापित हुए हैं।

आणविक एवं मानव आनुवंशिकी प्रभाग के व्यापक उद्देश्य भारतीय आबादी में आम बीमारियों के आणविक आनुवंशिक आधार को समझना है ताकि स्तनपायी कोशिकाओं एवं पैथोजेनिक माइक्रोऑर्गेनिज्म में जीन प्रकटीकरण एवं कार्य का अध्ययन किया जा सके तथा जीन चिकित्सा के लिए नए उपकरण विकसित किए जा सकें। इस प्रभाग के विशेष उद्देश्यों में कार्यात्मक आरएनए के साथ अन्तर्कोशिकीय मिटोकोंड्रिया को रूपांतरित करने हेतु पद्धतियों के विकास शामिल हैं ताकि उन पद्धतियों के द्वारा आरएनए डिलिवरी की क्रियाविधि की जाँच की जा सके, इन विट्रो एवं इन विवो मिटोकोंड्रियल कार्य पर आरएनए डिलिवरी के प्रभाव की जाँच की जा सके, आनुवंशिक खराबियों बाले परिवारों में डीएनए मार्कर सूचना की पहचान की जा सके, खराबी के कारणों को उत्पन्न करने वाले उम्मीदवार जीनों में त्रुटियों के लक्षण का निर्धारण किया जा सके, पैथोजेनेसिस के आणविक आधार को समझने हेतु आनुवंशिक भिन्नताओं का कार्यात्मक वैधीकरण किया जा सके, कैंसरपूर्व स्थिति की घातक संभावनाओं को समझने हेतु डीएनए मरम्मत एवं मेटाबोलिक जीनों में कोलेगन प्रकार तथा आनुवंशिक पोलिमॉर्फिज्म के प्रकटीकरण के एसोसिएशन का अध्ययन किया जा सके, संभावनायुक्त हस्तक्षेप रणनीति के निर्माण हेतु गैस्ट्रोइंटेसटाइनल संक्रमण में सिगनेलिंग नेटवर्क के आणविक विच्छेदन, स्पिंडल एसेम्बली चेकप्वायंट जीनों के रूपांतरणीय नियंत्रण तथा (क) चेकप्वायंट जीनों के पी53 मध्यस्थ नियमन तथा (ख) इन जीनों के बीच रूपांतरणीय

rings, synthetic studies on heterocyclic chemistry, novel synthetic routes (enantioselective synthesis) to natural products, synthesis of anti-leishmanial compounds, studies on bacterial cell surface antigens, plant polysaccharides and neoglycoproteins, chemical investigation of medicinal plants for bioactive substances and studies on nucleic acid binding properties of natural products. This division has also adapted them to Green Chemistry that will deliver more environmentally benign products and processes. Expertise in natural products chemistry has attracted a number of collaborative industrial research programs that established meaningful link with several major pharmaceutical industries.

The broad aims of the **Molecular and Human Genetics Division** are to understand the molecular genetic basis of diseases common in Indian populations, to study gene expression and function in mammalian cells and pathogenic microorganisms, and to develop new tools for gene therapy. The specific objectives of this division include developing methods for transforming intracellular mitochondria with functional RNAs, to investigate the mechanism of RNA delivery by such methods, to examine the effects of RNA delivery on mitochondrial function in vitro and in vivo, identification of DNA markers informative in the families affected with genetic disorders, characterization of defects in the candidate genes causing the disorders, functional validation of the genetic variants to understand the molecular basis of the pathogenesis, to study the association of expression of collagen types and genetic polymorphisms in DNA repair and metabolic genes to understand the malignant potentiality of the precancerous conditions, molecular dissection of signaling networks in gastrointestinal infections for design of potential intervention strategies, investigating transcriptional control of spindle assembly checkpoint genes and its impact on chromosome instability with the objective to decipher (a) p53 mediated regulation of the checkpoint genes, and (b) the transcriptional crosstalk between these genes, to study the

क्रॉसटॉक को समझने के उद्देश्य से क्रोमोजोम स्थिरता पर उसके प्रभाव की जाँच, पेय जल के माध्यम से होने वाले आर्सेनिक से स्वास्थ्य पर पड़ने वाले प्रभाव के आणविक आधार का अध्ययन और स्तनपायी कोशिकाओं में एम आइ आर एन ए–मध्यस्थ जीन नियमन की क्रियाविधि की जाँच शामिल है।

संक्रामक रोग एवं इम्युनोलोजी प्रभाग भारतीय विसरल लिसमानियासिस (वीएल), कोलरा एवं अन्य रोगों, इम्युनोलोजी तथा न्यूक्लियर औषधि के विभिन्न पहलुओं के अध्ययन में शामिल है। इन अध्ययनों में लक्षित थेराप्यूटिक्स, बुनियादी डीएनए एंजाइमोलोजी एवं वीएल में प्रोग्राम्ड कोशिका मृत्यु का अध्ययन शामिल है। इस प्रभाग में एक वर्ग ने इस प्रश्न पर विचार किया कि किस प्रकार *लिसमानिया* पारासाइट संक्रमण को प्रमाणित करने वाले मैक्रोफेज की जोरदार रक्षात्मक मशीनरी को न्यूट्रियलाइज करता है, जबकि दूसरा वर्ग नई प्रकार की चिकित्सा के लिए डीएनए टीका के विकास तथा इंजीनियर पेप्टाइड एवं प्रोटीन के विकास की दिशा में कार्य कर रहा है। इस प्रभाग के सदस्य वीएल के विरुद्ध पारासाइट मध्यस्थ इम्युन रक्षात्मक प्रतिक्रिया से आशोधित ग्लाइकोस्फिनिगोलीपिड एवं ग्लाइकोप्रोटीन की खोज करके चिकित्सा में इम्युनिटी की क्रियाविधि तथा प्रभावी टीका तथा इम्युनोपैथोलोजी के विकास, नए पैथोजेनिक क्लोन के विभिन्न सीटीएक्स फेज उत्पादित आविष्कारों की खोज हेतु विभिन्न कार्यनीतियों की जाँच कर रहा है और *वी. कोलरा* में कठोर प्रतिक्रिया के आणविक आधार को समझने की कोशिश कर रहा है, मलेरिया पर कार्य कर रहा है तथा 99एम टेक्नीशियम लेबल वाली औषधि युक्त नैनेकणों के संश्लेषण तथा ट्यूमर लक्षित रेडियोफार्मास्यूटिकल्स के रूप में उनके उपयोग के कार्य में लगा है। इस प्रभाग का इम्युनोलोजी वर्ग स्वास्थ्य एवं रोग में डब्लूएनटी एवं डब्लूआईएसपी नियामक नेटवर्क के आणविक आधार, बीसीआर–एबीएल+ सीएमएल कोशिकाओ के क्लोरोजेनिक अम्ल–प्रेरित एपाप्टोसिस की संलग्नता को समझने, संभावित विशुद्ध कैंसररोधी पादप यौगिकों की पहचान तथा सिगनेलिंग पथ की खोज पर कार्य कर रहा है ताकि विभिन्न प्रकार के कैंसरों के यौगिक–कोशिका अंतर्क्रिया एवं प्रोटियोमिक्स अध्ययन के आधार पर नए लक्ष्यों की पहचान की जा सके, परीक्षण एवं पुनराक्रांत की संभावना के लिए बायोमार्कर के रूप में सियालिलेटेड ग्लाइकोप्रोटीन तथा ग्लाइकोलिपिड और आणविक टारगेट के रूप में सियालिलेटेड एंजाइम की पहचान तथा ग्लाइकोप्रोटियोम/प्लाज्मा प्रोटियोम

molecular basis of health hazard caused by the exposure to arsenic through drinking water and to investigate the mechanism of miRNA-mediated gene regulation in mammalian cells.

The **Infectious Disease and Immunology Division** is involved in studies on different aspects of Indian visceral leishmaniasis (VL), cholera and other diseases, Immunology and nuclear medicine. These studies include targeted therapeutics, basic DNA enzymology and programmed cell death in VL. Here in this division one group addressed the question that how *Leishmania* parasites neutralize the robust defensive machinery of macrophages for establishing infection whereas another group is attempting to establish new tools for monitoring drug resistance and treatment response, develop DNA Vaccine and engineer peptides and proteins for new generation therapies. The members of this division are examining different strategies for the development of an efficacious vaccine and immunopathology and mechanism of immunity in the therapy, exploring purified glycosphingolipid and glycoprotein from parasites mediated immune protective response against VL, exploring diverse CTX phage driven evolution of new pathogenic clones and tries to understand the molecular basis of stringent response in *V. cholerae*, working on malaria and are engaged in synthesis of 99mTechnetium labelled drug conjugated nanoparticles and their application as tumor targeted radiopharmaceuticals. The Immunology group of this division is working to understand the molecular basis of WNT & WISP regulatory network in health & disease, involvement of ROS in chlorogenic acid-induced apoptosis of Bcr-Abl^{+} CML cells, identifying potential pure anti-cancer herbal compounds and exploring signaling pathways to identify new targets on the basis of compound-cell interaction and proteomics study on several cancers, identifying sialylated glycoproteins and glycolipids as biomarker and sialylating enzymes as molecular target for diagnosis, prediction of relapse and monitoring patients through glycoproteome/plasma proteome

दृष्टिकोण के माध्यम से रोगियों की मोनिटरिंग तथा ल्यूकेमिया में उनकी भूमिका की खोज की जा सके।

कोशिका जीवविज्ञान तथा फिजियोलोजी प्रभाग के फिजियोलोजिस्टों तथा आणविक जीववैज्ञानिकों के एक दल का लक्ष्य कुछ खास मेटाबोलिक एवं अनुत्पादक रोगों, कैंसर तथा पुनरूत्पादक चिकित्सा की पैथोफिजियोलोजी को समझना है। कैंसर, स्टेम सेल जीवविज्ञान, हृदय हाइपरट्रोफी, मधुमेह, नशासेवन, न्यूरोडिजेनरेटिव रोगो, यूटेरो-ओवेरियन डिस्कंक्शन तथा हेमाटोपोयटिक पद्धति में पैथोजीन में प्रतिक्रिया आदि पर इस दल द्वारा कार्य किया जा रहा है। इस प्रभाग ने विभिन्न मानव रोगों के लिए अनेक मोडलों का विकास तथा उनका परीक्षण किया है तथा आपसी हित के सहयोगात्मक कार्यक्रमों को प्रारंभ करने के इच्छुक लोगों के लिए पर्याप्त लाभ की संभावना प्रकट करता है। इस प्रभाग का एक अनोखा 'कोशिका जीवविज्ञान तथा फिजियोलोजी अनुसंधान त्योहार' मनाया गया जिसका लक्ष्य आने वाले वर्षों में उसे जारी रखा जाएगा। इस प्रभाग के अनेक उल्लेखनीय अनुसंधानों में शामिल हैं : पेरोक्साइरेडोक्सिन II के द्वारा कार्डियोमायोसाइट मृत्यु की सुरक्षा तथा मेलाटोनिन मेडिएशन, एक्रोजोम रिएक्शन के दौरान मेम्ब्रेन फुशन के नए नियामकों के रूप में स्पर्म एक्टो-प्रोटीन किनेस, तथा एक एंडोजेनस न्यूरोटॉक्सिन की खोज 6-हाइड्रोक्सीडोपामाइन का अंतर्जात उत्पादन, जो लंबे समय तक एल-डोपा देने के कारण मस्तिष्क में डोपामिनर्जिक कोशिका मृत्यु का कारण बनता है तथा नशे वाले ड्रग की लत के विकास की दिशा में आनुवंशिक जोखिम कारकों में योगदान देने वाले तत्वों की पहचान।

औषधि विकास, परीक्षण एवं जैवप्रौद्योगिकी प्रभाग बुनियादी तथा व्यवहारिक अनुसंधान के कार्य में संलग्न है, जिसमें स्वास्थ्य, कृषि तथा प्रक्रिया जैवप्रौद्योगिकी के क्षेत्र के अधीन विभिन्न विषय शामिल हैं। इस प्रभाग ने मुख्य रूप से अनुसंधान के चार प्रमुख क्षेत्रों पर बल दिया (क) पादप उत्पादों की संवीक्षा, विस्फीतिकरण, गैस्ट्रिक अल्सर, लिसमानियासिस तथा कैंसर को रोकने हेतु भारतीय सांपों तथा बिच्छुओं के विष पर अनुसंधान, (ख) नए एंटीबडी आधारित खोज पद्धति तथा लिपोसोम आधारित ड्रग डिलिवरी का विकास, (ग) गैस्ट्रिक अल्सर तथा कैंसर का बुनियादी जीवविज्ञान तथा आणविक क्रियाविधि, तथा (घ) बुनियादी जीवविज्ञान तथा फंगी के विभिन्न स्ट्रेनों का एंजाइम लक्षणनिर्धारण।

approaches and exploring their immunological role in leukemia.

The **Cell Biology and Physiology Division**, a team of physiologists and molecular biologists have a common goal of understanding the pathophysiology of certain metabolic and degenerative diseases, cancer and regenerative therapy. Cancer, stem cell biology, cardiac hypertrophy, diabetes, drug addiction, neurodegenerative diseases, utero-ovarian dysfunction and responses to pathogens in hematopoietic system are dealt with by the group. This division has developed and tested a number of models for various human diseases, and foresees immense benefit to all who want to initiate cooperative collaborative program of mutual interest. A unique 'Cell Biology & Physiology Research Festival' of the Division has been celebrated with an aim to continue it in the years to come. Among the many research highlights from the division are: protection of cardiomyocyte death via peroxiredoxin II and melatonin mediation, sperm ecto-protein kinase as novel regulators of membrane fusion during acrosome reaction and detection of an endogenous neurotoxin, endogenous production of 6-hydroxydopamine that causes dopaminergic cell death in the brain due to long-term L-DOPA administration, identification of genetic risk factors contributing towards development of addiction to drugs of abuse.

The **Drug Development, Diagnostics & Biotechnology Division** is involved in both basic and applied biological research covering various topics within the areas of health, agriculture and process biotechnology. The division mainly focuses on four frontier areas of research: (a) Screening of herbal products, venoms of Indian snakes and scorpions in combating inflammation, gastric ulcer, leishmaniasis and cancer; (b) Development of novel antibody based detection methods and liposome based drug delivery, (c) Basic biology and molecular mechanism of gastric, ulcer and cancer, and (d) Basic biology and enzyme characterization of various strains of fungi.

संरचनागत जीवविज्ञान एवं जैव-सूचना प्रभाग की उपलब्धि तथा क्षमता उचित जीववैज्ञानिक परिप्रेक्ष्य में महत्वपूर्ण मैक्रोमोलेक्यूल्स की संभावना व्यक्त करने तथा अंत:क्रिया को दर्शाने तथा स्टेट ऑफ द आर्ट उपकरणों की सहायता से परमाणविक संकल्पना करने में है। संरचनागत लक्षणनिर्धारण तथा संपुष्टिकारक विशिष्टता काफी हद तक सभी जैविक मैक्रोमोलेक्यूल के बीच अंतर्क्रिया की पद्धति के निर्धारण करने में है, जिससे उनके नियमित कार्यों का पता चलता है। इस प्रभाग का लक्ष्य उन क्षेत्रों में अनुसंधान करना है जो संभावित परिप्रेक्ष्ययुक्त जैविक मैक्रोमोलेक्यूलों के संरचनागत लक्षणनिर्धारण तथा विभिन्न रोगों, जैसे यक्ष्मा, लिसमानियासिस, कलरा, कैंसर, मधुमेह तथा विस्फीतिकारकरोधी, एंटीकनवल्सेंट तथा इम्यूनोमोडुलेटरी क्रियाकलापों के विरुद्ध चिकित्सीय हितो के अन्य छोटे अणुओं पर बल देना है। इस प्रभाग द्वारा नाभिकीय चुंबकीय निनाद (एनएमआर), एक्स-रे क्रिस्टेलोग्राफी, विश्लेषणात्मक अल्ट्रासेंट्रीफ्यूज, सतह प्लासमोन निनाद, प्रदीप्तिकरण सहसंबंध स्पेक्ट्रोस्कोपी, डायोड एरे अवरुद्ध-प्रवाह स्पेक्ट्रोफोटोमेट्री, मास-स्पेक्ट्रोमेट्री, प्रमात्रात्मक संरचना क्रिया संबंध (क्यूएसएआर) तथा 3डी-क्यूएसएआर जैसे आधुनिक परिष्कृत प्रौद्योगिकी का प्रयोग करते हुए प्रोटीन के कार्य, प्रोटीन-प्रोटीन एवं प्रोटीन-न्यूक्लिक अम्ल अंतर्क्रिया का मौलिक अध्ययन किया जा रहा है। प्रोटीन या पेप्टाइड समुच्चयन निर्माण की क्रियाविधि और क्रम का अध्ययन पूरे विश्व में पूरे जोर-शोर से किया जा रहा है क्योंकि उनका संबंध अनेक न्यूरोलोजिकल रोगों से है। इस प्रभाग के सदस्य इन प्रक्रियाओं के अनेक निषेधकों तथा आरंभिक परीक्षणों की जाँच कर रहे हैं। इसके अतिरिक्त बड़े रोगों के लिए सिलिको दवा निर्माण तथा संबंधित सॉफ्टवेयर का विकास किया जा रहा है। ये सॉफ्टवेयर जेनोम/प्रोटियोम विश्लेषण, संभावना की अभिव्यक्ति, मैक्रोमोलेक्यूलर संरचना के परिशोधन तथा विश्लेषण तथा जैव-सक्रिय अणुओं के साथ उनकी अंतर्क्रियाओं की व्याख्या के लिए किया जा रहा है। एक संपूर्ण प्रोटियोमिक्स सुविधा विकसित की जा रही है, जिसमें अद्यतन जानकारी वाली जनशक्ति तथा उपकरण दोनों उपलब्ध हैं, जो प्रोटियोमिक्स अध्ययन के लिए सहायक होगी। एक उल्लेखनीय सफलता रोगों का निदान करने हेतु उच्च मान वाले फिटोस्यूटिकल के उत्पादन के लिए पद्धति जीवविज्ञान को शामिल करने के रूप में प्राप्त हुई है।

समीक्षाधीन अवधि के दौरान पच्चीस (25) बाहरी परियोजनाएँ

The achievement and ability of the **Structural Biology & Bio-informatics Division** is to predict and demonstrate interaction of important macromolecules in proper biological perspectives and at atomic resolution with the aid of state-of-the art instruments. Structural characteristics and conformational specificity to a large extent determine the mode of interaction between/or among all the biological macromolecules, leading to expression of their regulated functions. The charter of this division is to carry out research in areas that focus on structural characterization of potentially prospective biological macromolecules and other small molecules of therapeutic interest against various diseases, e.g. tuberculosis, leishmaniasis, cholera, cancer, diabetes and for anti-inflamatory, anticonvulsant and immunomodulatory activities. Fundamental studies on protein functions, protein-protein and protein-nucleic acid interactions applying modern sophisticated technologies like nuclear magnetic resonance (NMR), X-ray crystallography, analytical ultracentrifuge, surface plasmon resonance, fluorescence correlation spectroscopy, diode array stopped-flow spectrophotometry, mass-spectrometry, quantitative structure activity relationship (QSAR) and 3D-QSAR are being pursued. The mechanism and course of protein or peptide aggregate formation have gained thrust worldwide for their relation with a number of neurological diseases. Members of this division are investigating several inhibitors and early dynamics of these processes. Further additions are in silico drug designing for major diseases and development of related software. Softwares are being developed for genome/proteome analysis, prediction, modification and analysis of macromolecular structures and for elucidating their interactions with bio-active molecules. A full-fledged proteomics facility, both in terms of updated manpower and instrumentation, is being developed for future catering of proteomics studies. A prominent success is the inclusion of systems biology for the production of high valued phytoceuticals to combat diseases.

During the reporting period twenty five (25)

संस्थान के विभिन्न वैज्ञानिकों द्वारा विभिन्न निधिप्रदाता एजेंसियों को प्रस्तुत की गई हैं, जिनमें एनआईएच, अमेरिका तथा वेलकम ट्रस्ट, लंदन शामिल है। अनेक नई परियोजनाओं को स्वीकृत किया गया है। वैज्ञानिक प्रयासों के माध्यम से उपलब्ध विशेषज्ञताओं के आधार पर सीएसआईआर-आईआईसीबी को **ग्यारहवी पंचवर्षीय योजना** के दौरान सीएसआईआर की बाइस (22) योजनागत परियोजनाएँ सौंपी गई हैं और इन परियोजना में अब तक हुई प्रगति की इस संस्थान की अनुसंधान परिषद (आरसी) ने काफी सराहना की है। इन परियोजनाओं ने अन्य सीएसआईआर प्रयोगशालाओं के साथ नेटवर्क स्थापित किया है और सीएसआईआर-आईआईसीबी के वैज्ञानिकों की क्षमताओं का उपयोग किया है तथा राष्ट्र के प्रति सीएसआईआर की सेवाओं के कुल योगदान को बेहतर प्रमाणित किया है।

सीएसआईआर-आईआईसीबी ने नेशनल इंस्टिट्यूट ऑफ फार्मास्यूटिकल एडुकेशन एंड रिसर्च **(एनआईपीइआर)**, कोलकाता के **वार्षिक दीक्षांत सम्मेलन** का आयोजन किया है। सत्ताईस (27) विद्यार्थियों ने अपना एम. एस. (फार्मा) डिग्री स्क्रॉल प्राप्त किया। प्रो. समीर कुमार ब्रह्मचारी, महानिदेशक, सीएसआईआर इस अवसर पर मुख्य अतिथि के रूप में उपस्थित थे। इस मांगलिक समारोह में बड़ी संख्या में उल्लेखनीय अतिथियों के साथ-साथ सीएसआईआर-आईआईसीबी के सभी विद्यार्थियों तथा स्टाफ सदस्यों ने भाग लिया।

'सिगनलिंग नेटवर्क तथा कैंसर' विषय पर एक चार दिवसीय सम्मेलन तथा **अंतर्राष्ट्रीय संगोष्ठी** का आयोजन इंडियन इंस्टिट्यूट ऑफ केमिकल बायोलोजी (आईआईसीबी) तथा आईएसीआर द्वारा संयुक्त रूप से किया गया। यह संगोष्ठी संस्थान के **75वें वर्ष** को मनाने के लिए किए गए आयोजन का अंग भी थी। विभिन्न देशों, जैसे यूके, अमेरिका, जापान, कनाडा, आस्ट्रेलिया, सिंगापुर, कोरिया तथा भारत के वैज्ञानिकों एवं तकनीशियनों ने इस सम्मेलन में भाग लिया। सम्मेलन में दो सौ से अधिक प्रतिनिधियों ने प्रतिभागिता की।

पश्चिम बंगाल में विज्ञान में युवा नेतृत्व, वर्ष 2010 (**सीपीवाईएलएस-2010**) पर सीएसआईआर कार्यक्रम का संयोजन इंडियन इंस्टिट्यूट ऑफ केमिकल बायोलोजी द्वारा किया गया। दो दिवसीय कार्यक्रम में विद्यार्थियों को सीएसआईआर-आईआईसीबी एवं सीएसआईआर-सीजीसीआरआई में चल रहे क्रियाकलापों को दिखाने के लिए विभिन्न प्रयोगशालाओं में ले जाया गया। आजीविका संबंधी अवसर पर भी एक कार्यक्रम आयोजित किया गया। सीबीएसइ

extramural projects have been submitted by different scientists of the institute to different funding agencies, which include NIH, USA and Wellcome Trust, London. Several new projects have been sanctioned. Based on the expertise available through scientific endeavour, CSIR-IICB was assigned with twenty two (22) Planned Projects of CSIR in the **Eleventh Five Year Plan** and the progress so far made of these projects have been highly appreciated by the Research Council (RC) of this institute. These projects networked with other CSIR labs, have exploited the potential of CSIR-IICB's scientists and synergized with the total output of CSIR services to the nation.

CSIR-IICB has organized the first **Annual Convocation** of National Institute of Pharmaceutical Education and Research **(NIPER)**, Kolkata. Twenty seven (27) students received their M.S.(Pharm.) degree scrolls. Prof. Samir Kumar Brahmachari, Director General, CSIR was present in the occasion as the Guest-in-Chief. The auspicious ceremony was attended by all the Staff members and students of CSIR-IICB alongwith a large number of distinguished guests.

A four day conference and **International Symposium** on "Signaling Network and Cancer" was jointly organized by Indian Institute of Chemical Biology (IICB) & IACR The symposium was also a part of the celebration to commemorate the **75th year** of this institution. Scientists and clinicians from different countries, namely UK, USA, Japan, Canada, Australia, Singapore, Korea and India participated in the conference. More than two hundred delegates participated in the conference.

CSIR Programme on Youth for the Leadership in Science for the year 2010 **(CPYLS-2010)** in West Bengal was coordinated by the Indian Institute of Chemical Biology. During the two days programme, the students were taken to different laboratories for demonstration of the on-going activities at CSIR-IICB & CSIR-CGCRI. A programme on career opportunities was also arranged. 107 students from the CBSE and

तथा डब्लूबीबीएसइ बोर्ड के 107 विद्यार्थियों ने इस कार्यक्रम में भाग लिया।

पशु, माइक्रोबियल, पादप विषाक्तता तथा सांप काटने पर प्रबंधन पर प्रथम राष्ट्रीय सम्मेलन (**एएमपीटीओएक्स 2010**) का आयोजन इंडियन इंस्टिट्यूट ऑफ केमिकल बायोलोजी तथा केपीसी मेडिकल कॉलेज एंड हॉस्पीटल द्वारा संयुक्त रूप से किया गया। इस कार्यक्रम में विभिन्न देशों, जैसे यूके, अमेरिका, रूस, स्लोवेनिया, ऑस्ट्रेलिया, सिंगापुर, मलेशिया, श्रीलंका, बंगलादेश, नेपाल एवं भारत के वैज्ञानिकों एवं तकनीशियनों ने भाग लिया।

सोसाइटी फॉर इनफॉर्मेशन साइंस (एसआईएस) का 27वां वार्षिक सम्मेलन तथा 'ओपेन एक्सेस : गेटवे टू ओपेन इनोवेशन' पर सम्मेलन बसु विज्ञान मंदिर, कोलकाता के साथ मिलकर सीएसआईआर–आईआईसीबी द्वारा आयोजित किया गया। इस संगोष्ठी का मुख्य उद्देश्य ओपेन एक्सेस मोडल के कुछ पहलुओं पर चर्चा करना था, जो विद्वतापूर्ण साहित्य को ऑनलाइन पढ़ने के लिए नि:शुल्क अवसर प्रदान करता है जो उचित लेखकीय योगदान के साथ और भी विस्तारित हो सकता है। इस तीन दिवसीय सम्मेलन का उद्देश्य इस दिशा में सक्रिय संलग्नता हेतु राष्ट्रीय स्तर पर वैज्ञानिक एवं तकनीशियन समुदाय के लोगों को अभिप्रेरणा प्रदान करना था। इस बैठक में पूरे देश के विभिन्न संस्थानों तथा पुस्तकालयों के विद्वान व्यक्तियों तथा विभिन्न अंतरराष्ट्रीय प्रकाशकों के ज्ञानवान अनेक लोगों ने भाग लिया।

ननलाइनियर डायनामिक्स ऑफ इलेक्ट्रोनिक सिस्टम पर 19वीं आईईईई अंतरराष्ट्रीय कार्यशाला (एनडीइएस 2011) सीएसआईआर–आईआईसीबी में साहा इंस्टिट्यूट ऑफ न्यूक्लियर फिजिक्स, कोलकाता के साथ संयुक्त रूप से आयोजित की गई। बैठक में इलेक्ट्रोनिक पद्धति पर विशेष बल देते हुए ननलाइनियर गतिकी के विभिन्न मुद्दों पर विचार–विमर्श किए गए। सीएसआईआर–आईआईसीबी से संबंधित कुछ संगत विषय थे — कार्डिएक मोडल, न्यूरोडायनामिक्स तथा सिंथेटिक जीवविज्ञान। तीन दिवसीय बैठक में विभिन्न देशों, जैसे अमेरिका, फ्रांस, जर्मनी, आस्ट्रिया, ताईवान, स्पेन, नाइजेरिया, चीली, बंगलादेश तथा भारत के एक सौ से अधिक अनुसंधानकर्ताओं, संकाय सदस्यों एवं विद्यार्थियों ने भाग लिया।

संस्थान ने 9 से 14 सितंबर के दौरान **हिंदी सप्ताह** का आयोजन किया, जिसमें हिंदी में वाद–विवाद प्रतियोगिता, प्रारूपण एवं आलेखन प्रतियोगिता का आयोजन और साथ ही हिंदी में

WBBSE boards attended the programme.

A four day conference and the 1st National Conference on Animal, Microbial, Plant Toxins & Snakebite Management **(AMPTOX 2010)** was organized jointly by Indian Institute of Chemical Biology & KPC Medical College & Hospital. This programme was also attended by Scientists and clinicians from different countries, namely UK, USA, Russia, Slovenia, Australia, Singapore, Malayasia, Sri Lanka, Bangladesh, Nepal and India.

The 27th **Annual Convention of Society for Information Science** (SIS) and conference on "Open Access: Gateway to Open Innovation" was organized by CSIR-IICB in association with Bose Institute, Kolkata. The main objective of the symposium was to discuss some aspects of Open Access model which provides opportunities for free and online access to scholarly literature that can be disseminated further with proper author attribution. The three day conference was intended for motivation of scientific and technological community at national level for their active involvement in this direction. The meeting was attended by a significant number of knowledge resource personnel nationwide from different institutions and libraries and also personnel from different international publishers.

The 19th **IEEE International Workshop on Nonlinear Dynamics of Electronic System** (NDES 2011) was held in the CSIR-IICB jointly with the Saha Institute of Nuclear Physics, Kolkata. The different issues of nonlinear dynamics with an emphasis on electronic system were discussed in the meeting. Some of the relevant topics to CSIR-IICB were cardiac models, neurodynamics, and synthetic biology. The three day meeting was participated by more than one hundred researchers, faculties and students, from different countries, namely, USA, France, Germany, Austria, Taiwan, Spain, Japan, Nigeria, Chile, Bangladesh and India.

The institute observed **Hindi Week** from 9-14 September by organizing different competitions like debate in Hindi, noting & drafting

वैज्ञानिक एवं तकनीकी शब्दावली के निर्माण पर एक कार्यशाला का आयोजन किया गया। संस्थान ने 14 सितंबर को एक राष्ट्रीय हिंदी दिवस का आयोजन भी किया।

समीक्षाधीन अवधि के दौरान सीएसआईआर–आईआईसीबी में बड़ी संख्या में राष्ट्रीय एवं अंतरराष्ट्रीय स्तर के ख्यातनामा वैज्ञानिकों तथा तकनीशियनों का आगमन हुआ, जिन्होंने व्याख्यान दिए तथा विभिन्न अनुसंधानकर्ताओं के साथ विचार–विमर्श किया। इनमें से डब्लूबीजीइडीसीएल के प्रबंध निदेशक श्री एस पी गोन चौधुरी द्वारा 'राष्ट्रीय सौर मिशन' पर दिया गया व्याख्यान; अमेरिका के यूनिवर्सिटी ऑफ टेक्सास के डॉ. चेंग मिंग चियांग का 'एपिजेनेटिक कंट्रोल ऑफ क्रोमेटिन–डेवलपमेंट ट्रांसक्रिप्शन' पर वैज्ञानिक व्याख्यान देने हेतु आगमन; अमेरिका के यूनिवर्सिटी ऑफ इलिनोयस, चिकागो के प्रो. आनन्द मोहन चक्रवर्ती का 'टेक्नोलोजी ट्रांसफर फ्रॉम बेंच टू बेडसाइड फ्यूचर जेनेरेशन ड्रग्स' पर व्याख्यान देने हेतु आगमन; एफएआई कंपनी, नीदरलैंड के निदेशक डॉ. डब्लू एम बुजिंग का 'एप्लिकेशन ऑफ ट्रांसमिशन इलेक्ट्रोन माइक्रोस्कोपी इन स्ट्रक्चरल एंड सेलुलर बायोलोजी' पर तकनीकी व्याख्यान देने हेतु आगमन तथा अमेरिका के यूनिवर्सिटी ऑफ टेक्सास, गालवेस्टन के प्रो. शंकर मित्रा का 'इंडोजेनस ऑक्सीडेटिव स्ट्रेस एंड सेल सरवाइवल' पर व्याख्यान देने हेतु आगमन बहुत ही उल्लेखनीय रहा। ग्रीष्म प्रशिक्षण तथा अन्य प्रशिक्षण कार्यक्रमों में भारत के विभिन्न संस्थानों तथा विश्वविद्यालयों के लगभग 107 विद्यार्थियों ने भाग लिया। हमारे संस्थान के काफी संख्यक वैज्ञानिक पड़ोसी विश्वविद्यालयों एवं संस्थानों में शिक्षण एवं प्रशिक्षण कार्यक्रमों से जुड़े रहे। संस्थान ने संस्थान का स्थापना दिवस तथा सीएसआईआर स्थापना दिवस का आयोजन भी किया।

इस अवधि के दौरान हमारे संस्थान ने पूरे भारत में छह प्रदर्शनियों में प्रतिभागिता की, जिनमें **सीएसआईआर टेक्नो फेस्ट 2010** तथा **98वां भारतीय विज्ञान कांग्रेस** 'विज्ञान प्रदर्शिनी' शामिल है। इन सभी प्रदर्शिनियों में सीएसआईआर–आईआईसीबी के चल रहे अनुसंधान एवं विकास कार्यक्रमों की उपलब्धियों को रोचक तरीके से पोस्टर एवं फोटोग्राफ लगाकर प्रदर्शित किया गया।

उच्च प्रभाव कारक वाली पत्रिकाओं में गुणवत्तायुक्त बड़ी संख्या में आलेखों का प्रकाशन इस संस्थान के अनुसंधान के क्षेत्र में हुई प्रगति को द्योतित करता है और प्रकाशनों का औसत प्रभाव कारक लगातार बढ़ रहा है। 2010 –11 की

competitions and a workshop was conducted on "Scientific and Technical vocabulary in Hindi". The institute also celebrated National Hindi Day on 14th September.

A large number of scientists and technologists of national and international repute visited our institute, delivered lectures and held discussions with different research groups in CSIR-IICB during this reporting year. Among which a lecture on "National Solar Mission" by Mr. S P Gon Choudhury, Managing Director, WBGEDCL, visit of Dr. Cheng Ming Chiang, University of Texas, USA for scientific lecture on "Epigenetic Control of Chromatin- Development Transcription", visit of Prof Ananda Mohan Chakraborty, University of Illinois, Chicago, USA for a lecture on "Technology transfer from bench to bedside – future generation drugs", visit of Dr. W M Busing, Director, FEI Company, Netherlands with a technical lecture on "Application of Transmission Electron Microscopy in Structural and Cellular Biology" and visit of Prof. Sankar Mitra, University of Texas, Galveston, USA for a lecture on "Endogenous Oxidative Stress and Cell Survival" are most significant. About 107 students from different universities and institutes of India participated in summer training and other training programmes. A large number of Scientists of our institute were involved in teaching and training programmes of neighbouring universities and institutes. The institute also pertinently observed Institute Foundation day and CSIR Foundation day.

During the period our institute participated in six exhibitions all over India which includes **CSIR Techno Fest 2010** and **98th Indian Science Congress** "Science Exhibition". In all of these exhibitions the achievements and on going R&D works of CSIR-IICB were presented in popular ways with posters and photographs.

A steady number of quality publications in journals of high impact factors are the hallmark of the institute's progress in research and the average impact factor of publications is increasing

निदेशक की कलम से
FROM DIECTOR'S DESK

अवधि में वैज्ञानिक प्रकाशनों की कुल संख्या **145** तक पहुँच गई। मुझे यह कहते हुए गर्व महसूस होता है कि सीएसआईआर–आईआईसीबी के अनुसंधान से संबंधित प्रकाशनों का औसत प्रभाव कारक इस वर्ष **3.3** तक पहुँच गया है।

पूरी समीक्षाधीन अवधि के दौरान सीएसआईआर–आईआईसीबी ने अस्थमा, गैस्ट्रोपैथी, कैंसर तथा अन्य सामान्य मानवीय रोगों के रोकथाम के लिए पादप संसाधनों से जैवसक्रिय यौगिकों के संश्लेषण, नि:स्रवण तथा कालाजार के परीक्षण हेतु पद्धति के लिए ग्यारह राष्ट्रीय एवं अंतरराष्ट्रीय पेटेंट दायर किया हैं। इस अवधि में विदेश में कुल तीन पेटेंटों की मंजूरी हुई है तथा भारत में एक पेटेंट स्वीकृत हुआ है।

सीएसआईआर–आईआईसीबी सदैव जैविक एवं रासायनिक क्षेत्रों में कार्य करने की अभिलाषा रखने वाले प्रतिभाशाली अनुसंधानकर्ताओं के लिए पसंदीदा केन्द्र रहा है। इस वर्ष इस संस्थान ने पूरे देश से बड़ी संख्या में मेधावी युवा अनुसंधानकर्ताओं एवं अनुसंधान एसोसिएटों को आकर्षित किया है जिससे जीवविज्ञान तथा रसायन के क्षेत्र में तथा संबंधित विभिन्न क्षेत्रों में पर्याप्त तथा प्रशिक्षित मानव संसाधन का निर्माण होगा और सीमान्त अनुसंधान की जरूरतों की पूर्ति होगी। 2010–11 के दौरान लगभग 274 फेलो एवं अनुसंधान एसोसिएटों ने इस संस्थान में कार्य किया। हमारे संस्थान में सीएसआईआर–आईआईसीबी में पीएच.डी. विद्यार्थियों के लिए आयोजित पाठ्यक्रम कार्य के संदर्भ में सीएसआईआर द्वारा हाल ही में प्रारंभ किए गए एकेडमी ऑफ साइंटिफिक एंड इनोवेटिब रिसर्च (एसीएसआईआर) के द्वारा परीक्षा लेना, उम्मीदवारो का मूल्यांकन तथा कार्यक्रम के एकीकरण का कार्य किया गया।

मैं अपने संस्थान के सभी वैज्ञानिक, तकनीकी तथा प्रशासनिक स्टाफ सदस्यों के प्रति उनके वर्ष व्यापी गहन क्रियाकलापों तथा सीएसआईआर–आईआईसीबी के विकास एवं प्रतिष्ठा को बनाए रखने में सहयोग के लिए हार्दिक आभार व्यक्त करता हूँ। मैं यह भी मानता हूँ कि हमारे सहकर्मियों द्वारा जो निष्ठा प्रदर्शित की गई है, वह आने वाले दिनों में इस संस्थान को नई ऊँचाइयों पर प्रतिष्ठित करेगी।

प्रो. सिद्धार्थ राय
सीएसआईआर–आईआईसीबी
कोलकाता

continuously. For the period of 2010-11 the total number of scientific publications reached **145**. I am proud in finding that the average impact factor of research publications of CSIR-IICB has reached **3.3** this year.

Throughout the reporting period CSIR-IICB has filed eleven national and international patents related to synthesis, extraction of bioactive compounds from herbal resources to combat asthma, gastropathy, cancer and other common human diseases, and method for diagnosis of kala azar. Total three patents have been granted abroad and one in India in this period.

CSIR-IICB has always remained as a centre of choice for promising researchers with ambition to work in biological and chemical fields. This year the institute has attracted a large number of bright, young research fellows and research associates from all over the country to generate adequate and trained human resource in the different fields of Biology and Chemistry and related areas for meeting the requirement of cutting edge research. During 2010-11 around 274 fellows and research associates worked in this institute. In the context of course work conducted for the PhD students at CSIR-IICB, taking examination, evaluation of the candidates and integration of the programs with recently launched Academy of Scientific and Innovative Research (AcSIR) by CSIR, an Academic Affairs Division has been established in our institute.

I extend my cordial gratitude to all the scientific, technical and administrative staff members of our institute for their year long sincere activity and cooperation in sustaining the growth and maintaining the reputation of CSIR-IICB. I also believe that the dedication offered by my colleagues will take the institute to a new height in coming days.

Prof. Siddhartha Roy
CSIR-IICB
Kolkata

उपलब्धियों की एक झलक

सम्मान

- डॉ. पिजुस के दास को सितंबर 2010 में विज्ञान और प्रौद्योगिकी विभाग, भारत के द्वारा सर जे.सी. बोस राष्ट्रीय अध्येता पुरस्कार से पुरस्कृत किया गया।
- डॉ. के. पी. मोहनाकुमार को वर्ष 2010–2011 के दौरान वरिष्ठ भारतीय वायोमेडिकल वैज्ञानिक के लिए आई.सी.एम.आर अन्तरराष्ट्रीय अध्येता के रूप में सम्मानित किया गया।
- डॉ. चित्रा मंडल को जनवरी–2011 में विज्ञान और प्रौद्योगिकी विभाग द्वारा सर. जे. सी. बोस राष्ट्रीय अध्येता पुरस्कार से पुरस्कृत किया गया।
- डॉ. श्यामल राय को वर्ष 2010 में राष्ट्रीय विज्ञान अकादमी (एफएनएएससी) भारत के अध्येता (फेलो) के लिए मनोनीत किया गया।
- डॉ. अरूण बन्दोपाध्याय को वर्ष 2010 में पश्चिम बंगाल अकादमी विज्ञान और प्रौद्योगिकी (डब्ल्यू.ए.एस.टी) के अध्येता के रूप में मनोनीत किया गया।
- डॉ. स्नेहसिक्ता स्वर्णकार को वर्ष 2010 में पश्चिम बंगाल अकादमी विज्ञान और प्रौद्योगिकी (डब्ल्यू.ए.एस.टी) के अध्येता के रूप में मनोनीत किया गया।
- डॉ. देबाशीष भट्टाचार्य को अक्टूबर 2010 में एसबीसीएन (सोसाइटी फॉर वायो क्रोमेटोग्राफी एण्ड नैनोसेपारेसन), लेयोन, फ्रांस के सम्मानीय सदस्य के रूप में मनोनीत किया गया।
- डॉ. देबाशीष भट्टाचार्य को फरवरी–2011 में भारतीय स्पेक्ट्रोफिजिक्स ऐसोसिएसन पुरस्कार 2009 से पुरस्कृत किया गया।
- डॉ. आशिष कुमार सेन को वर्ष 2010 में एसोसिएसन ऑफ कार्बोहाइड्रेट केमिस्ट एण्ड टेक्नोलोजिस्ट, भारत के जीवन–काल उपलब्धि पुरस्कार से पुरस्कृत किया गया।
- डॉ. सुभेन्द्र भट्टाचार्य को वर्ष 2010 में भारतीय विज्ञान अकादमी, बैंगलोर के एक सहयोगी के रूप में मनोनीत किया गया।

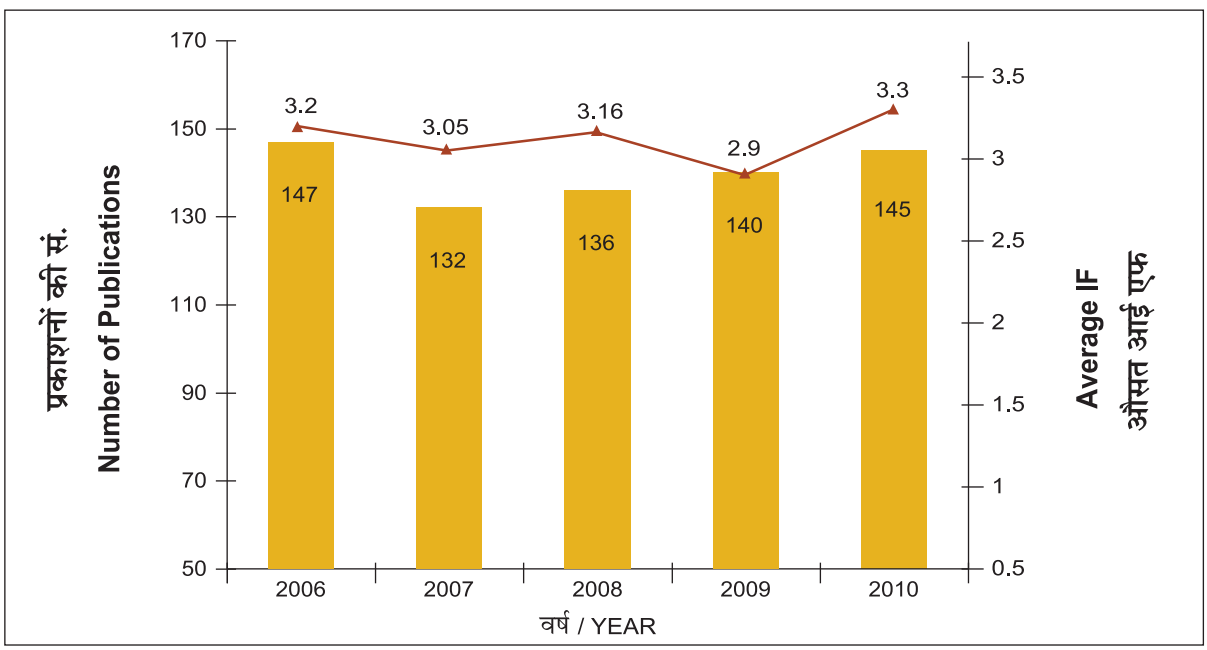
उपलब्धियों की एक झलक

प्रकाशन

अनुसंधान प्रकाशन – 2010	
कुल प्रकाशित कागजात	145
पुनर्निरीक्षण एवं वैगर एससीआई प्रकाशन	13
अनुसंधान प्रकाशन	132
कागजातों की संख्या आई.एफ. के संग ≥ 6	04
कागजातों की संख्या आई.एफ. के संग ≥ 5 < 6	07
कागजातों की संख्या आई.एफ. के संग ≥ 4 < 5	23
कागजातों की संख्या आई.एफ. के संग ≥ 3 < 4	38
कागजातों की संख्या आई.एफ. के संग ≥ 2 < 3	39
कागजातों की संख्या आई.एफ. के संग ≥ 1 < 2	15
कागजातों की संख्या आई.एफ. के संग < 1	06
कुल एम्पैक्ट फैक्टर	437.051
आई.एफ. प्रति कागजात	3.310
आई.एफ. प्रति वैज्ञानिक	6.070

संस्थान में प्रत्येक वर्ष स्थायी रूप से कई पेटेन्ट का पंजीकरण एवं स्वीकृति। निम्नलिखित आरेखों के द्वारा गत पाँच वर्षों का स्वीकृत पेटेन्टस* एवं पंजीकृत पेटेन्टस चित्रित है :

आई आई सी बी प्रकाशन

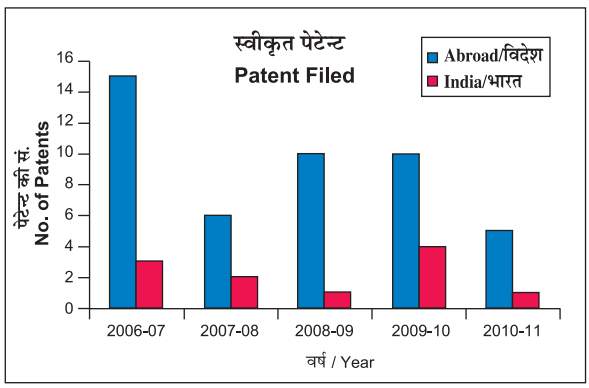


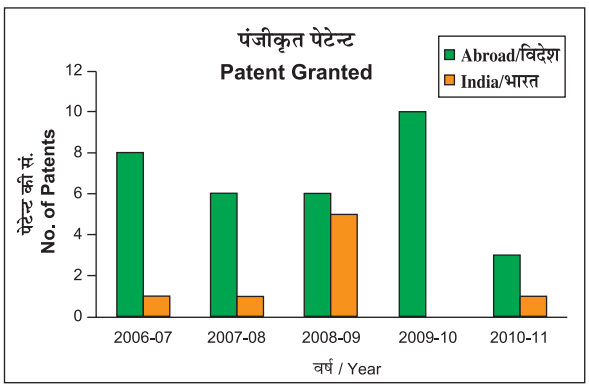
*2010–11 के लिए प्रकाशनों की विस्तृत सूची अन्दर अलग दिया गया है।

उपलब्धियों की एक झलक

पेटेन्ट

संस्थान में प्रत्येक वर्ष स्थायी रूप से कई पेटेन्ट* का पंजीकरण एवं स्वीकृति। निम्नलिखित आरेखों के द्वारा गत पाँच बर्षों का स्वीकृत पेटेन्टस एवं पंजीकृत पेटेन्टस चित्रित है :





*वर्ष 2010–11 में पंजीकृत एवं स्वीकृत पेटेन्ट की सूची संस्थान के प्रकाशन एवं सूचना विभाग के रिपोर्ट में दर्ज है।

उपलब्धियों की एक झलक

उद्योग–संस्थान का गठजोड़

संस्थान, उद्योग के साथ निरंतर एकीकरण बनाए रखा है एवं सफलतापूर्वक ज्ञान को धन में परिवर्तित कर रहा है। इस वर्ष आई. आई. सी. बी. के वैज्ञानिकों ने उद्योग के साथ पारस्परिक संबंध को बनाए रखने में एवं प्रर्याप्त मानवीय एवं वित्तीय संसाधन जुटाने में अपने को सक्षम बनाए रखा।

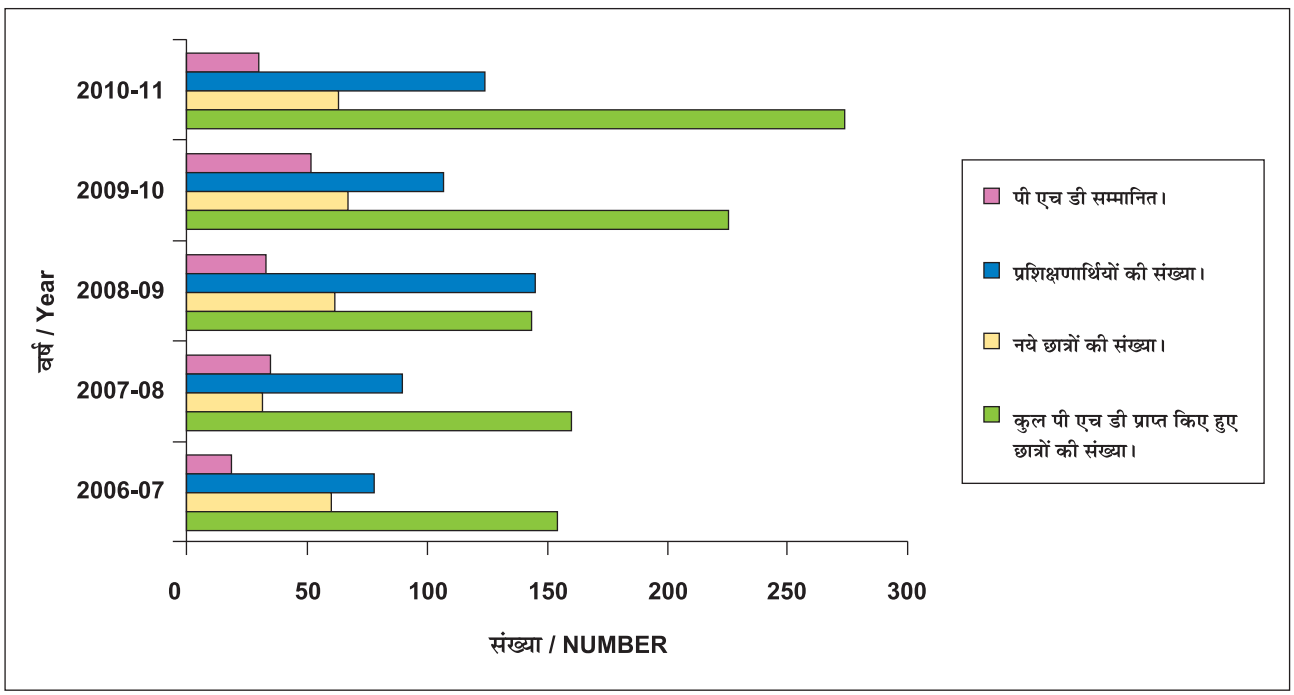
गेट (GATT)– भारत व्यवस्था के साथ सम्पूर्ण विकास के लिए हमारे सहयोगी इस प्रकार है:–

- चटर्जी मनेजमेन्ट सर्वीसेस प्राइवेट लिमिटेड, कोलकाता।
- ईस्ट इंडिया फार्मास्यूटिकल्स वर्क्स लिमिटेड, कोलकाता।
- एनजीओजेन फार्मास्यूटिकल्स (पीटीइ) लिमिटेड, आस्ट्रेलिया।
- केमबायोटेक रिसर्च इन्टरनेशनल प्राइवेट लिमिटेड, कोलकाता।
- डेज मेडिकल स्टोर्स (मैनुफैक्चरिंग) लिमिटेड, कोलकाता।
- बायोटेक कानसोरटीयम (आई) लिमिटेड, नई दिल्ली।
- शान्ता वायोटेकनिक्स लिमिटेड, हैदराबाद।
- पीरामल लाइफ सर्वीसेस लिमिटेड, मुंबई।
- एलबर्ट डेविड लिमिटेड, कोलकाता।
- क्वालप्रो डायग्नोस्टिक, गोवा।
- मेरियल एस ए एस लिन, फ्रांस।
- जेफिर बायोमेडिकल, गोवा।
- मोलोजेन एजी, जर्मनी।
- क्वायर वोर्ड, कोची।
- डी एन डी आई, फ्रांस।

उपलब्धियों की एक झलक

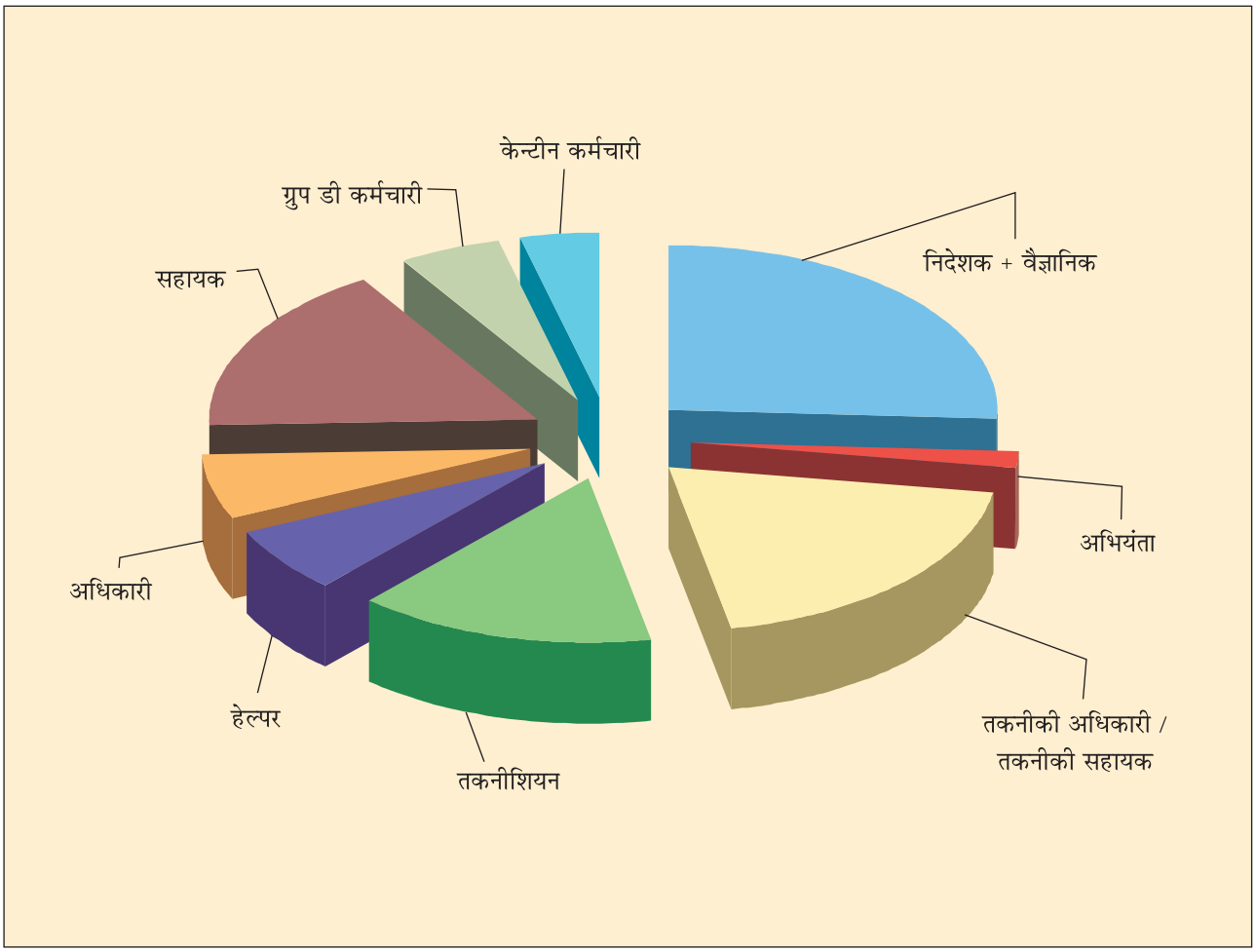
मानव संसाधन विकास

हर वर्ष कई अनुसंधानकर्ता डॉक्टरेट एवं पोस्टडॉक्टरेट स्तर पर अपना अनुसंधान जारी रखते हैं। देश के विभिन्न विश्वविद्यालयों से अनेक विद्यार्थी यहाँ हर वर्ष अल्पकालीन प्रशिक्षण प्राप्त करते हैं। गत पाँच वर्षों का आँकड़ा ग्राफ के माध्यम से प्रस्तुत है:-



उपलब्धियों की एक झलक

31 मार्च, 2011 तक कर्मचारी की संख्या



कुल कर्मचारी – 266

वैज्ञानिक एवं तकनीकी कर्मचारी – 181

निदेशक – 1, वैज्ञानिक – 68, अभियन्ता – 4, तकनीकी अधिकारी एवं सहायक – 52, तकनीशियन – 39, हेल्पर – 17

प्रशासनिक कर्मचारी – 85

अधिकारी – 17, सहायक – 44, ग्रुप डी – 14, कैन्टीन – 10

कर्मचारी अनुपात

वैज्ञानिक : तकनीकी कर्मचारी : सहायक कर्मचारी – 1:1.6:1.2

संस्थान में राजभाषा कार्यान्वयन

राजभाषा अधिनियम के अनुसार इस वर्ष संस्थान में राजभाषा कार्यान्वयन का दैनिक क्रियाकलाप में विभिन्न प्रयोगिक उपयोग का विशेष उल्लेख जैसे–दैनिक अनुवाद, हिन्दी शब्द लिखना एवं प्रदर्शन इत्यादि के साथ कार्यालय ज्ञापन तैयार करना, सामान्य आदेश, सूचना, निविदा इत्यादि को द्विभाषी रूप में जारी करने तक सीमित नही है, बल्कि राजभाषा अधिनियम 3(3) के अनुसार संस्थान में इसका सफलतापूर्वक पालन किया जा रहा है।

13 सितंबर 2010 को आयोजित हिन्दी सप्ताह के अंतर्गत हिन्दी वाद–विवाद प्रतियोगिता का आयोजन किया गया। वाद–विवाद का विषय था – ''लोक सेवा में महिलाओं के लिए आरक्षण अनिवार्य है''। इस प्रतियोगिता में डॉ. सिद्धार्थ मजुमदार और श्री प्रियंकर पालीवाल निर्णायक के रूप में उपस्थित थे।

तत्पश्चात अपराह्न 2.30 बजे से हिन्दी कार्यशाला का दूसरा सत्र सीजीसीआरआई के वरिष्ठ हिन्दी अधिकारी, श्री प्रियंकर पालीवाल की अध्यक्षता में आरम्भ किया गया। उन्होंने ''हिन्दी वैज्ञानिक लेखन एवं तकनीकी शब्दावली'' पर व्याख्यान प्रस्तुत किये। उन्होंने तकनीकी शब्दावली के प्रयोग के कई शब्दों का सटीक प्रयोग बताया एवं शब्दों के विभिन्न उपयोग तथा उनके विभिन्न व्यावहारिक प्रयोगों का उदाहरण देते हुए सभी को नये–नये तकनीकी शब्दों से अवगत कराया एवं तकनीकी शब्दों के प्रयोग में आने वाली कठिनाईयों का हल बताया।

14 सितंबर, 2010 हिन्दी दिवस पर प्रो. अमरनाथ शर्मा, हिन्दी विभाग, कोलकाता विश्वविद्यालय, कोलकाता मुख्य अतिथि के रूप में तथा श्री रामनारायण सरोज, उप–निदेशक, हिन्दी शिक्षण योजना, निजाम पैलेस, कोलकाता सम्मानीय अतिथि एवं विभिन्न प्रतियोगिताओं के निर्णायक के रूप में विराजमान थे। निदेशक की अस्वस्थता के कारण संस्थान के वरिष्ठतम वैज्ञानिक डॉ. समीत अड्या को अध्यक्ष बनाया गया। वरिष्ठ वैज्ञानिक डॉ. टी.के. धर ने प्रतियोगिता में भाग लेने वाले कर्मचारियों/अधिकारियों को पुरस्कार से प्रोत्साहित किए। हिन्दी दिवस पर आमंत्रित मुख्य अतिथि प्रो. अमरनाथ शर्मा जी ने हिन्दी के विकास तथा राजभाषा हिन्दी के प्रगामी प्रयोग पर कार्यान्वित करने पर प्रोत्साहित किया। संस्थान राजभाषा कार्यान्वयन में अभिरूचि रखते हुए कर्मचारियों के बीच प्रतियोगिताएँ आयोजित करता है जिसकी सराहना करते हुए उन्होनें संस्थान में हिन्दी में काम करने की कार्य संस्कृति की प्रशंसा किये। साथ ही साथ उन्होनें कहा कि हिन्दी एक ऐसी भाषा है जिसे देश के सभी लोग आसानी से समझ लेते है। श्री रामनारायण सरोज ने भी संस्थान के हिन्दी कार्यकलापों पर अपनी खुशी व्यक्त करते हुए इसे बनाए रखने के लिए सभी से आग्रह किया। सभा में दिये गए 50 हिन्दी शब्द को पुरस्कृत किया गया। इस दिन कई और प्रतियोगिताओं का आयोजन किया गया जिसमें निर्णायक के रूप में डॉ. सिद्धार्थ मजुमदार, तकनीकी अधिकारी, आईआईसीबी एवं श्री विजय शंकर मिश्रा, हिन्दी शिक्षक जी विराजमान थे। काव्य–आवृत्ति एवं तत्काल भाषण जैसे प्रतियोगिता में कई अधिकारी एवं कर्मचारी के साथ–साथ नाईपर के विद्यार्थियों ने भी हिस्सा लिया और पुरस्कार ग्रहण किया।

अंत में संस्थान के श्री एस. के. चौधुरी, प्रशासनिक अधिकारी द्वारा धन्यवाद ज्ञापन के साथ हिन्दी दिवस सम्पन्न हुई। आईआईसीबी के वरिष्ठ हिन्दी अनुवादक श्रीमती ए. नाग ने इस हिन्दी दिवस का संचालन सफलतापूर्वक किया।

Science Exhibition

Science Exhibition

Performance at a Glance

THE LAURELS

- Dr. Pijush K. Das received Sir J.C. Bose National Fellowship Award by Dept. of Science & Technology, India - September 2010.
- Dr. K.P. Mohanakumar was awarded ICMR International Fellowship for Senior Indian Biomedical Scientists during the year 2010 - 2011.
- Dr. Chitra Mandal received J.C. Bose Fellowship award by Department of Science and Technology in January, 2011.
- Dr. Syamal Roy was elected as Fellow of National Academy of Sciences India (FNASc) in 2010.
- Dr. Arun Bandyopadhyay was elected as Fellow of West Bengal Academy of Science and Technology (WAST) in 2010.
- Dr. Snehasikta Swarnakar was elected as Fellow of West Bengal Academy of Science and Technology (WAST) in 2010.
- Dr. Debasish Bhattacharyya was elected as a Member of Honor of the SBCN (Society for Bio-Chromatography and Nanoseparation), Lyon, France in October, 2010.
- Dr. Debasish Bhattacharyya received Indian Spectrophysics Association Award 2009 in February, 2011
- Dr. Asish Kumar Sen received Life Time Achievement Award of the Association of Carbohydrate Chemists & Technologists, India in 2010.
- Dr. Suvendra Bhattacharyya was selected as an Associate of the Indian Academy of Sciences, Bangalore in 2010.

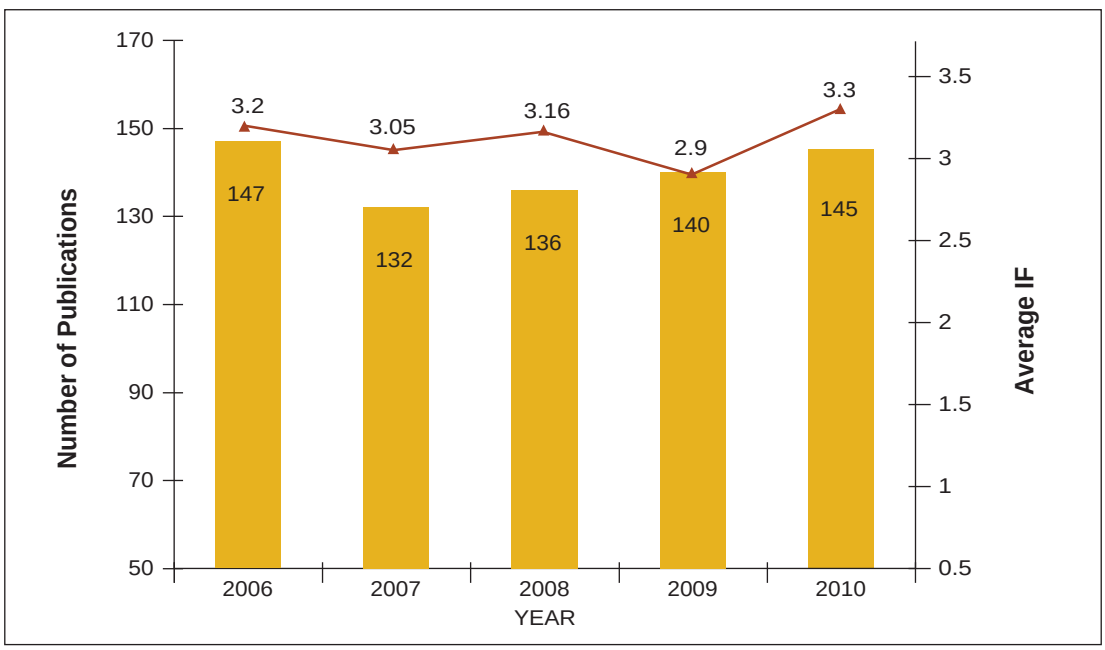
Performance at a Glance

PUBLICATIONS

Research Publication – 2010				
Total Publications	...	...	...	145
Review & Non SCI Publications	...	...	...	13
Research Publications	...	...	...	132
No. of Papers with IF ≥ 6	...	...	...	04
No. of Papers with IF ≥ 5 < 6	...	...	...	07
No. of Papers with IF ≥ 4 < 5	...	...	...	23
No. of Papers with IF ≥ 3 < 4	...	...	...	38
No. of Papers with IF ≥ 2 < 3	...	...	...	39
No. of Papers with IF ≥ 1 < 2	...	...	...	15
No. of Papers with IF < 1	...	...	...	06
Total IF	...	...	...	437.051
IF per Paper	...	...	...	3.310
IF per Scientist	...	...	...	6.070

A steady number of quality publications are the hallmark of the Institute's progress in research. Year-wise publications* and average impact factor (IF) for the last five years are given below:

IICB PUBLICATION

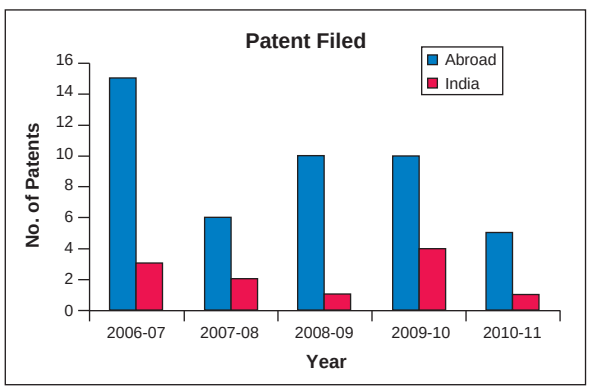


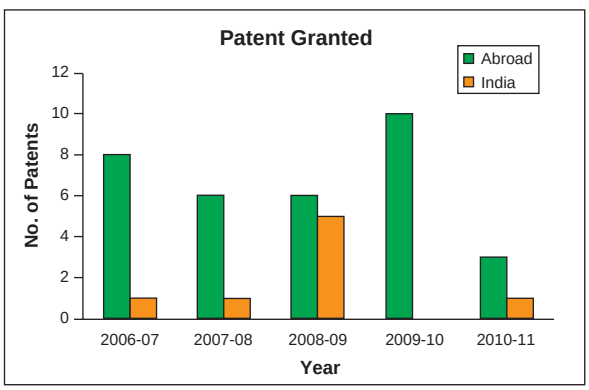
*Detailed list of publications for 2010-11 is given inside separately.

Performance at a Glance

PATENTS

A steady number of patents* are filed every year from the Institute and are granted.





*Lists of patents filed and granted in 2010-11 are given inside in the reports of P&I-PME Division.

Performance at a Glance

INSTITUTE - INDUSTRY TIE UP

The Institute is continuously building synergy with the industries and successfully converting knowledge into wealth. This year, IICB scientists have managed to sustain the same level of interaction with the industry and earn a considerable amount of resources both human and financial.

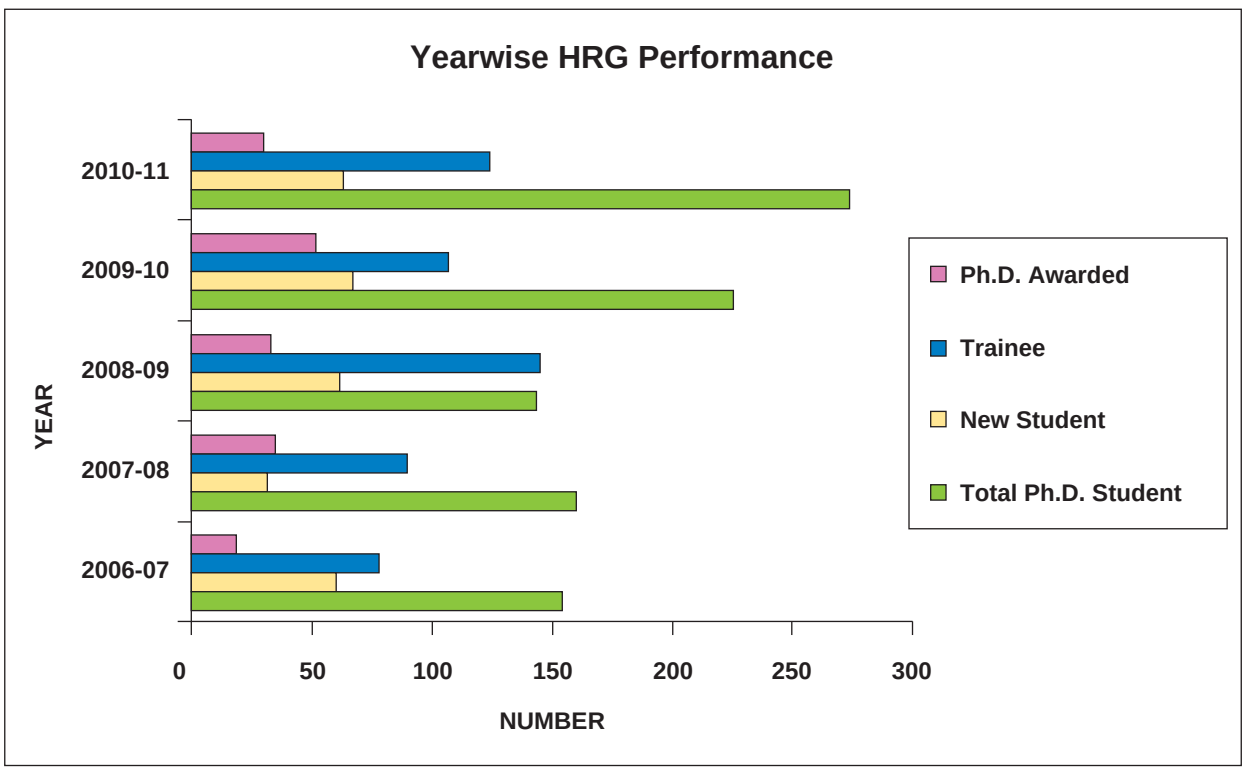
Our partners for the overall growth are as follows:

- ⇨ Chatterjee Management Services Pvt. Ltd., Kolkata
- ⇨ East India Pharmaceutical Works Ltd., Kolkata
- ⇨ Angiogen Pharmaceuticals Pte. Ltd., Australia
- ⇨ Chembiotech Research Int. Pvt. Ltd., Kolkata
- ⇨ Dey's Medical Stores (Mfg.) Ltd., Kolkata
- ⇨ Biotech Consortium (I) Ltd., New Delhi
- ⇨ Santha Biotechnics Ltd., Hyderabad
- ⇨ Piramal Life Sciences Ltd., Mumbai
- ⇨ Albert David Ltd., Kolkata
- ⇨ Qualpro Diagnostics, Goa
- ⇨ Merial SAS Lyn, France
- ⇨ Zephyr Biomedical, Goa
- ⇨ Mologen AG, Germany
- ⇨ Coir Board, Kochi
- ⇨ DNDi, France

Performance at a Glance

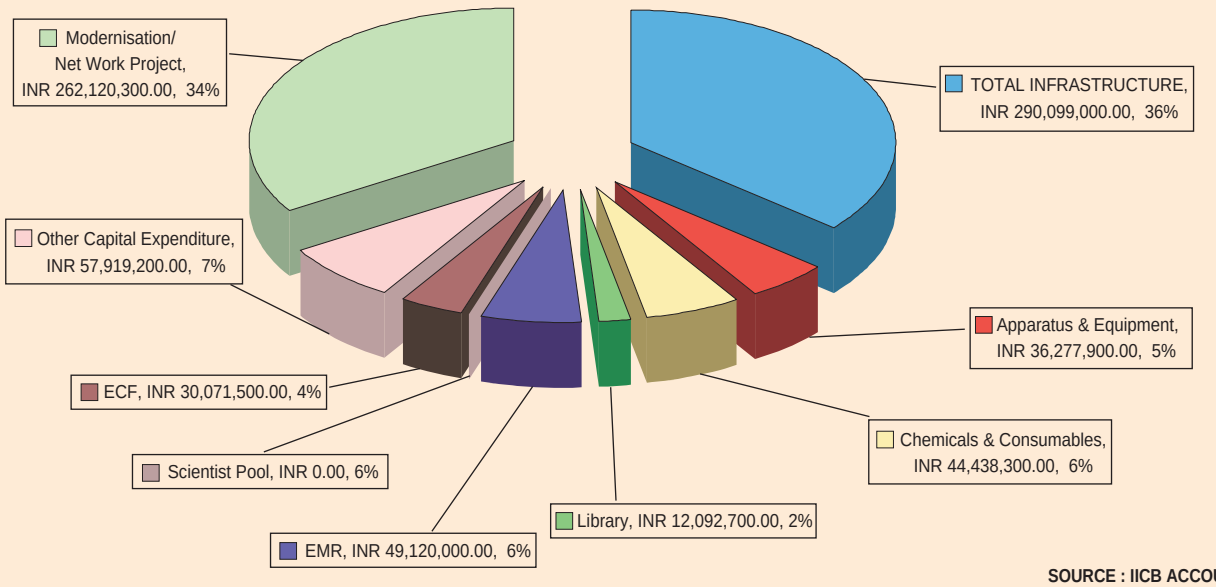
HUMAN RESOURCE DEVELOPMENT

A good number of research scholars carry out research at Doctoral and Post-doctoral levels each year. Several students from various universities of our country get short-term training in every year. Data for the last five years are presented graphically.



Performance at a Glance

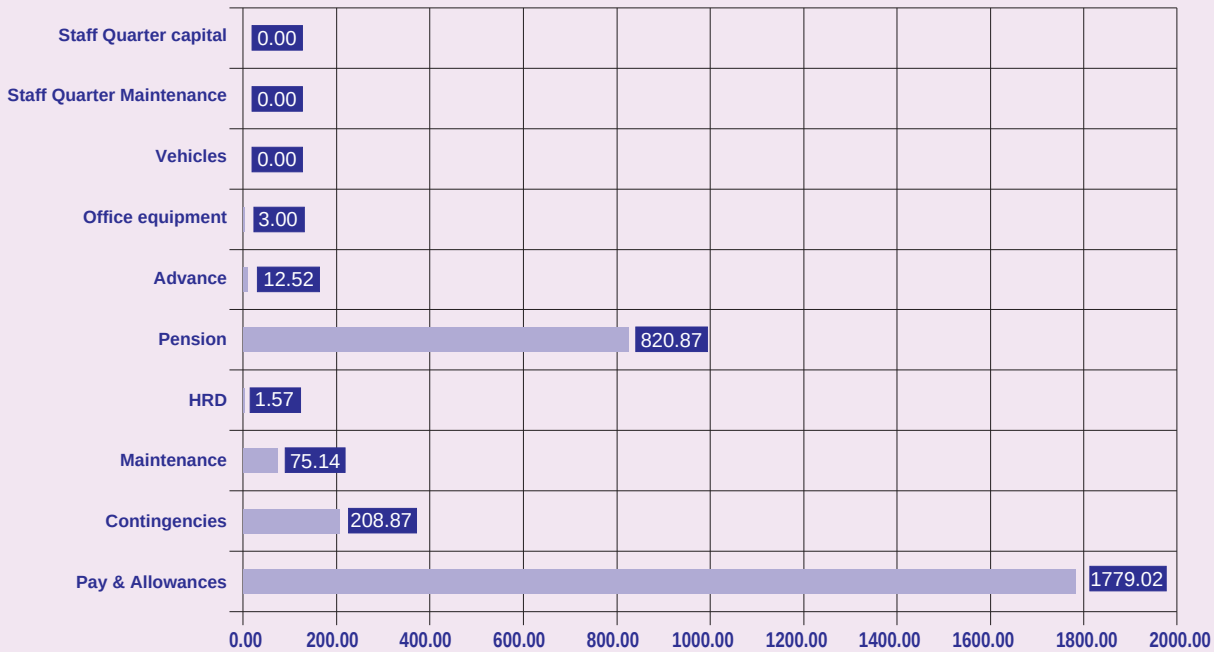
R & D AND TOTAL EXPENDITURE BREAK-UP 2010-11



SOURCE : IICB ACCOUNTS

SOURCE : IICB ACCOUNTS

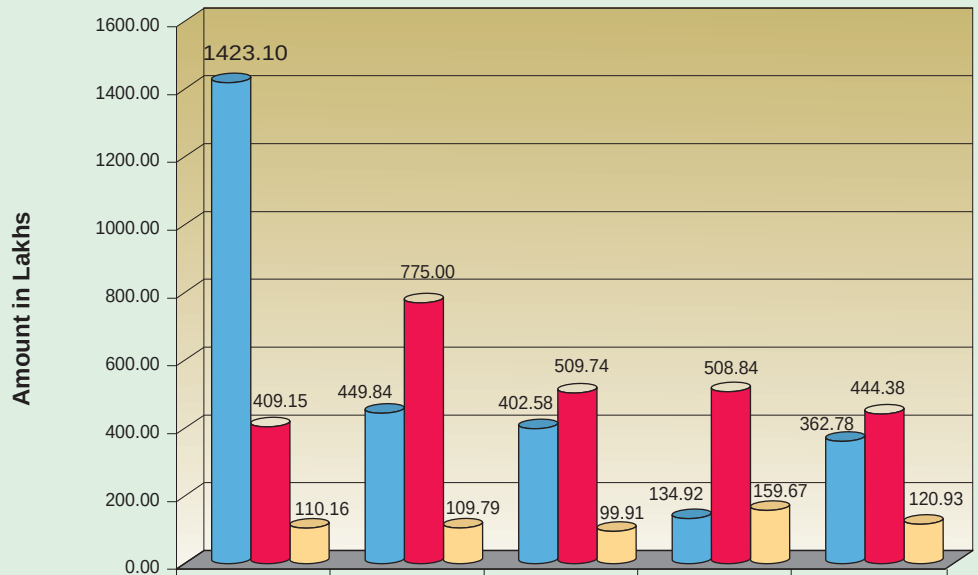
INFRASTRUCTURAL BREAKUP 2010-11



	Pay & Allowances	Contingencies	Maintenance	HRD	Pension	Advance	Office equipment	Vehicle	Staff Quarter Maintenance	Staff Quarter Capital
Amount in Lakhs	1779.02	208.87	75.14	1.57	820.87	12.52	3.00	0.00	0.00	0.00

Performance at a Glance

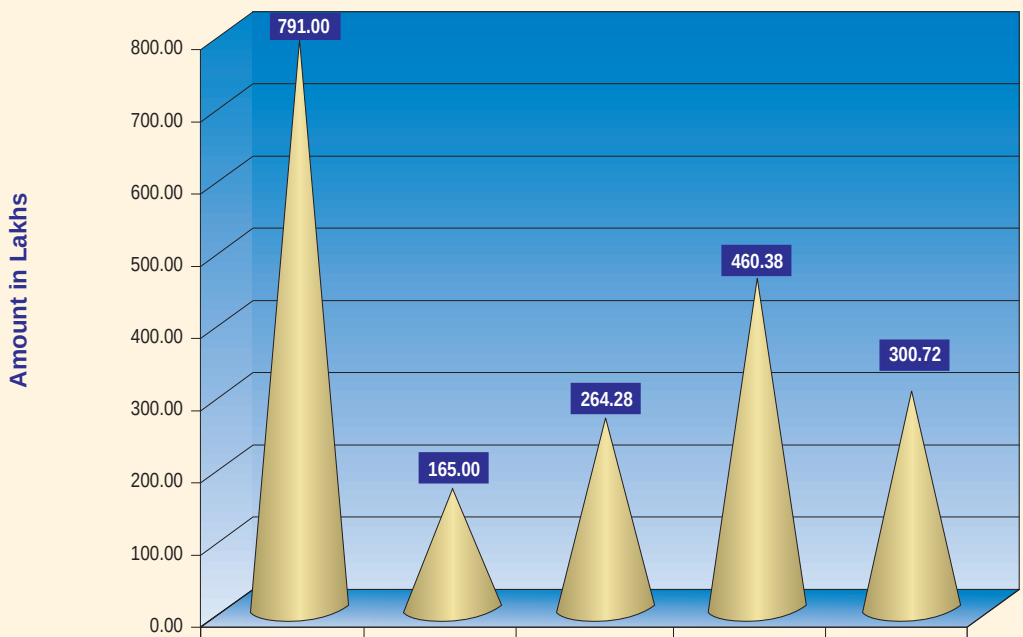
YEARLY EXPENDITURE W.E.F. 2006-07 TO 2010-11



	2006-07	2007-08	2008-09	2009-10	2010-11
Apparatus & Equipment	1423.10	449.84	402.58	134.92	362.78
Chemicals & Consumables	409.15	775.00	509.74	508.84	444.38
Library	110.16	109.79	99.91	159.67	120.93

SOURCE : IICB ACCOUNTS

EXTERNAL CASH FLOW OF IICB

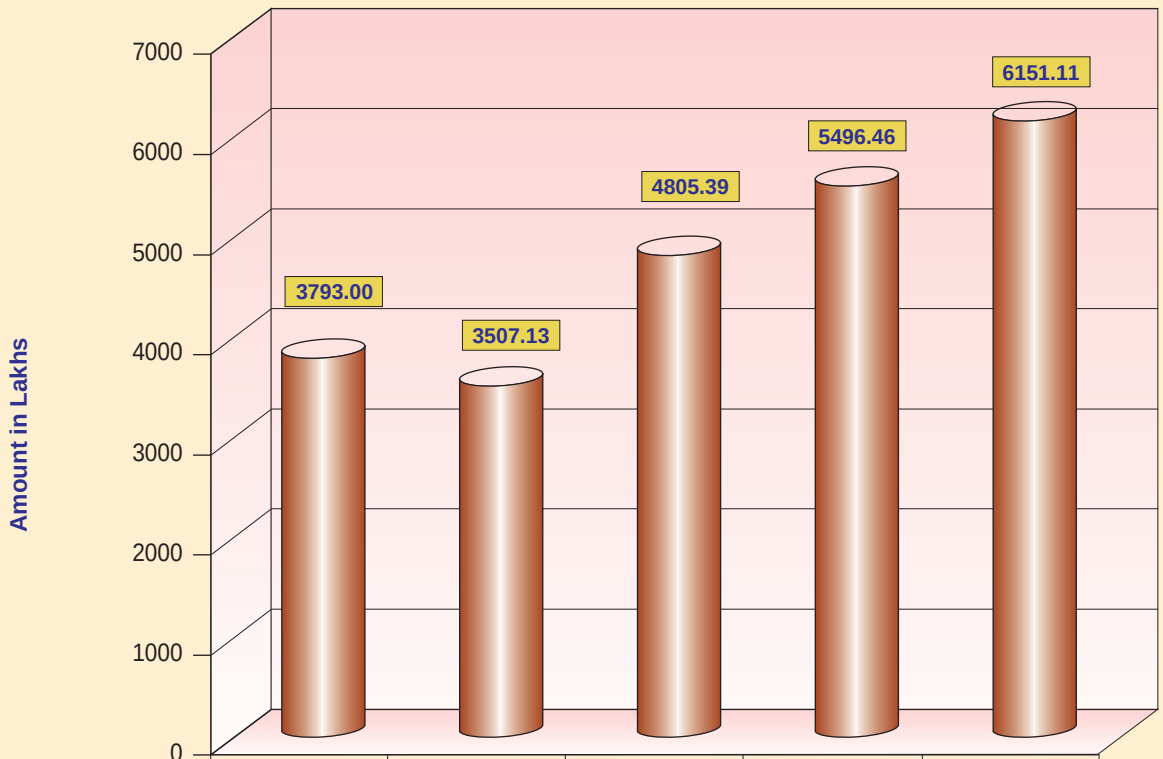


	2006-07	2007-08	2008-09	2009-2010	2010-11
Amount in Lakhs	791.00	165.00	264.28	460.38	300.72

SOURCE : IICB ACCOUNTS

Performance at a Glance

YEARWISE GRANT RECEIVED FROM CSIR

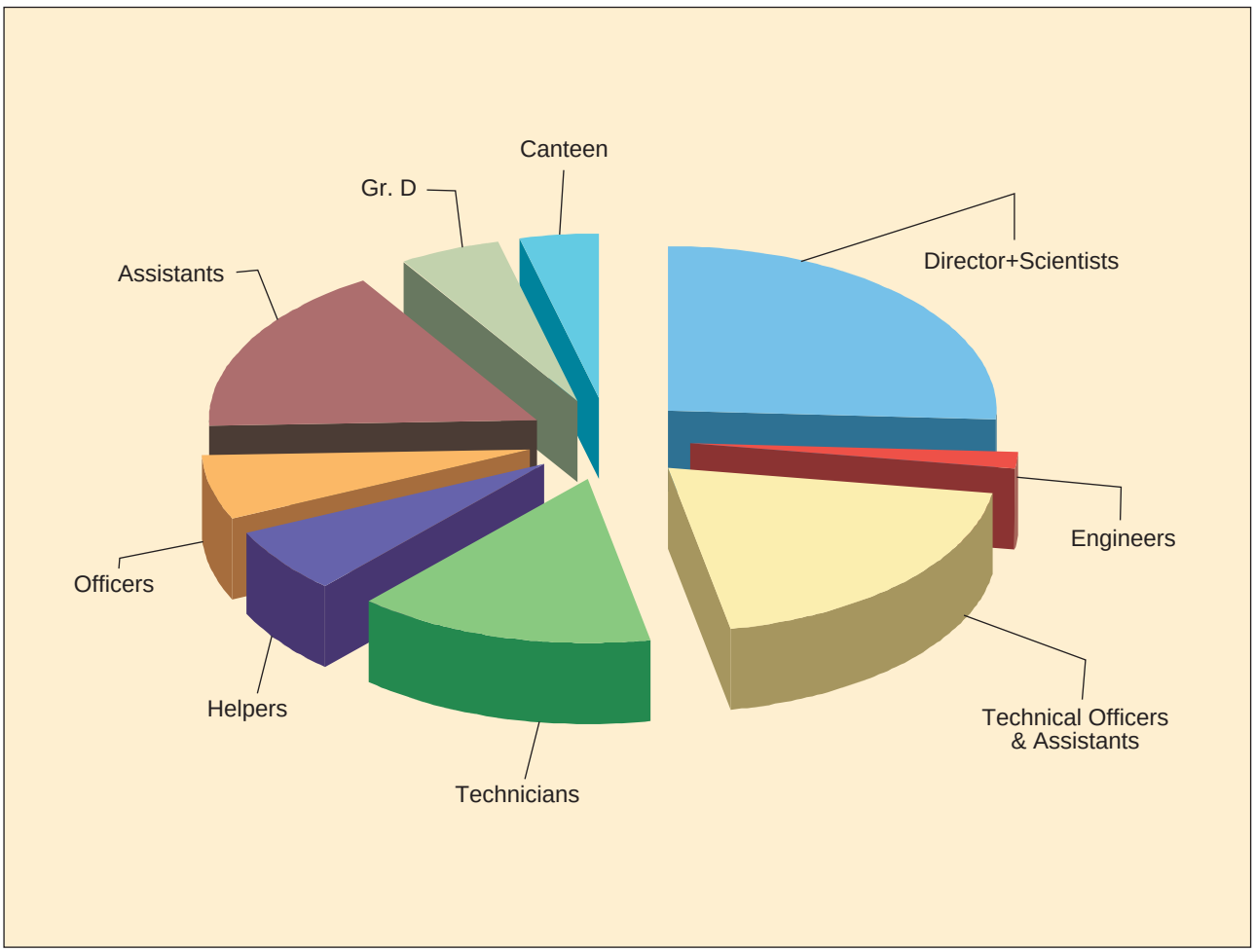


	2006-07	2007-08	2008-09	2009-10	2010-11
Grant	3793.00	3507.13	4805.39	5496.46	6151.11

SOURCE : IICB ACCOUNTS

Performance at a Glance

STAFF STRENGTH AS ON 31.03.2011



Total Staff – 266

Scientific & Technical Staff – 181

Director – 1, Scientists – 68, Engineers – 4, Technical Officers & Assistants – 52, Technicians – 39, Helpers – 17

Administrative Staff – 85

Officers - 17, Assistants - 44, Group D - 14, Canteen - 10

Staff Ratio

Scientist : Technical Staff : Supporting Staff = 1 : 1.6 : 1.2


भारतीय रासायनिक जीवविज्ञान संस्थान
4, राजा एस. सी. मल्लिक रोड, कोलकाता – 700032
68वाँ सीएसआईआर स्थापना दिवस समारोह
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INFECTIOUS DISEASES AND IMMUNOLOGY

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Research activity of infectious diseases and immunology group involves various fields of biological sciences with special interest to Leishmania and Cholera.

Dr. H. K. Majumder

Involvement of autophagy in cryptolepine induced cell death of L. donovani promastigotes

Leishmania donovani is the causative agent of visceral leishmaniasis worldwide. Lack of vaccines and emergence of drug resistance warrant the need for improved drug therapy and newer therapeutic intervention strategies against leishmaniasis. In this study, we have investigated the effect of the natural indoloquinoline alkaloid cryptolepine on *L. donovani* AG83 promastigotes. Our results show that cryptolepine induces cellular dysfunction in *L. donovani* promastigotes, which leads to the death of this unicellular parasite. Interestingly, this study suggests that initial autophagic features elicited by the cells counteract cryptolepine-induced cell death of *L. donovani*. For the first time, we show that autophagy serves as a survival mechanism in response to cryptolepine treatment in *L. donovani* promastigotes and inhibition of autophagy causes an early increase in the number of cell death. This study can be exploited for designing better drugs and better therapeutic strategies against leishmaniasis in future.

Identification of tyrosyl DNA phosphodiesterase 1 (Tdp 1), a DNA repair enzyme

This study describes for the first time the cloning and functional characterization of tyrosyl DNA phosphodiesterase 1 (Tdp1) in DNA damage repair pathway in kinetoplast parasite *L. donovani*. Tdp1 is a member of phospholipase D superfamily, conserved from yeast to humans, which cleaves a broad range of 3' DNA adducts, the best characterized of which is the phosphodiester bond formed between DNA and topoisomerase IB. The protein is termed as LdTdp1. Sequence analysis study confirmed conservation of the active site motifs typical for Tdp1 family. Transcriptional down regulation of the gene was observed during CPT and H_2O_2 mediated apoptotic death of the parasites indicating a regulatory role, played by the gene. Enforced expression of the active enzyme protected the parasites against CPT and H_2O_2 mediated cytotoxicity. Overproduced Tdp1 reduced the DNA damage mediated by CPT inside the cells whereas its down regulation rendered the parasites hypersensitive to CPT. LdTdp1 activity was identified inside the nucleus as well as in the kinetoplast of *Leishmania* parasites. The protein harbors the nuclear localization signal (NLS) at its C-terminus. The active site residues of LdTdp1 have been identified by site directed mutagenesis. LdTdp1 transcripts and protein levels were observed to be higher during non-dividing and oxidative stress resistant stationary phase of *L. donovani* parasites compared to proliferative logarithmic phase suggesting a role of LdTdp1 in handling DNA damage repair in highly oxidative environment. Recombinant LdTdp1 was found to be active

in vitro on 3-tyrosine linked oligonucleotide substrate that mimicked the in vivo substrate of the enzyme. This study shows for the first time a tyrosyl DNA phosphodiesterase 1 protein in kinetoplastid parasites, which actively participate in removing trapped topoisomerase 1 from topo I-DNA dead end complexes generated from endogenous or exogenous sources, enabling the parasites to gain resistance against topoisomerase inhibitors.

Identification of DNA topoisomerase IA and III

Role of IB type of topoisomerase is well studied in *L. donovani*. Apart from this, three type IA topoisomerases are there in the parasite genome, termed as topoisomerase IA, and two topoisomerase III.

DNA topoisomerase IA of *Leishmania* (LdTOPIA) has been identified and functionally characterized for the first time *in vitro* and *in vivo* in the lab. LdTOPIA has a strong prokaryotic lineage that is evident from the conservation of active site residues and its ability to complement bacterial TopA null mutant strains. The Mg^{2+} dependent relaxation activity of only negatively supercoiled plasmids and the preference for single stranded substrates exhibited by recombinant LdTOPIA overexpressed in *Leishmania* conclusively establishes its evolutionary ancestry from prokaryotes. But eukaryotic features include adaptation for the compartmentalized structure wherein the enzyme localizes in the nucleus and kinetoplast and has a codon bias for expression. The enzyme prevents DNA gyrase induced hypernegative supercoiling and thereby inhibits R-loop formation inside the TopA null mutant bacterial strain. All these properties of LdTOPIA make it an attractive molecular target for drug development. Purification of this protein is currently in progress and our study on the basic understanding of the properties of LdTOPIA will pave a future path in therapeutic interventions against leishmaniasis.

The role of topoisomerase III in DNA metabolism has remained largely enigmatic. Genes encoding topoisomerase III enzymes are highly conserved in evolution from bacteria to human, and the phenotypic consequences of loss of topoisomerase III function are generally quite severe. It has been shown to possess a weak, ATP independent relaxation activity towards negatively supercoiled DNA only and strict dependence on magnesium. We have, for the first time, identified and characterized *L. donovani* homologue of bacterial and eukaryotic topoisomerase III *in vivo*, in order to get insight into its importance in *Leishmania* biology. The two topoisomerase III genes (α and β) were cloned and amino acid sequence analysis revealed that one of the two proteins shares 47.84 identity with *H. sapiens* Topo IIIβ and 45% identity with *D. melanogaster* Topo IIIβ and termed as LdtopIIIβ. The second Topo III showed to be divergent from the first one and shares significant homology with Topo III of *A. thaliana*, termed as LdTopIIIα. Complementation study of wild-type and mutant LdTopIIIβ with slow-growing topoisomerase III mutant yeast *S. cerevisiae* revealed the functional conservation of the leishmanial counterpart of topoisomerase IIIβ protein, the 327 tyrosine being the active site amino acid. A C-terminal deletion construct of LdTopIIIβ could not suppress the slow-growth phenotype of mutant yeast, indicating the requirement of C-terminal region for the enzyme function *in vivo*. LdTopIIIβ localized inside the nucleus and kinetoplast of the parasite. Taken together, our study indicates functional conservation and possible role of LdTopIIIβ in parasite DNA processing.

The genes for LdTOP1A, LdtopIIIα and LdtopIIIβ have been successfully expressed in *in vitro* transcription-translation system of *E. coli*. All the proteins are able to show their activities in crude extracts. Purification of the proteins and further characterization are in progress.

Effect of ATP on the ATP independent type IB topoisomerase of L. donovani

Most type IB topoisomerases do not require ATP and Mg^{2+} for activity. However, as shown previously for vaccinia topoisomerase I, we demonstrate that ATP stimulates the relaxation activity of the unusual heterodimeric type IB topoisomerase from *L. donovani* (LdTOP1L/S) in the absence of Mg^{2+}. The stimulation is independent of ATP hydrolysis but requires salt as a co-activator. ATP binds to LdTOP1L/S and increases its rate of strand rotation. Docking studies indicate that the amino acid residues His93, Tyr95, Arg188 and Arg190 of the large subunit may be involved in ATP binding. Site directed mutagenesis of these four residues individually to alanine and subsequent relaxation assays reveal that the R190A mutant topoisomerase is unable to exhibit ATP-mediated stimulation in the absence of Mg^{2+}. However, the ATP-independent relaxation activities of all the four mutant enzymes remain unaffected. Additionally, we provide evidence that ATP binds LdTOP1L/S and modulates the activity of the otherwise ATP-independent enzyme. This study establishes ATP as an activator of LdTOP1L/S in the absence of Mg^{2+}.

Development of therapeutics targeting type IB topoisomerase of Leishmania

Our laboratory has been involved in developing DNA topoisomerase targeted anti-leishmanial agents. 3,3'-Diindolylmethane (DIM), a novel poison targeting *L. donovani* topoisomerase I (LdTOP1LS), induces programmed cell death in *Leishmania* parasites. Forced molecular evolutionary approach revealed that F270L mutation of large subunit confers DIM resistance to parasites. To deal with the problem of future DIM resistance, we have prepared three derivatives of DIM namely DPDIM (2,2'-diphenyl 3,3'-diindolyl methane), DMDIM (2,2'-dimethyl 3,3'-diindolyl methane) and DMODIM (5,5'-dimethoxy 3,3'-diindolyl methane) from parent compound DIM. Interestingly, DPDIM is more potent than the parent compound DIM against parasite growth. We have also synthesized a large number of derivatives of betulin which is a natural triterpene isolated from the cork layer of Betula plants and exhibits several pharmacological properties. Three compounds viz. disuccinyl betulin, diglutaryl dihydrobetulin and disuccinyl dihydrobetulin inhibit growth of the parasite as well as relaxation activity of the enzyme type IB topoisomerase (LdTOP1LS) of the parasite. Mechanistic studies suggest that these compounds interact with the enzyme in a reversible manner. These compounds slow down the strand rotation event that ultimately affects the relaxation of supercoiled DNA. Interestingly, these compounds reduce the intracellular parasite burden in macrophages infected with wild type *Leishmania* as well as with sodium antimony gluconate resistant parasite (GE1). Taken together, our data suggest that these betulin derivatives can be exploited as potential drug candidates against threatening drug resistant leishmaniasis.

Future Plan:

- Exploring Type IA DNA topoisomerase of *Leishmaina* as therapeutic target.
- Overexpression and purification of Type II DNA topoisomerase of *Leishmania*.

Dr. (Mrs.) Chitra Mandal

Understanding molecular basis of cancer

Sialic acids and its derivatives are found in nearly all higher animals studied and in certain bacteria and have been recognized to play a pivotal role in modulating various biological and pathological

processes such as cell-cell and virus-cell adhesion, signalling, differentiation, immune reactions including apoptosis and malignancy.

The main attention of my laboratory is focused on identification of modified sialylated structures, the understanding the importance of modulation of sialylation, its biological role and their utility as potential disease-associated biomarkers/molecular target in cancer and visceral leishmaniasis (VL).

Additionally, our aim also is to understand the molecular basis of different cancers. Accordingly, emphasis is given on identification of potential lead molecule from herbal sources, novel targets and target-specific leads for development of novel therapeutics through cell signaling, proteomics, physicochemical and in silico approaches.

Induction of apoptosis by targeting the activation of neutral sphingomyelinase-ceramide cascade in leukemias

Natural products are rich source of medicine from the ancient time for diseases since the beginning of civilization. Vedas, Ayurveda is the oldest system of medicine in the world. In Ayurvedic medicine, Ashwagandha (*Withania somnifera*, Dunal) is an important plant due to its wide range health attributing properties. Recently, extensive study in morphology and phytochemical composition of *W. somnifera* led to the isolation of important development of pharmacologically active compounds named withanolides by a venture of Indian Government under the auspices of new Millenium Indian Technology Leadership Initiative (NMITLI) steered by CSIR. They are ergostane based C28-steroids nomenclatured as 22-hydroxy ergostane-26-oic acid 26, 22-lactones with structures further diversified through position specific hydroxylations leading to the myriad of individual chemical entities. Among the Withanolides, Withaferin A, Withanolide D, Withanolide A and Withanone are lead molecules.

We showed that Withanolide D (WithaD) could effectively induces cell death in a dose and time dependant manner both in myeloid (K562) and lymphoid (MOLT-4) cells being nontoxic to normal lymphocytes and control proliferative cells. Ceramide is a known inducer of apoptosis. In leukemia, chemoresistance generally developed due to deregulated ceramide metabolism. In combinatorial treatment strategies of leukemia, manipulation in ceramide production by physiological and pharmacological modulators therefore may give additive effect in leukemia chemotherapy. Hence, we checked the ability of WithaD for Ceramide production and we observed that WithaD potentially augment ceramide production in leulemic cells. Downstream of ceramide, WithaD acted on MKK group of proteins and significantly increased JNK and p38MAPK phosphorylation. Pharmacological inhibition of p38MAPK and JNK significantly reduced WithaD-induced cell death thereby proves their cooperative action. Dissecting the cause of ceramide production, we found activation of neutral sphingomyelinase and showed neutral-sphingomyelinase 2 (N-SMase 2) is a critical mediator of WithaD-induced apoptosis. Knockdown of N-SMase 2 by siRNA and inhibitor of N-SMase significantly reduced WithaD-induced ceramide generation and phosphorylation of MKK4 and MKK3/6, whereas phosphorylation of MKK7 was moderately regulated in leukemic cells. Also, both by silencing of N-SMase 2 and/or blocking by GW4869 protects these cells from WithaD-mediated death and suppressed apoptosis, whereas fumonisin B1, an inhibitor of ceramide synthase, did not have any effect. Additionally, WithaD effectively induced apoptosis in freshly isolated lymphoblasts from patients and the potent cell killing activity was through JNK and p38MAPK activation. Our results demonstrate that WithaD enhance the ceramide accumulation by activating N-SMase 2, modulate phosphorylation of the JNK and p38MAPK and induced apoptosis in both myeloid and lymphoid cells along with primary cells

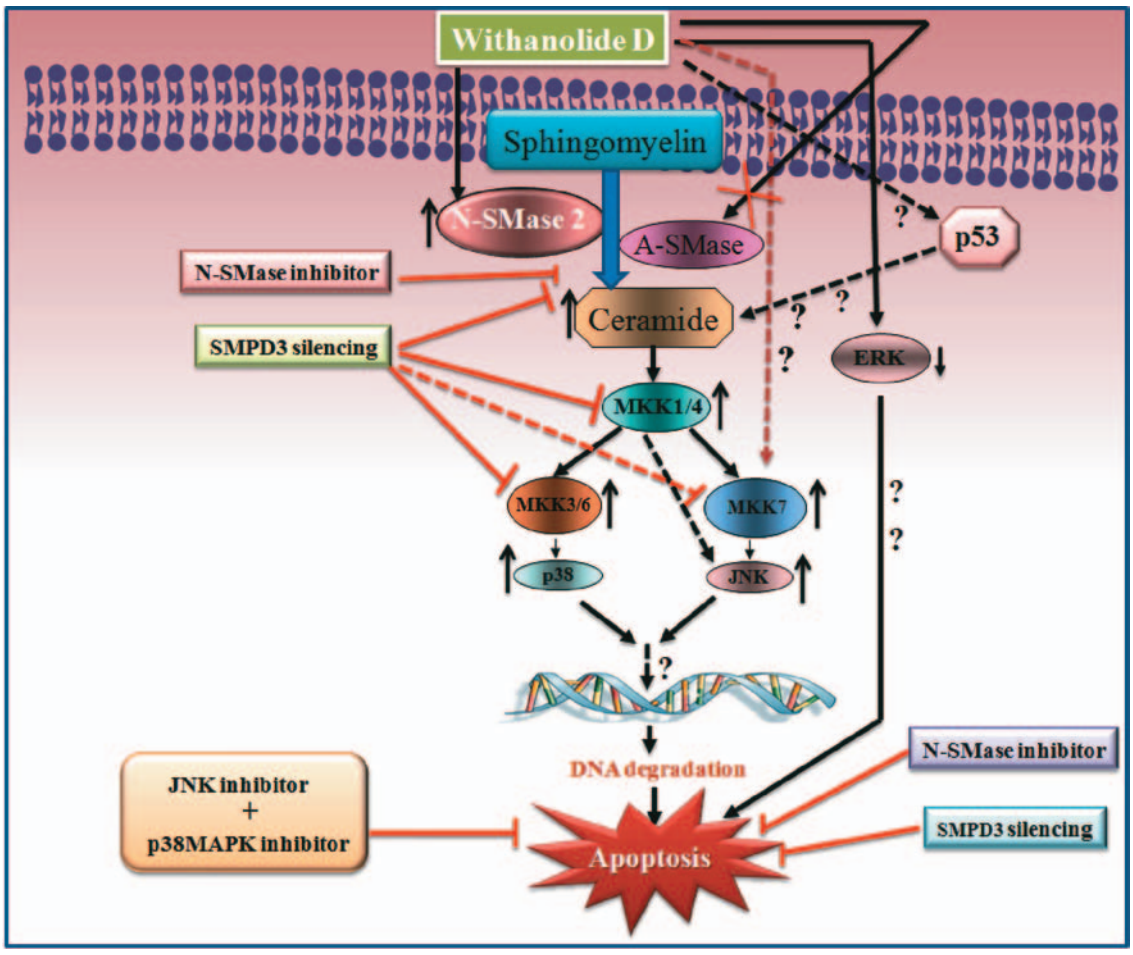

Fig. 1.

derived from leukemia patients (Fig. 1). Taken together, this pure herbal compound may consider as a potential alternative tool with additive effects in conjunction with traditional chemotherapeutic treatment, thereby accelerate the process of conventional drug development [Mondal et.al. **(2010)** *Molecular Cancer* **9**, 239].

Future plan:

- Modulation of the expression of sialic acid modulator enzymes to understand their involvement in the cancer progression
- Relation of GD3 and sialylating enzymes with angiogenesis in pancreatic cancer
- Glycoproteomics of leukemia-associated sialoglycans and their functional role
- Cell cycle regulation and G1/S check point function and other pathway interaction in glioblastoma multiforme.
- Intervention of dysregulation in Wnt/β-catenin signaling and its correlation with cell cycle in pancreatic adenocarcinoma.
- Identification of target protein in non small cell lung cancer using novel anti-cancer agent.

These *9-O*-AcSGs trigger the alternate complement pathway in VL. We have also demonstrated the

contributory role of these sialoglycotopes as immunomodulatory determinants leading towards a beneficial immune response influencing the disease pathology.

Sialic acids in visceral leishmaniasis (VL)

An enhanced presence of *9-O*-acetylated sialoglycoconjugates (*9-O*-AcSGs) on erythrocyte of VL patients (RBC_{VL}) has been exploited to develop a user friendly, simple blood based assay for the diagnosis and monitoring of these patients. Sequence data of one of this sialoglycoprotein revealed a cytoskeleton protein namely spectrin. Extensive studies through several biochemical and physicochemical means demonstrated for the first time the glycosylation of eythrocytic-spectrin, in normal erythrocytes and its enhanced sialylation in RBC_{VL}. Molecular modelling studies also suggest that a sugar moiety can fit into the potential glycosylation sites.

Future plan:

- Glycoproteomic approaches of sialoglycans induced on immune cells/plasma of VL patients in search of candidate marker and their biological significance
- Role of siglecs in recognition of pathogen and impairment of macrophage function.

Dr. Pijush K. Das

The work in my laboratory is centered on studying macrophage biology using visceral leishmaniasis as a model disease of macrophage. In this period, first of all we made a fundamental observation that although enhanced macrophage-specific arginase activity is directly related to increased parasite burden in both cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL), but while IL-4-induced arginase pathway is operative in CL, IL-10 plays crucial role in modulating arginase activity in VL though a synergism with IL-4 is required. In VL, IL-10 regulated both in vivo and ex vivo arginase induction in a STAT6 and C/EBPβ-dependent fashion in combination with IL-4. Actually, the induction of STAT3-dependent IL-10-mediated cascade in VL triggers the expression and surface localization of IL-4 receptor alpha (IL-4Rα) which, in turn, enhances IL-4 responsiveness towards STAT6 and C/EBPβ-dependent signaling for arginase (Fig. 2). This could also offer a mechanistic explanation for the fact that in spite of low level of IL-4 in VL, enhanced IL-4Rα expression by IL-10 might markedly amplify IL-4 mediated arginase signaling and provide a possible mechanism of synergistic induction of arginase.

In our comprehensive understanding of the various mechanisms exploited by *Leishmania* to frustrate macrophage defense machinery, we have identified uncoupling protein 2 (UCP2), a mitochondrial inner-membrane protein and a negative regulator of mitochondrial ROS (mROS) generation, as a possible candidate. We have demonstrated that *Leishmania* infection strongly up-regulates the expression of UCP2, thereby preventing mROS generation in the macrophages. To assess the functional significance of UCP2 during infection, expression of UCP2 was suppressed by siRNA or shRNA-mediated knock-down. Interestingly, knocked-down macrophages produced considerably higher amount of mROS and were able to eliminate parasite burden successfully. It was found that, in knocked-down macrophages the higher amount of mROS generation deactivated protein tyrosine phosphatises (PTPs), thereby facilitating positive mitogen activated ptotein kinase (MAPK) signal transduction, ultimately culminating in heightened expression of disease-healing proinflammatory cytokines like IL-12 and TNF-α, both *in vitro* and *in vivo* conditions. Whereas, quenching of mROS in UCP2 knocked-down infected

macrophages resulted in elevated level of disease-progressing anti-inflammatory cytokines (IL-10, TGF-β) emphasizing the significance of parasite-mediated induction of UCP2 to suppress mROS generation. The role of UCP2 in *Leishmania* infection is explained by a schematic representation (Fig. 3). Thus, this study for the first time has shed light on a novel pathway involving a mitochondrial uncoupler favouring parasite persistence and a better understanding of this will help in developing intervention strategies, not only for visceral leishmaniasis, but also for other macrophage associated diseases.

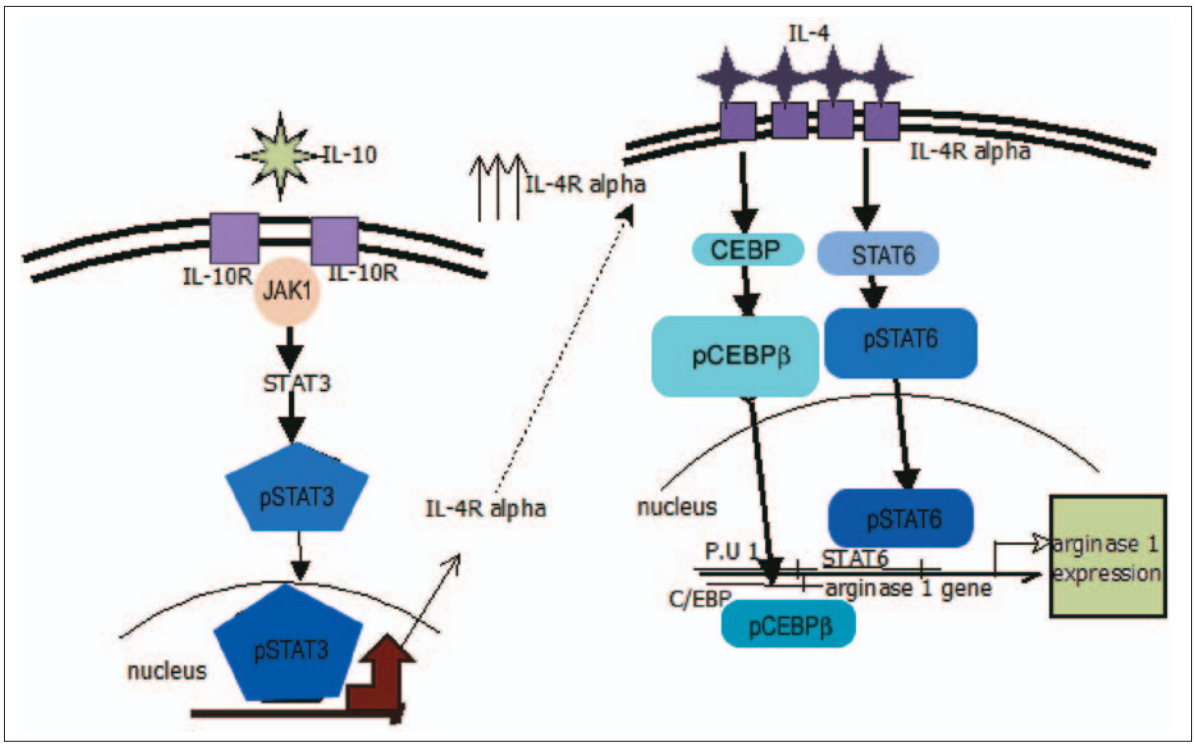

Fig. 2 : Model for IL-10-mediated regulation of arginase 1 gene expression in VL. IL-10-mediated cascade results in activation of STAT3, which triggers the expression and surface localization of IL-4Rα. This, in turn, amplifies IL-4-mediated arginase 1 signaling through STAT6 and C/EBP activation in spite of low level of IL-4 in VL.

In our efforts towards unraveling the role of cAMP signaling in parasite survival and infectivity, we first showed that differentiation-coupled induction of resistance of *Leishmania* parasites to macrophage oxidative damage is associated with increased intracellular cAMP and cAMP-mediated response. Parasites having increased cAMP-response elements were more cytoprotective, having higher levels of antioxidant enzymes and having more free radical scavenging capacity. For comprehensive understanding of cAMP signaling, we carried out detailed studies on all the enzymes involved in cAMP metabolism in the parasite e.g. the cAMP synthesizing enzyme, adenylate cyclase, the degrading enzyme phosphodiesterase (PDE), the regulatory enzyme pyrophosphatase (PPase) and the functional enzyme, cAMP-dependent protein kinase (PKA) (Fig. 4).

In the reporting period, we concentrated in determining the downstream effector molecules of cAMP-mediated events. In mammalian cells, there are a number of intracellular effectors of cAMP, most important of which is cAMP-dependent protein kinase (PKA). PKA exists as inactive R_2C_2 heterotetramer

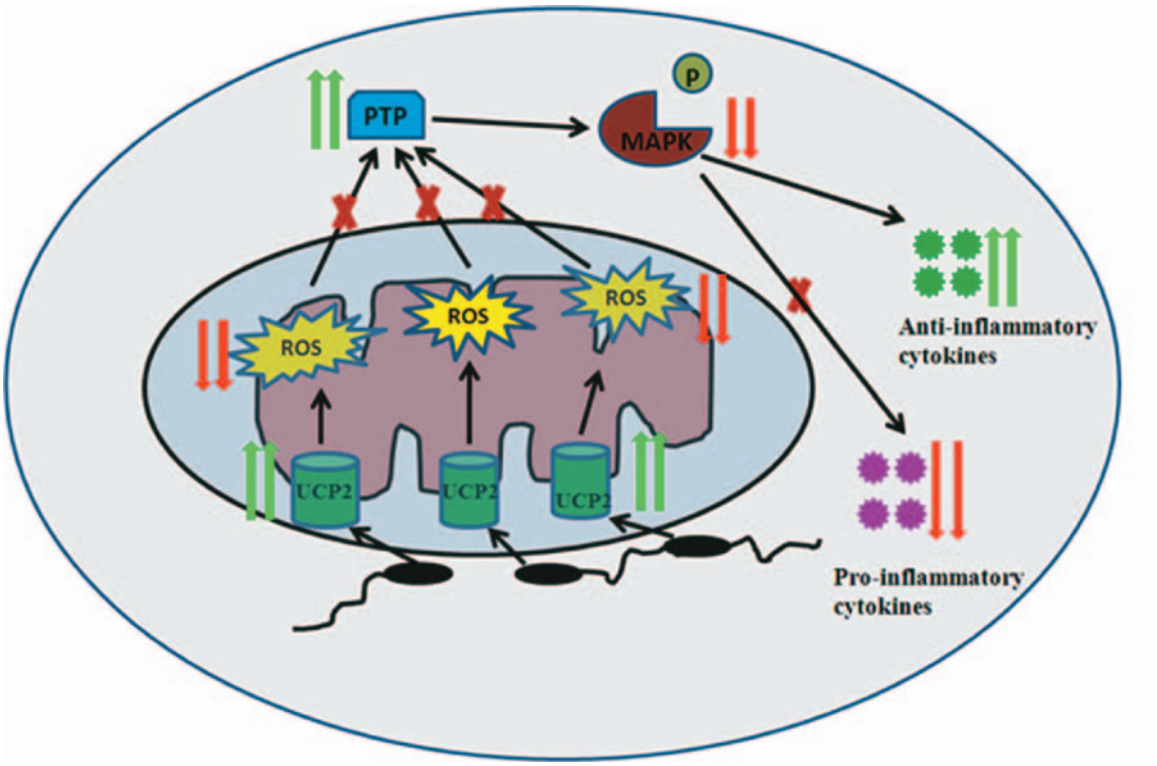

Fig. 3 : *L. donovani* infection strongly up-regulated UCP2, a mitochondrial inner-membrane protein, which down-regulated mitochondrial ROS generation thereby preventing ROS-mediated PTP inactivation. This in turn led to deactivation of MAPKs thereby shifting the pro/anti-inflammatory cytokine balance to anti-inflammatory phenotype facilitating parasite survival.

consisting of two catalytic and two cAMP-binding regulatory subunits. Binding of cAMP to the regulatory subunits releases the active catalytic subunits, which are then free to phosphorylate a broad range of substrates. PKA catalytic subunits (PKAC) have been cloned and characterized from different *Leishmania* species, but the regulatory subunit has not yet been characterized from any *Leishmania* species. We identified a regulatory subunit of PKA from *L. donovani* (LdPKAR), which is expressed in all life cycle stages. Its expression attained maximum level in stationary phase promastigotes which are biochemically similar to infective metacyclic promastigotes. Starvation condition, the trigger for metacyclogenesis in the parasite, elevated PKAR expression and under starvation condition, promastigotes overexpressing PKAR attained metacyclic features earlier than normal cells. Furthermore, PKAR overexpression accelerated autophagy, a starvation-induced cytological event necessary for metacyclogenesis and amastigote formation. Conditional silencing of PKAR delayed the induction of autophagy in the parasite. The study, for the first time, reports the identification of a functional cAMP-binding effector molecule from *L. donovani* that may modulate important cytological events affecting metacyclogenesis. Since no *bona fide* cAMP-binding protein of defined function has yet been identified in *Leishmania* or in any other kinetoplastidae, the biological significance and molecular mechanism behind cAMP signaling is still an open field to be explored.

Future plans:

(i) Sequestering itself inside the cells of the host allows *Leishmania* to hijack host-signaling systems, which primarily involve MAPK as well as TLR signalling cascades. We would like to continue our studies on comprehensive understanding of the homeostasis including both positive and negative

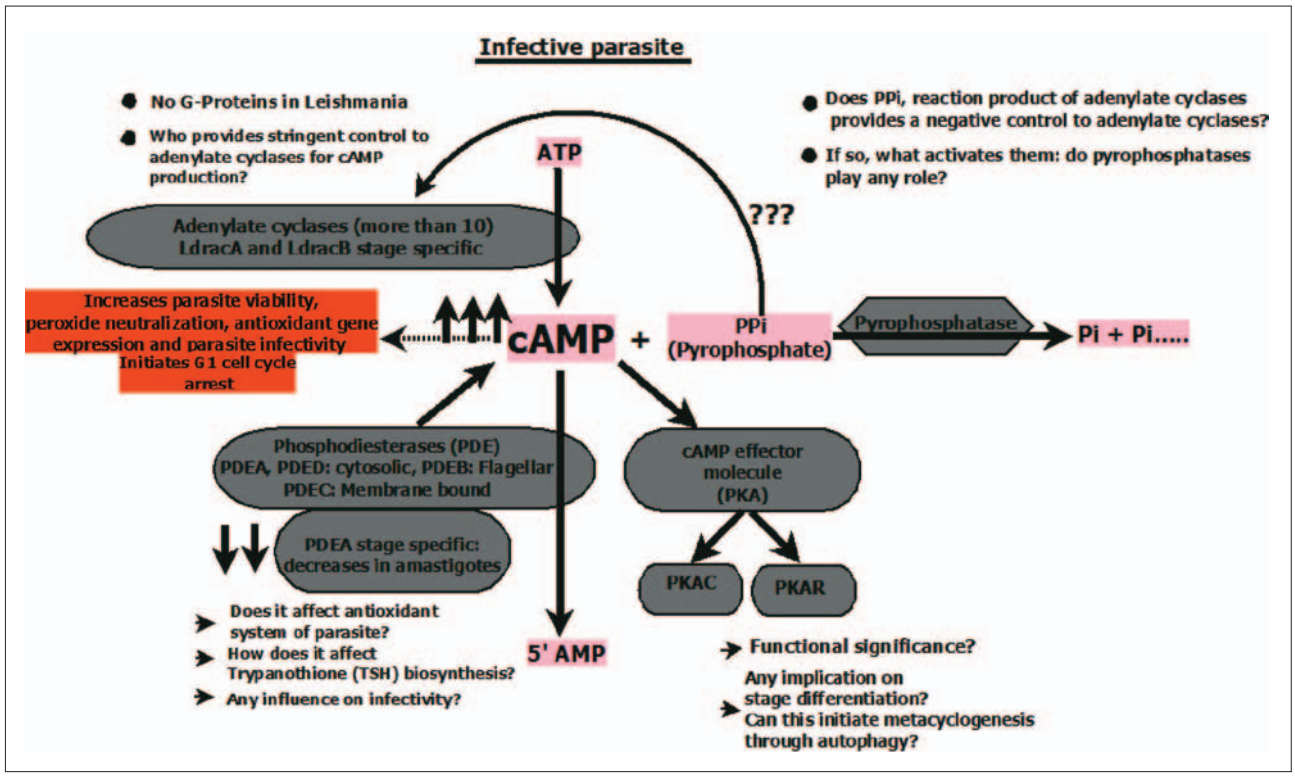

Fig. 4 : Enzymes intimately associated with cAMP metabolism in *Leishmania*. cAMP is formed from ATP by adenylate cyclases where pyrophosphate (PP_i) is also produced as one of the reaction products which is hydrolyzed by pyrophosphatases to inorganic phosphate (P_i). Downstream to cAMP, leishmanial phosphodiesterases (PDE) hydrolyzes cAMP to 5' adenosine monophosphate (5'AMP). There are 5 different PDEs in the parasite (PDEA, PDEB1, PDEB2, PDEC and PDED). cAMP dependent protein kinase A (PKA) exists as an inactive tetramer consisting of two catalytic subunits (PKAC) and two regulatory subunits (PKAR). Binding of cAMP to regulatory subunit releases catalytic subunit.

regulators of these signaling systems. (ii) Role of mitochondrial UCPs will be studied in relation to the establishment of infection in the hostile environment of macrophages. Upstream events leading to modulation of UCPs in infected condition will be assessed. Finally, the transport of UCPs in the inner membrane of mitochondria will be investigated. (iii) We would also like to continue our studies on comprehensive understanding of cAMP signaling in *Leishmania* parasites.

Dr. Syamal Roy

Understanding the mechanism of immune suppression in leishmaniasis

Kala-azar patients at the active stage of the disease fail to show antigen specific T-cell proliferation - the cause of which is still largely unknown. The causative agent, *Leishmania donovani*, replicate within the macrophage of the mammalian hosts. The parasites during their intracellular line cycle quench membrane cholesterol which causes increase in membrane fluidity. Parasitized macrophages are unable to stimulate antigen specific T-cells but this can be corrected by liposomal delivery of cholesterol. The mechanism by which parasites influence cholesterol homeostasis is not known. As the conformations of a number of membrane proteins are dependent on membrane cholesterol, we endeavoured to study the rate of dissociation of the peptide-MHC complex as a functional read out

to assess the early event of T-cell activation. It was observed that $t_{1/2}$ for the peptide-MHC complex in normal, infected and cholesterol-liposome treated infected macrophages were 128 h, 3 h and 108 h respectively. This observation collectively indicated that the membrane is more fluid in parasitized macrophages as compared to normal. This may cause poor stability of the peptide-MHC complex but such defects could be corrected by liposome delivery of cholesterol.

Differential immune modulation by antimony sensitive (SbS) and antimony resistant (SbR) Leishmania donovani (LD)

The disease visceral leishmaniasis or kala-azar is widening its base in the Indian subcontinent and the evolution of antimony unresponsiveness in *Leishmania* parasites is compounding the problem further. Analysis of the functional ability of dendritic cells upon infection either with Sb^R-LD or Sb^s-LD demonstrated that Sb^R-LD, but not Sb^s-LD, differentially modulate dendritic cell function upon infection. This showed that Sb^R-LD parasites, unlike Sbs-LD parasites, express neoglyconjugates on their surface with terminal N-acetyl-D-galactosaminyl residue. In contrast to Sb^R-LD, Sb^R-LD exploits Toll 2 receptor to induce IL-10 production from infected macrophages and causes upregulation of the Multidrug Resistant (MDR) protein pGP-1 in the infected host cells. Upregulation of MDR was found to be IL-10 dependent. Using a variety of pharmacological inhibitors, it was shown that upregulation of IL-10 is NFKB dependent. Thus Sb^R-LD may modulate host immune response more efficiently than Sb^R-LD parasites by producing the disease promoting cytokine IL-10.

Development of a DNA vaccine for visceral leishmaniasis

Protozoan parasites in the genus *Leishmania* are responsible for a spectrum of human diseases termed Leishmaniasis. To compound the problem further, the parasites are increasingly becoming resistant to common anti-leishmanial pentavalent antimony drugs. DNA vaccination is a promising new approach for the prevention and treatment of many diseases because of its ability to induce both humoral and cellular immune response. The aim is to formulate MIDGE (Minimalistic Immunogenically Defined Gene Expression) vector based DNA vaccines encoding candidate antigens such as Kinetoplastid Membrane Protein-11 (Kmp-11), Thiol-Specific Antioxidant (TSA), P74, Cystein Protease A and B (CPA & CPB) and assess their efficacy against experimental visceral leishmaniasis model. So far we have studied the vaccine formulation with KMP-11, TSA and P74 and the results are very promising. The study on a vaccine formulation including all the five antigens (KMP-11, TSA, P74, CPA and CPB) at different doses is under way to find the optimal formulation of this DNA vaccine to combat leishmaniasis.

Dr. Santu Bandopadhyay

We described anti-chronic myeloid leukemia activity of Piper betel leaf extract (several international patent applications filed). Hydroxychavicol (HCH) was identified as one of the active principles of this activity. In this study, we try to elucidate the mechanism and potential signaling involved in apoptosis of Bcr-Abl+ CML cells mediated by one synthetic analogue of hydroxychavicol, ICB3E. ICB3E was synthesized by Dr. Parasuraman Jaisankar, Division of Chemistry.

ICB3E induces iNOS expression by ROS-dependent JNK and Erk activation for apoptosis of leukemic cells

Hydroxychavicol (HCH), a Piper betle leaf component, induces apoptosis of KB carcinoma cells by ROS-dependent mechanism. Here we report that ICB3E, a synthetic analogue of HCH is four to five times more potent than HCH in inducing apoptosis of leukemic cells without having appreciable effects on normal human peripheral blood mononuclear cells, mouse fibroblast cell line NIH3T3 and monkey kidney epithelial cell line Vero. ICB3E causes early accumulation of mitochondria-derived reactive oxygen species (ROS) in K562 cells. ROS dependent activation of both c-Jun N-Terminal Kinase (JNK) and extracellular signal-regulated kinase (Erk) was noticed, both of which induced the expression of iNOS leading to generation of nitric oxide (NO). This causes cleavage of caspase 9, 3 and PARP leading to apoptosis. Our data reveal a novel ROS-dependent JNK/Erk-mediated iNOS activation pathway which leads to NO mediated cell death in leukemic cells by ICB3E. This molecule merits further testing in pre-clinical studies as anticancer agent.

Dr. (Mrs.) Nahid Ali

The effect of C-terminal domain deletion on the catalytic activity of Leishmania donovani surface proteinase GP63: Role of Ser446 in proteolysis

The kinetoplastid protozoan *Leishmania* encodes major surface glycoprotein GP63; a zinc metallo-peptidase (EC.3.4.24.36) expressed both in promastigote and amastigote life stages. In the present study, we explored for the first time the role of C-terminal domain (CTD) in proteinase activity by serial truncation of *L. donovani* GP63 (LdGP63) from carboxyl terminal end (CTend). Deletion of 180-211 amino acids from CTend (Δ420 and Δ389) resulted in almost 50% loss of catalytic activity against azocasein, casein and gelatin (Fig. 5). Moreover, all the truncated constructs showed reduced activity towards immunoglobulin (IgG). Upon homology modeling, we identified two residues, S446, and F448 in CTD, conserved in different *Leishmania* species, which were positioned 6.8-11Å apart from the active site. To ascertain the role of S446 and F448 in catalysis, we replaced S446 with Ala and Thr, and F448 with Val and Tyr by site-directed mutagenesis. The variant enzymes (S446T, F448V, and F448Y) maintained near wild-type activity, whereas S446A demonstrated 50% loss of catalytic activity towards the cleavage of various biological substrates (Fig. 6). Kinetic analysis of S446A resulted in a 2.6-fold decrease in the affinity, 10-fold decrease in turn-over rates, and large increase in transition-state binding energy (1.4kcal/mol) for the quenched peptide substrates. These results emphasize the relevance of CTD in the proteolytic activity of LdGP63. Fluorescence spectroscopy, and CD analysis however, indicated that the reduced activities showed by Δ389 and S446A were not due to global changes in the enzyme structures. Indeed, identification of S446 and its possible role in the stabilization of transition-state binding between enzyme and substrate can be exploited towards understanding of structure-function relationship of GP63.

Potency, efficacy and durability of DNA/DNA, DNA/protein and protein/protein based vaccination using gp63 against L. donovani in BALB/c mice

Visceral leishmaniasis (VL) caused by an intracellular protozoan parasite *Leishmania*, is fatal in the absence of treatment. At present there are no effective vaccines against any form of leishmaniasis.

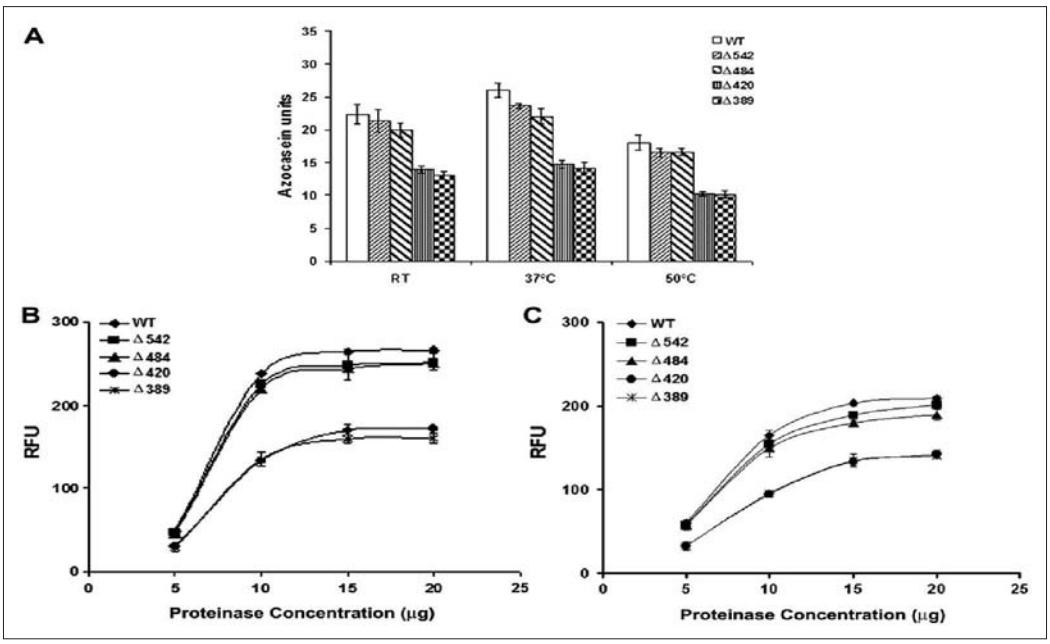

Fig. 5 : Caseinolytic, and gelatinolytic activities of WT, and truncated LdGP63. (A) Temperature dependence of the WT, truncated proteinases measured using azocasein. Azocasein (2%) was incubated with WT and different truncated proteinases at different temperatures (RT, 37 °C and 50(C) for 30 min in 25 mM Tris/HCl (pH 7.5), 100 mM NaCl. Absorbance was measured spectrophotometrically at O.D 440 nm. The activity is represented as the mean of the azocasein unit. Error bars represent (S.E of three independent experiments. (B) Proteinase activity of the WT, and truncated GP63 measured using FTC-casein. FTC-casein (20 mg/ml) was incubated with different quantities (5-20 mg) of proteinases at 37 °C for 1 h in 25 mM Tris/HCl (pH 7.2), containing 150 mM NaCl and fluorescence (RFU) resulting from hydrolysis was measured using excitation and emission filters of 485 and 538, nm respectively. The average value of the RFU is indicated with (S.E. and (C) Proteinase activity of the WT, and truncated GP63 measured using DQ-gelatin. DQ-gelatin (10 mg/ml) was incubated with WT, and truncated GP63 with different quantities (5-20 mg) at 37 °C for 1 h in 50 mM Tris/HCl (pH 7.5), 150 mM NaCl, 0.2 mM sodium azide. Hydrolysis was monitored by RFU using excitation and emission filters 485 and 515 nm, respectively. The average value of the RFU is represented with ±S.E.

Thus, we evaluate the potency, efficacy and durability of DNA/DNA, DNA-prime/protein-boost, and protein/protein based vaccination against VL in a susceptible murine model. To compare the potency, efficacy, and durability of DNA, protein and heterologous prime-boost (HPB) vaccination against *L. donovani*, gp63 DNA based vaccination induced immune responses and conferred protection against challenge infection. However, vaccination with HPB approach showed comparatively enhanced cellular and humoral responses than other regimens and elicited early mixed Th1/Th2 responses before infection. Moreover, challenge with parasites induced polarized Th1 responses with enhanced IFN-γ, IL-12, nitric oxide, IgG2a/IgG1 ratio and reduced IL-4 and IL-10 responses compared to other vaccination strategies. Although, vaccination with gp63 DNA either alone or mixed with CpG-ODN or heterologously prime-boosting with CpG-ODN showed comparable levels of protection at short-term protection study, DNA-prime/Protein-boost in presence of CpG significantly reduced hepatic and splenic parasite load in long-term study. The extent of protection, obtained in this study has till now not been achieved in long-term protection through HPB approach in susceptible BALB/c model against VL. Interestingly, the HPB regimen also showed marked reduction in the footpad swelling of BALB/c mice against *L. major* infection. Thus, HPB approach based on gp63 in association with CpG, resulted in robust cellular and humoral responses correlating with durable protection against

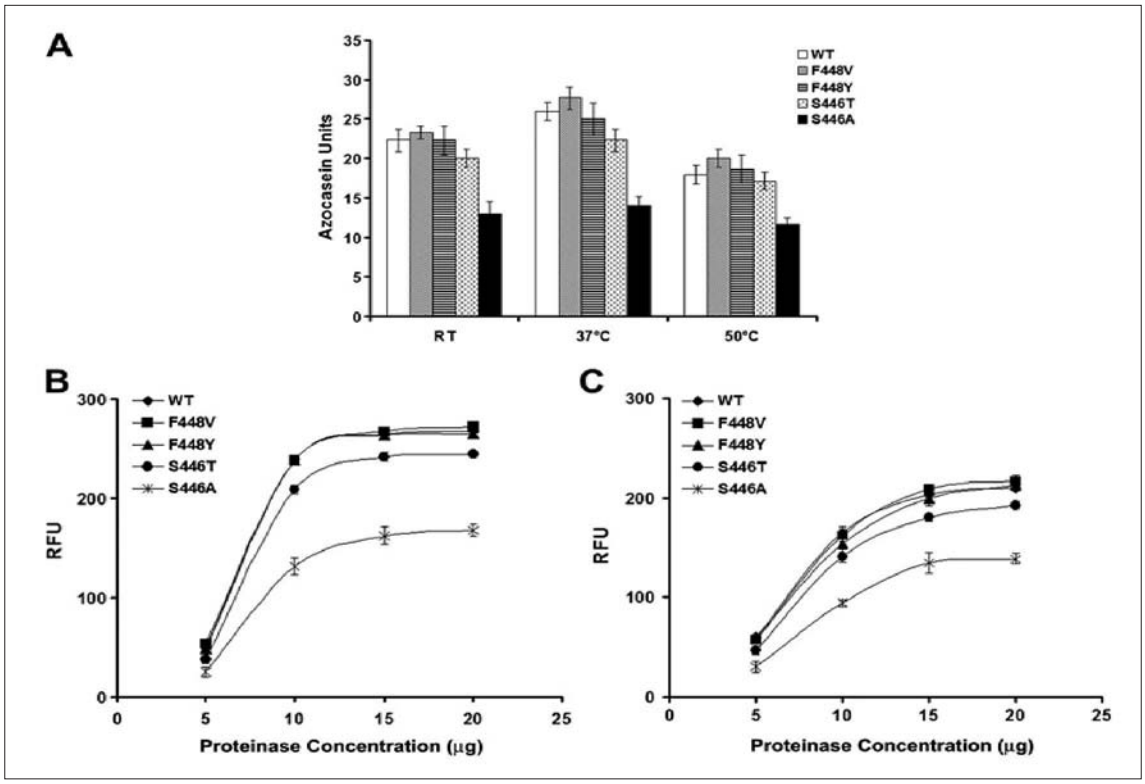

Fig. 6 : Caseinolytic, and gelatinolytic activities of WT, and mutated LdGP63. (A) Temperature dependence of the WT, and mutated proteinases measured using azocasein. Proteinase activity of the WT, and mutated GP63 measured using FTC-casein (B) and DQ-gelatin (C).

L. donovani challenge till twelve weeks post-vaccination. These results emphasize the potential of DNA-prime/Protein-boost vaccination over DNA/DNA and Protein/Protein based vaccination in maintaining long-term immunity against intracellular pathogen like *Leishmania*.

Comparison of BCG, MPL and cationic liposome adjuvant systems in leishmanial antigen vaccine formulations against murine visceral leishmaniasis

The development of an effective vaccine against visceral leishmaniasis (VL) caused by *Leishmania donovani* is an essential aim for controlling the disease, the latter being an invariably fatal disease in the absence of drug treatment. Till date there is no vaccine available against any form of human VL. Use of the right adjuvant is of fundamental importance in vaccine formulations for generation of effective cell-mediated immune response. The aim of the present study was to compare the effectiveness of two very promising adjuvants, Bacille Calmette-Guerin (BCG) and Monophosphoryl lipid A (MPL) plus trehalose dicorynomycolate (TDM) with cationic liposomes, in combination with LAg, to confer protection against murine VL. Our results demonstrated that although comparable level of protection was observed in BCG+LAg and MPL-TDM+LAg immunized mice, highest level of protection was exhibited by the liposomal LAg immunized group (Figs. 7 & 8). Significant increase in anti-LAg IgG levels were detected in both MPL-TDM+LAg and liposomal LAg immunized animals with higher levels of IgG2a than IgG1. But BCG+LAg failed to induce any antibody response. An important leishmanicidal effector mechanism is the production of IFN-γ by*Leishmania*-specific cells, which in

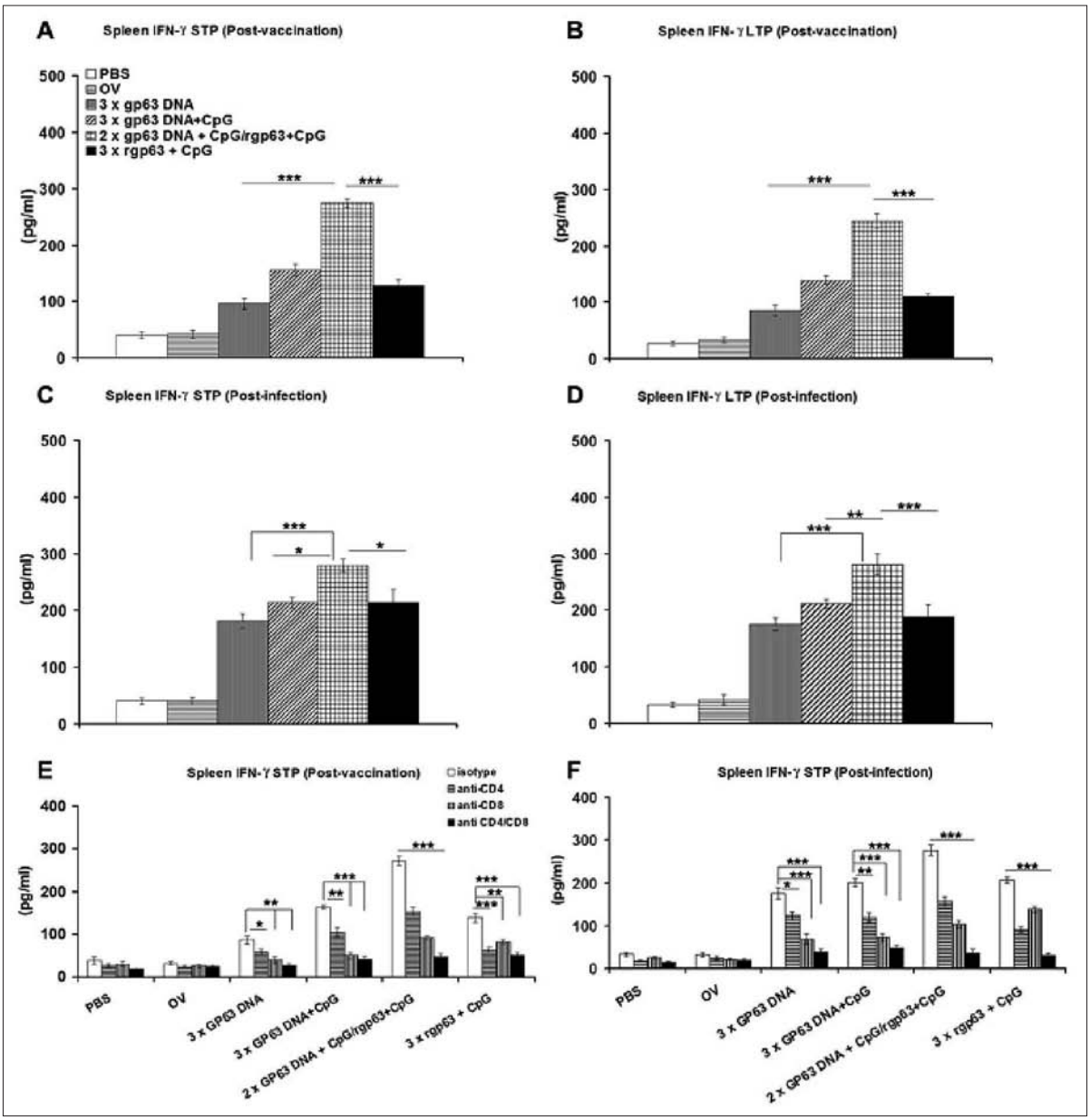

Fig. 7 : IFN-γ responses in BALB/c mice vaccinated with different vaccine approaches before and after 3 months challenge infection. Levels of IFN-γ ten days, short-term protection (STP), and twelve weeks, long-term protection (LTP) after final boosting (post-vaccination) (A, B), and 3 months after challenge infection (post-infection) (C, D). Splenocytes were isolated from vaccinated mice, stimulated with rgp63 (5 (g/ml) and were cultured for 96 h. The supernatants were collected, and assayed for IFN-γ through ELISA. Figures (E, F) represent in vitro blocking experiments either with anti-CD4+ or anti-CD8+ or both mAbs before (post-vaccination) and after *L. donovani* infection (post-infection). The results are shown as the mean absorbance values (S.E. of five individual mice per group, representative of two independent experiments with similar results. OV- only vector. * $p<0.05$, ** $p<0.01$, *** $p<0.001$ as assessed by one-way ANOVA and Tukey's multiple comparison test.

turn activates macrophages to kill intracellular parasites. Evaluation of IFN-γ and IL-4 responses in immunized mice revealed that MPL-TDM+LAg group produced the highest level of IFN-γ but lowest IL-4 level, while BCG+LAg demonstrated generation of suboptimum levels of both IFN-γ and IL-4 response (Fig. 9). The optimum levels of both the cytokines IFN-γ and IL-4 induced by the liposomal LAg vaccination substantiate earlier observations that a mixed Th1/Th2 response is essential for protection against VL. The degree of protection correlates with level of cytokine response and is inversely proportional with the liver and splenic parasite burden. Interestingly, mice immunized with liposomal LAg showed highest reduction in parasite load in liver after 2 as well as 4 months of

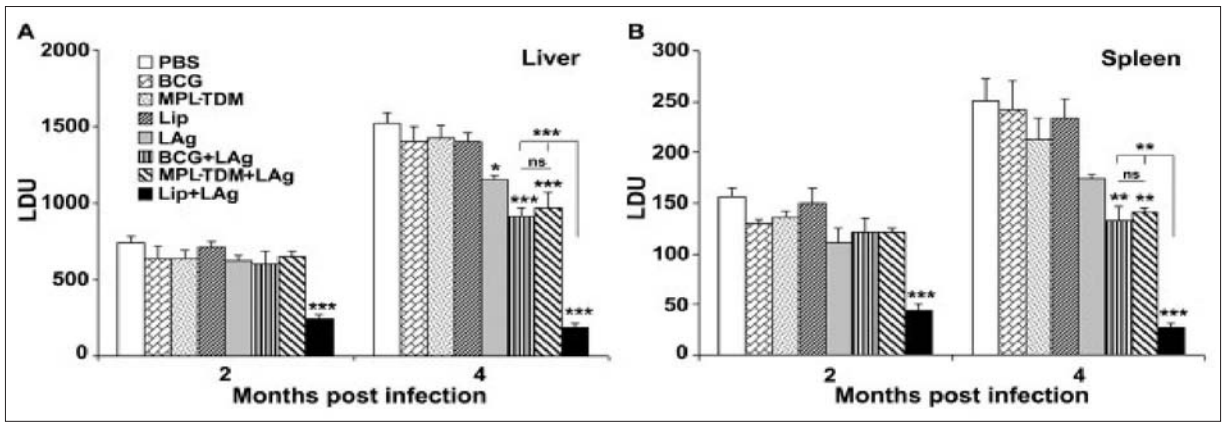

Fig. 8 : Evaluation of protection against *L. donovani* in differently adjuvanted LAg vaccinated mice. Kinetics of liver (A) and spleen (B) parasite burden of mice immunized intraperitoneally three times at 2-week intervals with BCG-LAg, MPL-TDM+LAg and LAg entrapped in cationic liposomes. Control animals received PBS or adjuvant only. At 10 days after the last immunization, mice were challenged intravenously with 2×10^7 promastigotes of *L. donovani*. Each bar represents the mean ± SE for five individual mice per group. Asterisks over each bar indicate significant differences in comparison to control groups. Asterisks over line indicate significant differences between groups. *, P < 0.05; **, P < 0.01; ***, P < 0.001; ns, not significant.

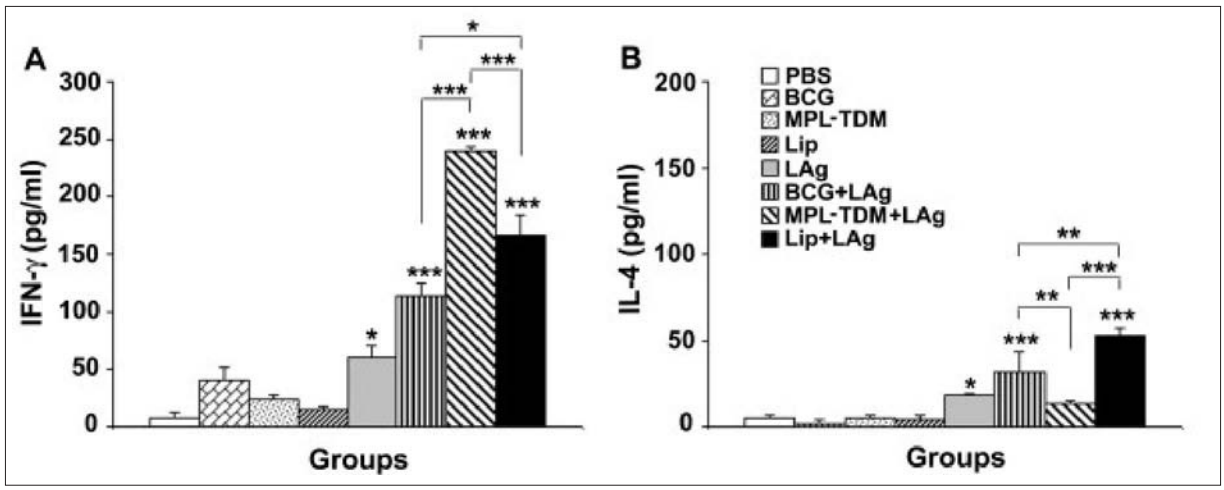

Fig. 9 : IFN-γ and IL-4 responses in differently adjuvanted LAg vaccinated mice. Mice were immunized three times at 2-week intervals. Ten days after last immunization spleens were collected from mice and restimulated in vitro with LAg (10 μg/ml). After 72 h concentrations of released IFN-γ (A) and IL-4 (B) levels were determined by ELISA. Each bar represents the mean ± SE for five individual mice per group. Asterisks over each bar indicate significant differences in comparison to control groups. Asterisks over line indicate significant differences between groups. *, *P* < 0.05; **, *P* < 0.01; ***, *P* < 0.001.

challenge which is significantly lower than BCG+LAg and MPL-TDM+LAg vaccinated groups. Thus this comparative study reveals greater effectiveness of the liposomal vaccine for protection against progressive VL in BALB/c. Again, evaluation of the immune responses by vaccination emphasizes the need of stimulation of potent cellular immunity based on both Th1 and Th2 cell responses to confer protection against VL.

Combination therapy with paromomycin-associated stearylamine-bearing liposomes cures experimental visceral leishmaniasis through Th1-biased immunomodulation

We, for the first time, used phosphatidylcholine (PC)-stearylamine (SA) liposome-associated paromomycin (PM) as a combination drug against experimental VL to achieve 88 to 98% parasite clearance from bone marrow, the liver, and the spleen, with a single-shot delivery (Fig. 10). Here, PC-SA-PM switched LAg-specific disease-resolving humoral as well as cell-mediated immunity over that of the disease-promoting immune response in *L. donovani*-infected BALB/c mice. PC-SA-PM induced the highest elevation of DTH, lymphoproliferation, IL-12, IFN-γ, TNF- α, and NO, followed by PM and PC-SA, and maximally reduced IL-4, IL-10, and TGF-β, followed by PC-SA and PM (Fig. 11). Thus, the combination drug augments the host protective immune mechanisms induced by the monotherapies. To prove that PC-SA-PM itself has immunomodulatory activity, we performed cytokine analysis of splenic supernatants from uninfected BALB/c mice 10 days after treatment with respective drugs. The present study showed that PC-SA at a molar ratio of 7:2 significantly enhanced the levels of IL-12, IFN-γ, and NO and reduced significantly not only IL-10 but also TGF-β. Maximum induction of IL-12, IFN- γ, and NO was observed with PC-SA-PM treatment in normal mice. All together, the findings make it evident that our present combination therapy incorporated both the IL-12, IFN- γ, and NO-promoting capacities of PM, and the IL-10 and TGF-β reducing capacity of PC-SA.

Therapy with sodium stibogluconate in stearylamine-bearing liposomes confers cure against SSG-resistant Leishmania donovani in BALB/c mice

Resistance of *L. donovani* to pentavalent antimonials, the first-line treatment of visceral leishmaniasis (VL), has become a critical issue worldwide. Suitable drug-delivery systems can improve the mode

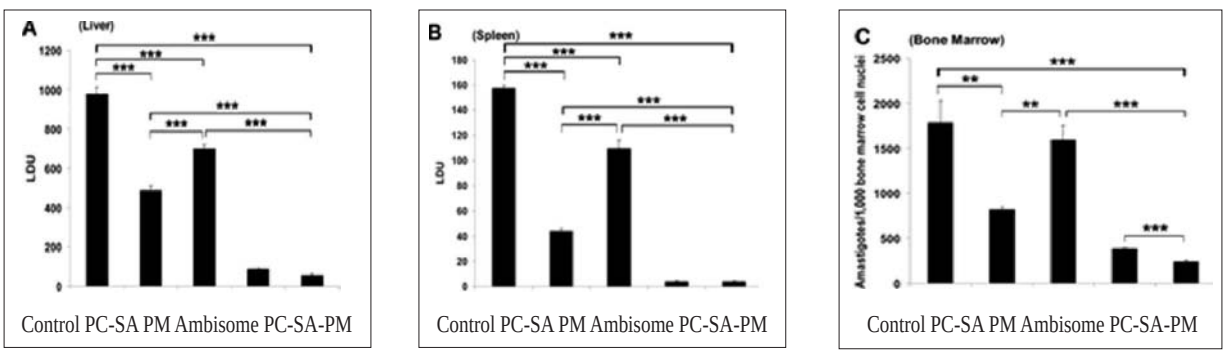

Fig. 10 : Effect of PC-SA-associated PM treatment on established *L. donovani* infection in BALB/c mice. Effect of PC-SA -associated PM was compared with those of treatment with drug-free PC-SA liposomes, free PM, and AmBisome on 12-week-infected mice. Untreated, infected mice were considered controls. Hepatic (A) and splenic (B) parasite burdens were determined by stamp-smear method and expressed as Leishman-Donovan units and bone marrow parasite load (C) was determined with cell smear prepared from femur bone marrow and expressed as amastigotes/1,000 bone marrow nuclei. Data represent the mean ± SE for five animals per group. Data were tested by ANOVA. Differences between means were assessed for statistical significance by Tukey's test (**, $P < 0.001$; ***, $P < 0.0001$).

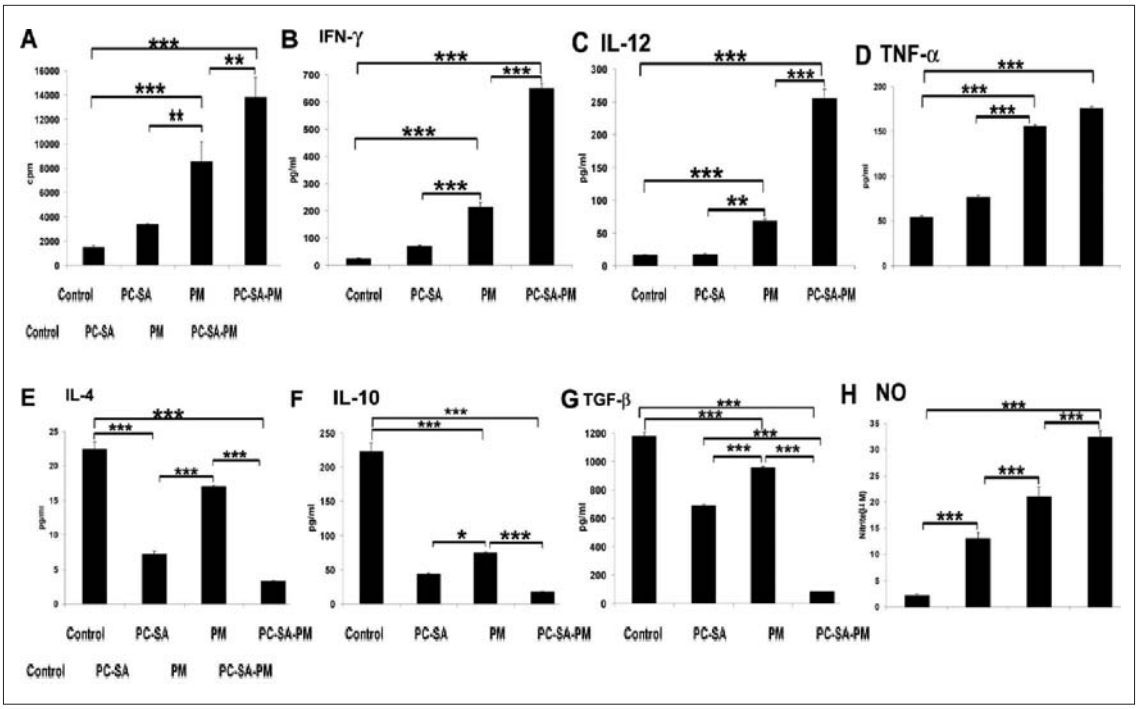

Fig. 11 : LAg-specific lymphoproliferation, cytokine, and NO levels in differently treated infected mice. Spleen cells of indicated treated animals were isolated 4 weeks posttreatment, plated aseptically (2 x 10^5 cells/well), and stimulated with LAg at 2 µg/ml for 48 h. (A) LAg-specific in vitro proliferation of spleen cells of differently treated animals was determined. IFN- (B), IL-12 (C), TNF- (D), IL-4 (E), IL-10 (F), TGF-β (G), and NO (H) in spleen cell culture supernatants of indicated treatment groups were determined by ELISA (for panels B to G) and the Greiss assay method (for panel H). Data represent the mean ± SE for five animals per group. Data were tested by ANOVA. Differences between means were assessed for statistical significance by Tukey's test (**, $P < 0.01$; ***, $P < 0.001$).

of administration and action of the existing antimonials, thus increasing their clinical life. We investigated the efficacy of sodium stibogluconate (SSG) in phosphatidylcholine (PC)-stearylamine-bearing liposomes (PC-SA-SSG), PC-cholesterol liposomes (PC-Chol-SSG) and free amphotericin B (AmB) against SSG-resistant *L. donovani* strains in 8-wk infected BALB/c mice. Animals were sacrificed and parasites in liver, spleen and bone marrow were estimated 4-wk post-treatment by microscopic examination of stamp smears and limiting dilution assay. Cytokine profile and immunomodulatory activity of different formulations in treated mice were determined. Uptake of free and liposomal SSG in intracellular amastigotes was determined by atomic absorption spectroscopy. Rhodamine 123 and 5-carboxyfluorescein, known substrates of Pgp and MRP transporter proteins, respectively, were used in free and liposomal forms for efflux studies to estimate intracellular drug retention. Unlike free and PC-Chol-SSG, PC-SA-SSG was effective in curing mice infected with two differentially originated SSG-unresponsive parasite strains (GE1F8R and CK1R) at significantly higher levels than AmB. Successful therapy correlated with complete suppression of disease-promoting interleukin (IL)-10 and tumour growth factor (TGF)-β, upregulation of T helper (Th)1 cytokines and expression of macrophage microbicidal nitric oxide (NO). Cure due to elevated accumulation of SSG in intracellular parasites, irrespective of SSG-resistance, occurs as a result of increased drug retention and improved therapy when administered as PC-SA-SSG versus free SSG. The design of this single-dose combination therapy with PC-SA-SSG for VL, having reduced toxicity and long-term efficacy

(Fig. 12), irrespective of SSG-sensitivity may prove promising, not only to overcome SSG-resistance in *Leishmania*, but also for drugs with similar resistance-related problems in other diseases.

A curative immune profile one week after treatment of Indian Kala-Azar patients predicts success with a short-course liposomal amphotericin B therapy

Visceral leishmaniasis (VL) is a potentially fatal disease without treatment, characterized by prolonged fever, enlargement of spleen and liver, anemia and weight loss. Treatment for VL is difficult, as it requires prolonged and painful application of toxic drugs with adverse side effects. It is therefore important to develop alternative satisfactory therapies for VL. In this paper, we report the efficacy

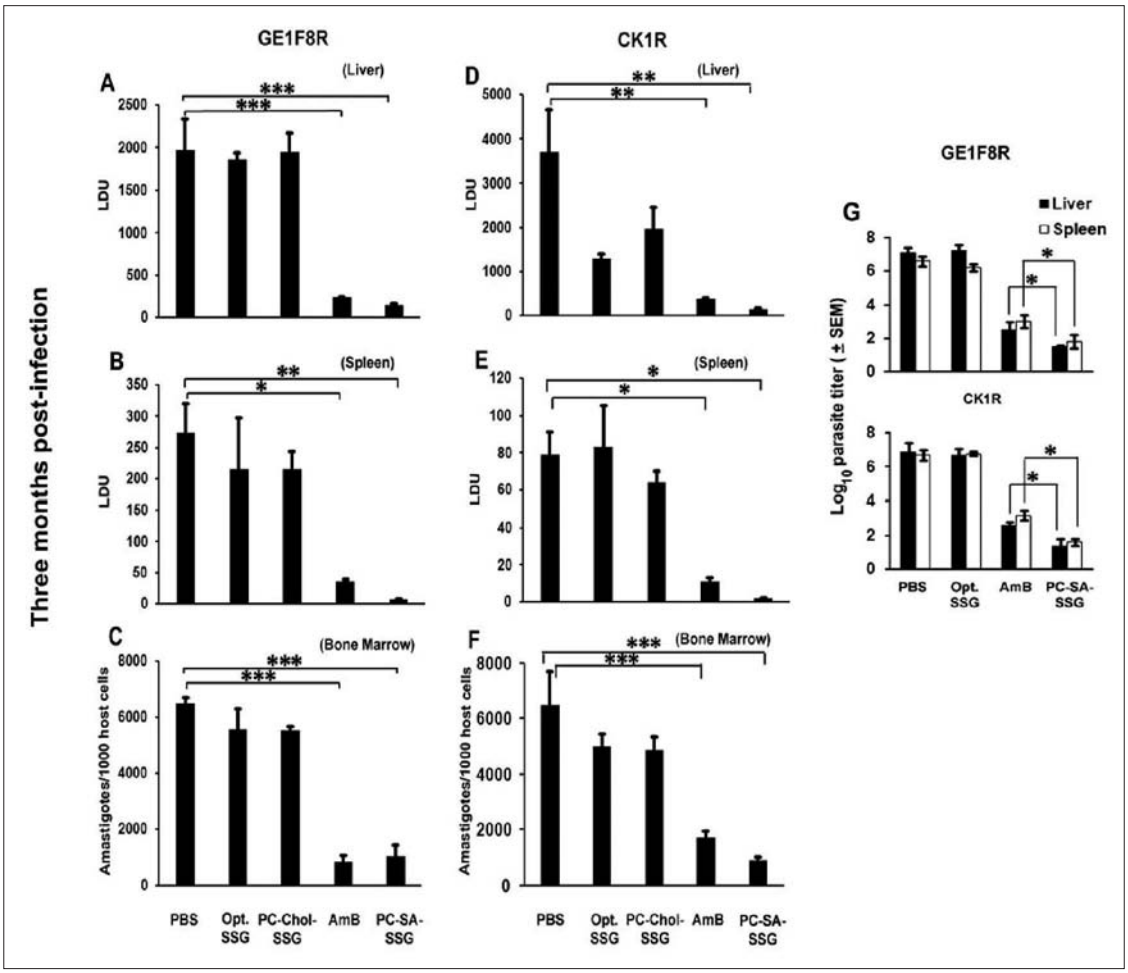

Fig. 12 : Parasite burden in treated BALB/c mice after *L. donovani* challenge infection. Parasite loads of liver, spleen, and bone marrow in murine model of established visceral leishmaniasis after treatment with 300 mg/kg of free sodium stibogluconate (SSG), 12 mg/kg of SSG entrapped in phosphatidylcholine-stearylamine (PC-SA) or phosphatidylcholine-cholesterol (PC-Chol) liposomes and 2 mg/kg amphotericin B (AmB). Mice were sacrificed after 4 weeks of treatment for determination of (A, D) liver, (B, E) spleen, and (C, F) bone marrow parasite loads. Untreated, infected mice were used as controls. Data represent mean ± SEM (n = 5 mice per group), representative of two similar experiments. * $p<0.05$; ** $p<0.01$; *** $p<0.001$. (G) Eight week infected mice received optimal SSG, PC-SA-SSG and AmB. Parasite burden determined 12 weeks following infection reflects the mean log10 parasite burden 6 SEM determined by the limiting dilution assay (LDA) (n = 5 mice per group) with PBS treated group as control. Data are representative of two similar experiments. * $p<0.05$ compared to AmB therapy.

of a new liposomal formulation of amphotericin-B, fungisome, and the immunological changes that take place 1-week after treatment. Patients treated with 5 and 7.5 mg/kg (single-dose) and 10 mg/kg (5 mg/kg double-dose) of fungisome showed 60%, 50% and 90% successful cure at 6-month post treatment, respectively. Successfully cured patients showed reduced IL-12 and IL-10 levels in the plasma and two-fold or more increase in Th1 type-cytokines IFN-γ, IL-12 and TNF, and down-

Table 1 : Plasma cytokine profile of Fungisome treated patients measured by ELISA from all the 3 groups, before treatment, 1 week after Fungisome treatment, at the time of relapse, and again after AmB treatment. Data are represented as mean (SEM). P values were calculated using Mann-Whitney U test for unpaired samples; P<0.05 was considered significant.

Cytokines (pg/ml)	Before treatment (n=21)	1 week after Fungisome treatment		At the time of relapse (n=8)	After AmB treatment (n=8)
		Responders (n=13)	Non-responders (n=8)		
IFN-γ	23.79 (2.07)	22.22 (1.79)	15.63 (2.65)	23.19 (4.6)	23.35 (2.33)
IL-12	222.8 (19.76)	107.2 (18.14)[a]	172.5 (25.83)	182.9 (27.20)	100.4 (19.93)[a, c]
TNF	19.44 (7.74)	28.22 (15.11)	17.13 (4.90)	22.36 (7.72)	11.18 (2.80)
IL-10	62.69 (6.01)	30.58 (2.65)[a, b]	47.69 (6.61)	48.31 (5.22)	28.50 (1.55)[a, c]
TGF-β	1507 (193.1)	1450 (330.8)	1700 (313.5)	1581 (393.2)	1400 (320.7)

Table 2 : LAg-specific lymphoproliferation and cytokine analysis before and after treatment with Fungisome. PBMCs were stimulated with 12.5 mg/ml LAg for 5 days and lymphoproliferation was measured by [3H]thymidine incorporation for the last 18-24 hours of culture. Cytokine levels were measured from supernatants of similar cultures after 96 hours calculated over background levels from all the 3 groups, before treatment, 1 week after Fungisome treatment, at the time of relapse and again after AmB treatment. Data are represented as mean (SEM). P values were calculated using Mann-Whitney U test for unpaired samples; P<0.05 was considered significant.

Before treatment (n=21)		1-week after Fungisome treatment		At the time of relapse (n=8)	After AmB treatment (n=8)
		Responders (n=13)	Non responders (n=8)		
Lymphoproliferation					
Stimulation index (SI)	1.20 (0.03)	1.84 (0.12)[a]	1.41 (0.12)[b]	1.37 (0.12)	2.90 (0.12)[a]
Cytokines (pg/ml)					
IFN-γ	15.35 (3.34)	60.48 (20.74)[a]	20.75 (4.67)[b]	46.25 (24.94)	60.13 (18.85)[a]
IL-12	34.46 (6.44)	91.03 (12.96)[a]	44.53 (4.48)[b]	58.09 (21.29)	135.05 (32.95)[a]
TNF	4.52 (1.68)	17.58 (3.42)[a]	4.91 (0.97)[b]	7.06 (3.32)[*]	19.00 (4.02)[a]
IL-10	58.19 (4.17)	37.86 (9.44)[a]	54.69 (8.31)[b]	52.63 (6.69)	24.22 (4.51)[a]
TGF-β	393.72 (60.75)	222.12 (41.31)[a]	258.1 (43.43)	400.30 (61.47)	208.30 (27.49)[a]

regulation of immunosuppressive factors IL-10 and TGF-β in the culture supernatants, 1-week after treatment independent of drug-dose (Table 1). Insignificant decrease of plasma IL-12 and IL-10, negligible increase of Th1-cytokines, and persistence of IL-10, despite decrease in TGF-β in culture supernatants, correlated with relapse within 6-months of treatment (Table 2). These interesting results pave the way for further testing of this drug as a new alternative in the chemotherapy of leishmaniasis.

Dr. (Mrs.) Rukhsana Chowdhury

Vibrio cholerae: Host pathogen interaction

Vibrio cholerae, a gram negative, non-invasive enteric bacterium is the causative agent of the diarrheal disease cholera. Cholera continues to be a major public health concern especially in developing countries. For successful infection, *V. cholerae* must first adhere to and colonize the intestinal epithelial cells. We have previously shown that the *V. cholerae* virulence genes are upregulated upon adherence to host cell lines. We have now demonstrated that immediately upon host cell contact *V. cholerae* upregulates genes involved in biofilm formation. The transcriptional regulation of these genes and the relevance of biofilm formation in infection are being investigated.

Competitive exclusion of classical biotype by El Tor biotype of V. cholerae.

V. cholerae strains of the O1 serogroup that typically cause epidemic cholera can be classified into two biotypes, classical and El Tor. The El Tor biotype emerged in 1961 and subsequently displaced the classical biotype as a cause of cholera throughout the world. We have demonstrated that when strains of the El Tor and classical biotypes were cocultured in standard LB medium, the El Tor strain clearly had a competitive growth advantage over the classical biotype starting from the late stationary phase and could eventually take over the population. The phenomenon is not due to the production of bacteriocins and is contact dependent. Furthermore, evidence has been obtained that indicate that the loss of viability of the classical biotype when cocultured with the El Tor biotype is due to conversion of the former to the Viable but Non-Culturable (VBNC) state. Next, to identify the genes for the above phenotype, a transposon mutant library of a classical strain was constructed and screened for mutants exhibiting a complete or partial competition resistant phenotype. Six mutants were obtained, five of them had mutations in different genes involved in flagellar motility and one had a mutation in the stationery phase specific sigma factor.

Helicobacter pylori: Host-pathogen interaction

H. pylori is a non-invasive bacterium that causes persistent gastric infections. The effect of adherence to the gastric epithelial cell line AGS , on expression of a number of H. pylori virulence has been investigated. The results obtained indicated that the expression of the major virulence gene *cagA* was upregulated 5-6 fold following adherence of *H. pylori* to host cell lines. Of particular interest is the identification of transcription factors that control the specific induction of *cagA* following adherence to host cells. We have demonstrated that transcriptional regulator Fur upregulates *cagA* expression in host cell associated *H. pylori*.

Helicobacter pylori: Regulation of gene expression by sRNA

H. pylori has a small genome (1.67 Mb) and a relatively small number of transcription factors have

been identified in the genome. Recently, however, it has been reported that *H. pylori* has a large repertoire of small non-coding RNAs (sRNA) which can provide insights into the regulation of gene expression in the bacterium. We have validated two sRNA candidates HPnc2620 and HPnc2630 encoded by the Cag Pathogenecity Island. Studies have been initiated to elucidate the roles of the two sRNAs under different conditions of growth, stress and adherence to host cells. HPnc2620 appears to act as an antisense sRNA regulating the expression of the virulence gene *cag*13. HPnc2630 acts as a 5′ UTR of *cag*15 and its role in regulating *cag*15 expression is currently under investigation.

Dr. Rupak K. Bhadra

Vibrio cholerae is a major human diarrhoeal pathogen causing frequent epidemics in most developing countries including India. The situation is further complicated by frequent emergence of new pathogenic clones with multiple drug resistance. In this regard recent spread of the hybrid *V. cholerae* El Tor strains carrying classical type CTX phages in Africa and Indian Subcontinent is noteworthy. However, recent progress in bacterial genomics and proteomics has dramatically altered the study of bacterial pathogenesis and designing of experiments for complete understanding the virulence mechanism, growth, survival and persistence of the pathogens in various environmental niches. As a result new genes and regulatory circuits of the above pathogens are identified. It is also necessary to understand the role played by various mobile genetic elements in the evolution of new pathogenic clones. Different physico-chemical stress signals including nutrition deprivation received by pathogens in environmental reservoirs as well as under in vivo situations are quite dissimilar and probably play critical roles in adaptation through genetic mutation and help a pathogen to evolve further. In this regard, role of quorum sensing and biofilm formation also appears to be important for survival and growth of *V. cholerae.*

Evolution of hybrid Vibrio cholerae O1 biotype El Tor

Pathogenicity of *Vibrio cholerae*, the cholera pathogen, is fully dependent on a filamentous bacteriophage, called CTXΦ. The genome of CTXΦ carries the *ctxAB* operon, which codes for cholera toxin, the principal virulence factor of *V. cholerae*. Diverse CTXΦ infects *V. cholerae* and helps the pathogen to evolve further and maintain its pathogenic and epidemic potentials. The classical biotype, a sixth pandemic strain, harbored $CTX^{Cl}\Phi$, but the current seventh pandemic El Tor biotype carries $CTX^{ET}\Phi$. Similarly, the newly evolved *V. cholerae* strain belonging to the new serogroup O139 may carry $CTX^{ET}\Phi$ as well as another diverse phage $CTX^{calc}\Phi$. More recent hybrid El Tor strains reported from this lab and other labs carry $CTX^{Cl}\Phi$ instead of $CTX^{ET}\Phi$ and the basis of evolution of this hybrid strain is currently unclear. Apart from CTX^{Cl} prophages certain hybrid El Tor strains also carry pre-CTX prophages, which are devoid of *ctxAB* genes. Furthermore, certain environmental toxigenic *V. cholerae* non-O1, non-O139 strains may carry pre-CTX prophage. To understand more clearly about the nature of pre-CTX prophages, we are sequencing the entire prophage genomes of a *V. cholerae* O1 El Tor hybrid strain VC106 and a non-O1, non-O139 strain VCE232. Preliminary analysis indicated that that they are different from $CTX^{Cl}\Phi$ or $CTX^{ET}\Phi$ indicating further the complex evolution of these elements.

Molecular basis of survival of V. cholerae under nutritional stress

Nutritional stress evokes stringent response in bacteria. RelA and SpoT enzymes of Gram-negative organisms, namely *E. coli, V. cholerae* etc., critically regulate cellular levels of (p)ppGpp, the cellular

alarmone. Previously we have dissected the *spoT* gene function of the *V. cholerae* by extensive genetic analysis and results suggested RelA-SpoT independent (p)ppGpp synthesis in *V. cholerae*. This was followed by discovery of a novel gene *relV*, which is responsible for (p)ppGpp synthesis under *relA spoT* negative condition. Thus, intracellular concentration of (p)ppGpp in *V. cholerae* appears to be critically regulated by *relA spoT* and *relV* and it is quite complex. Stringent response in bacteria is also regulated by a factor, called DksA (product of the gene *dksA*). We have generated several *dksA* mutants of *V. cholerae* and characterization of those mutants revealed that the DksA protein apart from its role in stringent response may control virulence factor production, motility, indole biosynthesis, biofilm formation etc. Role of stringent response genes *relA, spoT, relV* and *dksA* will be further explored for their involvement, if any, in quorum sensing, biofilm formation, long-term starvation survival and relation with stationary phase sigma factor gene *rpoS* and nitrogen metabolism related sigma factor gene *rpoN* expressions. Apart frome these genes, we also characterized the essential gene *cgtA*, the product of which is a GTP-binding protein. CgtA is involved in stringent response in *V. cholerae*. Previously we reported about the function of CgtA by studying different mutants and by deletion analysis showed that the C-terminal domain of CgtA is important for its function. We have now tried to characterize the promoter region of the cgtA gene of *V. cholerae*. There are two putative promoters, P_1 and P_2, of the *cgtA* operon and which one is active is not known. Therefore, the entire P_1+P_2 promoter region and only the P_2 region were individually cloned in a *lacZ* reporter vector and strength of these promoters were tested in a *V. cholerae* Δ*lacZ* strain. It was noted that the P_2 region is significantly less active than that of combine P_1+P_2 region. Therefore, more extensive deletion analysis is needed to pinpoint the exact promoter region of the *cgtA* gene of *V. cholerae*.

Currently we are engaged in dissecting the regulatory circuits of stringent response, quorum sensing of *V. cholerae* and trying to understand how these two major regulatory networks are linked with each other.

Dr. (Mrs.) Tripti De

Galactose-terminal glycans, lymphocyte activation and induction of protective immunity against Visceral Leishmaniasis.

Impact of glycosylation on the regulation of innate and adaptive immune responses is well documented. Pathogen-specific innate immune recognition through binding to different immune sensors viz, Toll-like receptors (TLR) lead to the activation of antigen-specific adaptive immune responses. The galactose-terminal glycans can modulate host responses in a Th-1 direction via IFN-γ and TLRs. Visceral leishmaniasis (VL) is characterized by parasite-specific immunosuppression. Interleukin-10 is thought to play an immunosuppressive role in VL, by restraining Th1 cell-type responses and/or deactivating parasitized tissue macrophages. In mice experimentally infected with *L. donovani*, the *in vivo* efficacy is primarily regulated by Th1-cell-type cytokines IL-12 and IFN-γ, and induction of macrophage leishmanicidal mechanisms. We investigated the immune response elicited in infected mice by the galactose-terminal glycans and the subsequent impact on the balance between Th1 and Th2 responses.

CD1d mediated T cell recognition of Leishmanial glycosphingophospholipid

An immunomodulatory glycosphingophospholipid (GSPL) was used to immunize BALB/c mice prior to *Leishmania donovani* infection. GSPL mediated activation of NKT cells efficiently induced long-

lived adaptive resistance. IL-17 and IFN-γ producing NKT cells induced the host protective Th1 immune response.

The host protective purified leishmanial glycoprotein [LGP]

Protein subunit vaccines are typically poorly immunogenic when administered alone and therefore require co-administration with adjuvants to boost the immune response. A successful vaccine, therefore, should not only contain protective antigen(s), but also a good adjuvant that can effectively amplify the protective immune responses. We have purified a galactose terminal glycoprotein (LGP) from an Indian strain of *L.donovani*. LGP acts as a self adjuvant to confer a protective immune response in murine visceral leishmaniasis. There was a strong correlation between elimination of the parasites and an increased *Leishmania*-specific IFN-γ/IL-10 ratio. Data indicated that IL-12 did not play a direct role in GP29 mediated protective immunity; protection was predominantly mediated via IL-12 induced IFN-γ production. Thus, IL-12 probably acts as an effective adjuvant for the initiation of protective cell-mediated immunity against leishmaniasis.

Mrs. Neeta V. M. Khalkho

We have been involved in the study of functional aspects of replication proteins. Targeting these proteins can be very much effective for anti-leishmanial drug development. Universal minicircle sequence binding protein (UMSBP) is one of the essential proteins playing a key role in the replication of kDNA minicircles in trypanosomatids. As an origin binding protein UMSBP is expected to act during the initiation of kDNA replication in the recruitment of other replication proteins to replication origin through protein protein interaction (Onn et al., 2004).

For better understanding of the structure of UMSBPs from *L. donovani*, we have earlier reported the cloning, over expression and purification of the LdUMSBP1 and LdUMSBP2 from bacterial expression vector. We have earlier reported LdUMSBP1 and LdUMSBP2 to recognize 12mer (5'-GGGGTTGGTGTC-3'), Universal Minicircle Sequence (UMS) present on the heavy strand is the site for replication origin of light strand. This time we have checked for the nucleoprotein complex formation of *Ld*UMSBP1 and *Ld*UMSBP2 with another oriH-associated 14-mer, H14 sequence containing the conserved hexamer "core" (5'-ACGCCC-3') and the 4 residues flanking both termini. We found binding of *Ld*UMSBP1 and *Ld*UMSBP2 to H14 sequence with the same efficiency as they did with UMS sequence.

To study the effect of temperature on the nucleoprotein complex formation, EMSA of UMS DNA ligand and H14 DNA ligand was done with *Ld*UMSBP1 protein and *Ld*UMSBP2 protein respectively in 0°C to 37°C, increasing temperature condition. Increase in temperature from 0°C to 37°C resulted in super shifting of nucleoprotein band due to enhanced nucleoprotein complex formation. These studies help us to better understanding of the biochemical nature of these proteins. Further detail study about the protein structure and interaction needs protein crystallization, NMR and co-immunoprecipitation studies.

Dr. Uday Bandopadhyay

Thioredoxin-like oxidoreductase and antioxidant activities of Plasmodium falciparum macrophage migration inhibitory factor

Plasmodium falciparum macrophage migration inhibitory factor (*Pf*MIF) exhibits thioredoxin (Trx)-

like oxidoreductase activity but the active site for this activity and its function has not been evaluated. The bioinformatics search revealed that the conserved CXXC motif which is responsible for Trx-like oxidoreductase activity is absent in *Pf*MIF. In contrast, N-terminal two adjacent cys-3 and cys-4 are conserved in MIF across the species of malaria parasites. Mutation of either vicinal cys-3 or cys-4 of *Pf*MIF abolished the Trx-like activity, whereas the mutation of the remaining cys-59 or cys-103 did not affect it. *Pf*MIF has antioxidant function. It prevents reactive oxygen species-mediated lipid peroxidation and oxidative damage of DNA as evident from DNA nicking assay. Interestingly, chemical modification of vicinal cysteines by phenylarsine oxide (PAO), a specific vicinal thiol modifier significantly prevented its antioxidant activity. Modification of cys-3 and cys-4 was confirmed by MALDI-mass spectroscopy of peptide fragments obtained after cyanogen bromide (CNBr) digestion of PAO-modified *Pf*MIF. Furthermore, mutation of either cys-3 or cys-4 of *Pf*MIF results in the loss of both Trx-like oxidoreductase and antioxidant activities of *Pf*MIF. Altogether, our results suggest that vicinal cys-3 and cys-4 play a critical role for Trx-like oxidoreductase activity and antioxidant property of *Pf*MIF.

Gallic acid prevents non-steroidal anti-inflammatory drug-induced gastropathy in rat by blocking oxidative stress and apoptosis

Non-steroidal anti-inflammatory drug (NSAID) - induced oxidative stress plays a critical role in the gastric mucosal cell apoptosis and gastropathy. NSAID induces the generation of hydroxyl radical ($^{\bullet}$OH) through the release of free iron, which plays an important role to develop gastropathy. Thus, molecule having both iron chelating and antiapoptotic properties will be beneficial to prevent NSAID-induced gastropathy. Gallic acid (GA), a polyphenol natural product has the capacity to chelate free iron. Here, we report that GA significantly prevents as well as heals NSAID-induced gastropathy. GA, *in vivo* blocks NSAID-mediated mitochondrial oxidative stress by preventing mitochondrial protein carbonyl formation, lipid peroxidation and thiol depletion. GA scavenges free radical and blocks (OH-mediated oxidative damage *in vitro*. GA also attenuates gastric mucosal cell apoptosis *in vivo* as well as in vitro in cultured gastric mucosal cell as evident from TUNEL assay. GA prevents NSAID-induced activation of caspase-9, a marker for mitochondrial pathway of apoptosis and restores NSAID-mediated collapse of mitochondroial transmembrane potential and dehydrogenase activity. Thus, the inhibition of mitochondrial oxidative stress by GA is associated with the inhibition of NSAID-induced mitochondrial dysfunction and activation of apoptosis in gastric mucosal cells, which are responsible for gastric injury or gastropathy.

Dr. (Mrs.) Malini Sen

We are interested in understanding the molecular basis of WNT5A and WISP3 mediated regulatory networks in health and disease. Our primary focus is on two aspects of signal transduction: (i) the role of WNT5A, a member of the WNT family of growth regulators in immune response / inflammation, and (ii) the role of WISP3, a connective tissue growth modulator in regulation of IGF signaling, oxidative stress and chondrocyte hypertrophy.

Our experimental results suggest that WNT5A signaling contributes to macrophage growth / differentiation and phagocytosis. This aspect of WNT5A signaling can be both beneficial for innate immunity and also enhance context dependent chronic inflammation. We also propose that WISP3 sustains chondrocyte / cartilage integrity by inducing collagen II and modulating IGF1 mediated effects, for example, oxidative stress and cellular hypertrophy.

Dr. (Mrs.) Mridula Misra

Development of new radiopharmaceuticals for different organ imaging

Tyr3Octreotide Derivatives: synthesis, radiolabelling and application as tumor targeted radiopharmaceuticals

Peptides are important regulators of growth and cellular functions not only in normal tissue but also in tumours. A wide variety of tumours express enhanced number of somatostatin receptors. Octreotide is a synthetic analogue of the peptide hormone somatostatin and octreotide is used clinically for tumour targeting. Octreotide is used in nuclear medicine imaging by labelling with indium-111 (Octreoscan) to non-invasively image neuroendocrine and other tumours expressing somatostatin-receptors. More recently, it has been radiolabelled with gallium-68 enabling imaging with positron emission tomography (PET), which provides higher resolution and sensitivity. Octreotide can also be labelled with a variety of radionuclides, such as yttrium-90 or lutetium-177 and ^{99m}Tc, to enable peptide receptor radionuclide therapy (PRRT) for the treatment of unresectable neuroendocrine tumours.

We have synthesized some more octreotide / octreotate derivatives semi automatically on a peptide synthesizer by using standard Fmoc solid phase synthesis. These peptides were purified by using a semi-preparative HPLC column and characterized by MALDI mass, ^{1}H NMR, ^{13}C NMR, and IR spectra, analytical HPLC. Peptides were radiolabeled with ^{99m}Tc by using SnCl2 method. The complexation efficiency and radiochemical purity of radiolabelled peptide complexes were analysed by ITLC and HPLC. Stability study was performed at different time intervals. And we found that compound were stable for 24 h. Biodistribution (Fig. 13), Protein binding and renal clearance (Fig. 14) study was performed for Octreotide as well as Octreotide derivatives.

In-vitro, In-vivo study and scintigraphic imaging work are in progress with these peptide radiopharmaceuticals.

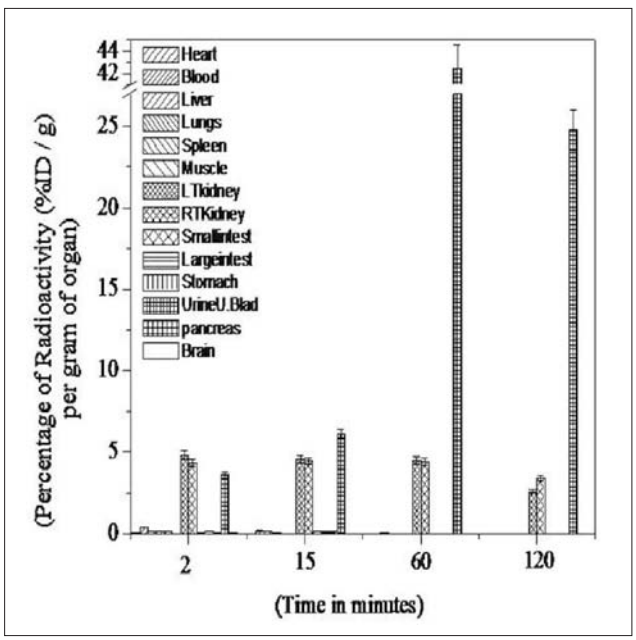

Fig. 13 : Biodistribution of Octreotide.

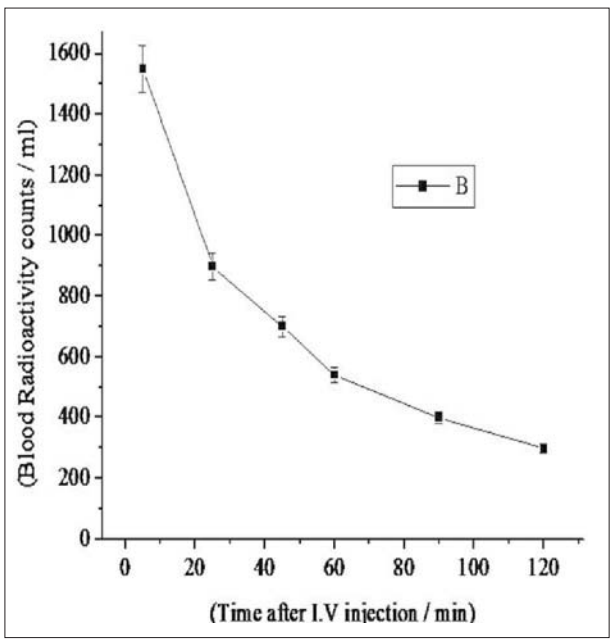

Fig. 14 : Renal clearance of Octreotide.

We also have directly labeled Tyr^3-Octreotide with ^{99m}Tc by using sodium ascorbate and tartarate method then we studied the stability of the radio peptide complex. We found that the compound was stable at room temperature and the radio labeling efficiency was found to be 90% and 95% respectively.

We have also tried to develop nanoparticles to target somatostatin receptor positive tumors and different physicochemical and biopharmaceutical properties of nanoparticles by using different octreotide derivatives.

Dr. Mita Chatterjee Debnath

99mTc(CO)$_3$-nitrofuryl thiosemicarbazone a novel infection imaging radiopharmaceutical

The high incidence of infection in daily life has prompted research into better and more accurate diagnostic methods, of these noninvasive diagnosis of infection / inflammation with suitable radiopharmaceuticals using nuclear medicine techniques is a major challenge, which allows prompt and successful treatment and reduces the risk of morbidity. The radiopharmaceuticals so far developed or proposed include various technetium-99m labeled agents e.g. polyclonal and monoclonal immunoglobulins hexamethyl propylene amine oxime WBC, cytokines peptides , antibiotics etc. Unfortunately, majority of these radiolabeled compounds cannot always distingwish between septic and aseptic processes. Antibiotics in general localize at the infection site, where they are taken up and metabolized by living microorganisms.The area of bacterial infection could be identifiable by gamma scintigraphic imaging technique with antibiotic suitably radiolabeled with technetium-99m.

Over the last few decades nitrofuran derivaties are used in the treatment of bacterial infection of the urinary tract. Semicarbazones and thiosemicarbazones prepared from 5-nitro-2-furaldehyde are found to exhibit profound antibacterial, antifungal and antiparasitic (antiprotozoal Trypanosoma Cruzi) activities. Antibacterial, antifungal properties of transitional metal (Cu(II), Ni (II)) chelates of thiosemicarbazones are also reported . These compounds produce oxidative stress in the microorganism. Recently *fac*[^{99m}Tc(CO)$_3$ (H_2O)$_3$]+ core has been widely used for radiolabeling of different types of bioactive molecules. Bearing in mind the high chemical and kinetic stability of ^{99m}Tc-tricarbonyl core leading to efficient labeling of low molecular weight biomolecules and as part of our ongoing development of novel infection imaging agent based on ^{99m}Tc-tricarbonyl precursor, we radiolabeled nitrofuryl thiosemicarbazone with fac-[^{99m}Tc(CO)$_3$(H_2O)$_3$]$^+$, the radiopharmaceutical was evaluated in *S. aureus* infected rat model. 5-Nitrofurfural- 2-thiosemicarbazone (NFT) was synthesised from 5-nitrofurfural and thiosemicarbazide in dry toluene using p-TsOH (catalytic amounts) room temperature under nitrogen atmosphere. ^{1}HNMR (CD_3OD) [δ (ppm) : 7.138 (d, 1H, J=3.9 Hz, furan-H), 7.57 (d, 1H, J=3.9 Hz, furan-H), 7.93(s, 1H, -CH=N)]. MS (ESI): m/z 215.10 (100%, M + H)$^+$. 5-Nitrofuryl-2-thiosemicarbazone was radiolabeled with freshly prepared ^{99m}Tc(CO)$_3$(H_2O)$_3$]$^+$ solution of (pH 6.0, 185-279 MBq), final pH of the reaction mixture was maintained between 6.1 to 6.2. The mixture was heated at 75ºC for 30 min, cooled. 5-nitrofuryl-2-thiosemicarbazone was also radiolabeled with ^{99m}TcO^{3+} core in ethanol- H_2O medium at room temperature using freshly prepared stannous chloride dihydrate solution (1mg/mL) as reductant. Instant thin layer chromatography (ITLC) was performed on silica gel strips in brine to detect free ^{99m}TcO$_4^-$ in ^{99m}Tc(CO)$_3$-NFT, ^{99m}Tc(V)O-NFT. ^{99m}Tc(CO)$_3$-NFT and ^{99m}Tc(V)O-NFT were further characterized by HPLC analysis using XTerra® RP_{18} column (4.6x250mm) eluted with a gradient mixture of 0.05 mol/L triethylammoniumphosphate pH 2.25

buffer (eluent A) and methanol (eluent B) (Fig. 15). The radiochemical purities were >96% and near about 80% in $^{99m}Tc(CO)_3$-NFT, $^{99m}Tc(V)O$-NFT respectively. The biodistribution studies (4hr) were performed in *S. aureus* infected Sprague, Dawley rats resulted urinary excretion of about 19%, hepatobiliary excretion of about 29% and blood activity was 6.5% of the injected dose/organ . Infected vs normal muscle ratios were 3.41 and 2.83 for $^{99m}Tc(CO)3$-NFT and $^{99m}Tc(V)O$-NFT respectively. Two well hydrated infected anaesthetised rats were injected intravenously with $^{99m}Tc(CO)_3$-NFT, (0.1 mL, 6 MBq). Whole body images of the animals were acquired in an anterior position at 4 h post-injection in GE Infinia Gamma Camera equipped with Xeleris Work Station. This procedure was repeated in separate experiments with equivalent doses of $^{99m}Tc(V)O$-NFT as above (Fig. 16). Scintigraphic studies showed definite uptake in infected thigh in comparison to that of normal thigh

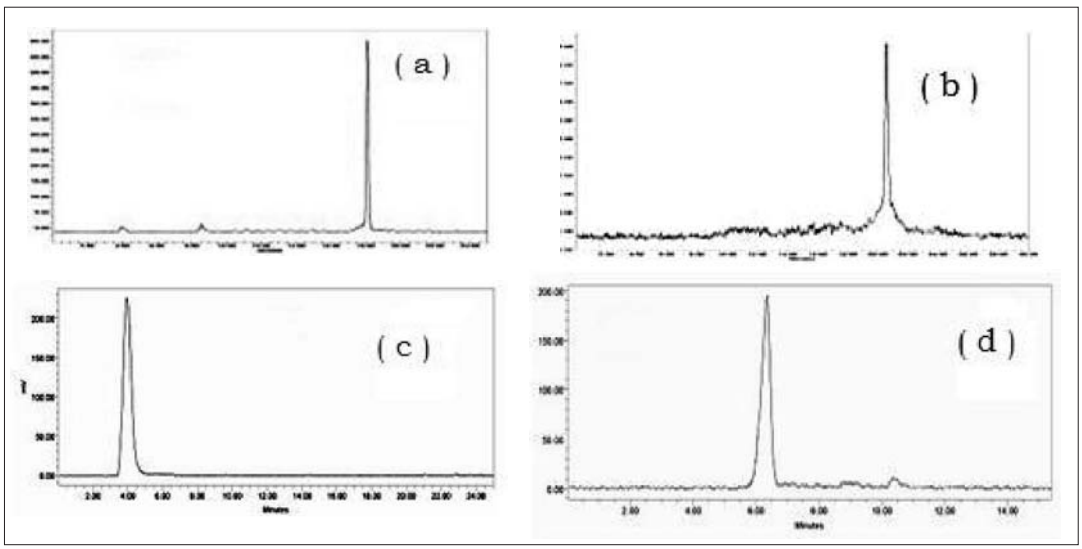

Fig. 15 : Radiochromatograms of $^{99m}Tc(CO)_3$-NFT (a), $^{99m}Tc(V)O$-NFT (b), $^{99m}Tc(CO)_3(H_2O)_3]^+$ (c) and $^{99m}TcO_4^-$ (d).

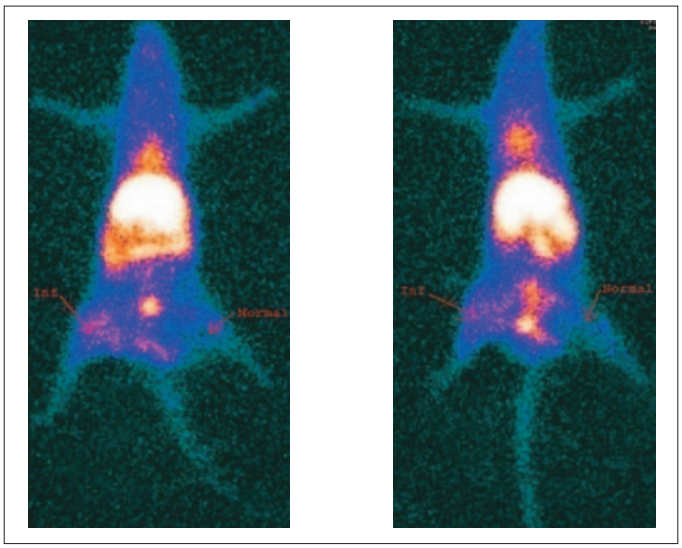

Fig. 16 : Scintigraphic images of $^{99m}Tc(CO)_3$ -NFT in rats with thigh muscle infections at 4 h post-injection (i.v.).

(Fig. 16). However the uptake in the infected area was much better for ^{99m}Tc(CO)3-NFT than ^{99m}Tc(V)O-NFT. The above method of radiolabelling with tricarbonyl precursor will also be extended for chelation of other nitrofuryl thiosemicarbazones as well as some fluoroquinolone antibiotics. This study will help us in uderstanding the pharmacokinetics of a series of antimicrobial agents with different spectrum of activity. In addition this study may lead to the development of a novel infection imaging agent having ability to localize in wide variety of deep seated bacterial infection.

Dr. Aparna Laskar

Transmission electron microscope (TEM) is one of the most sophisticated instrument in the research field for detail characterization of different samples. Now-a-days, TEM data is almost essentially required to validate most of research works, since it provides information regarding vivid details of the sample under analysis. TEM is performed in research works related to biological samples (bacterial cells, Leishmanial cells, sperm cells etc.), nanoparticles (gold, silver etc.), protein aggregates, monomers, dimer and oligo peptide detection and many more.

Tecnai G^2 Spirit BioTWIN (120kV) transmission electron microscope, made in Czech republic, and Leica EM UC6 ultramicrotome, is included in the *infrastructural facility* in the department of Infectious diseases and Immunology.

Scientific Activities

i) TEM is performed with internal samples (such as bacterial cells, Leishmanial cells, various nanoparticles, protein aggregates, monomers, dimer and oligo peptides etc.), as well as external samples (such as bacterial and fungal cells, nanoparticles etc.), on daily basis, all year long.

ii) Ultramicrotome, which is an accessory yet essential instrument of this lab, is undergoing calibration and standardization. It will provide ultrathin (in the nm.range) sections of various biological samples, including Leishmanial cells, cancer cells, sperm cells, plant cells, bacterial cells etc.

Other Scientific Activities

Work is also done in collaboration with some internal scientists in the structural Biology field related to Silicon Graphics Work Station.

Dr. Krishna Das Saha

Anticancer and immunomodulatory role of integral membrane proteins and sphingolipids of leishmanial origin

Recognition of microbial PAMP (pathogen associated molecular pattern) molecules like lipid, proteins, carbohydrate by an array of transmembrane proteins (mainly Toll receptors) of mammalian cells modulates different signaling cascades and cellular responses including cell growth, apoptosis, immune responses and inflammation. *Leishmania* is one of the simplest forms of eukaryotes. Any of its component as therapeutic agent may be compatible for host. To find a novel target for cancer, and a novel target for inflammation from microbial origins, we have used *Leishmania* sp.

Integral membrane proteins (IMPs) of *Mycobacteria, Mycoplasma* and leishmanial origin are immunologically active. Whether the integral membrane protein(s) from *Leishmania* sp. have anticancer

or immunomodulatory activity are being examined by us. Reports are coming to show that externally added sphingolipids (SPLs) specially the ceramides induce apoptosis in cancer cells either by enhancing cellular ceramide content or by altering ceramide ratio of lipid raft. Also, sphingolipids regulate cellular functions like immune responses. These evidences have encouraged us to find the anticancerous and immunomodulatory role of leishmanial integral membrane proteins (LIMPs) and leishmanial sphingolipids (LSPLs).

We are isolating IMPs, SPLs from *L. donovani* major, UR-6 as well as *L. donovani*, AG83 and separating each component, screening the (a) growth regulatory effect of each component on cancer cells of different origins, (b) anti-inflammatory effect on endotoxin stimulated macrophages and various inflammatory models, and (c) immunostimulatory role *in-vitro* and *in-vivo* studies. Next we are characterizing the active protein and sphingolipid components along with the elucidation of their mechanism of actions and involvement of Toll recptors (TLRs).

From Our study one integral membrane protein of approximate MW 58 KDa, was found to be a glycolipoprotein and one sphingolipid of inositol ceramide type as evident from preliminary studies show potent cytotoxic effect through induction of apoptosis on a number of cancer cell lines examined by us. The active leishmanial sphingolipid component suppresses the inflammatory responses in murine model of arthritis, on endotoxin stimulated macrophage cells, and synovial fluid cells of rheumatoid arthritis patients. Treatment of active sphingolipid (LSPL) (2mg/kg body weight /dose) on day 3, 5, 7, 10, and 15 in BALB/c mice significantly increases the survival rate of mice and reduce the B16F10 tumor growth. The active leishmanial sphingolipid component (LSPL) induces apoptotic like morphological changes in adherent synovial fluid cells of rheumatoid arthritis (RA) patients and significantly suppresses the paw swelling of collagen induced arthritis in rat 24 h after or prior to the challenge of it. The active sphingolipid (LSPL) potentially suppresses the inflammatory responses of endotoxin stimulated macrophages as well synovial fluid cells of RA patients.

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Lab Assistant

Mr. Narendra Pradhan, Mr. Biswajit Mandal, Mr. Shibkumar Sharma.

MOLECULAR & HUMAN GENETICS

Drs. Samit Adhya, Suvendra Nath Bhattacharyya, Keya Chaudhuri, Kunal Ray, Susanta Roychoudhury and Ashok Kumar Giri.

Brief Preamble

The broad aims of the division are to understand the molecular genetic basis of diseases common in Indian populations, to study gene expression and function in pathogenic microorganisms.

The specific objectives are : to decipher the molecular basis of the genomic instabilities in head and neck cancer (HNSCC) and to identify the putative tumor suppressor genes involved in the development of this cancer: to identify susceptibility alleles in *Helicobacter pylori* associated gastroduodenal diseases: to study the molecular pathogenesis of oral submucous fibrosis: to understand the molecular genetics of haemophilia, glaucoma, Wilson disease, and oculo-cutaneous albinism: to assess the health effects, genetic damage and genetic variants in populations exposed to arsenic through drinking water in West Bengal: to test the antimutagenic and anicarcinogenic effects of black tea polyphenols theaflavins and thearubigins: to identify differentially expressed *V. cholerae* genes following infection to host and their role in pathogenesis, and to study the response of human intestinal epithelial cells to *V. cholerae* infection: to study the molecular basis of the import of nuclear-encoded tRNAs into the mitochondria of the kinetoplastid protozoon *Leishmania* using a combination of biochemical and reverse genetic approaches; to develop gene delivery protocols for mitochondria; to identify, intracellular & extracellular factors regulating miRNA mechanism in animal cells.

MiRNAs are ~21-nt-long regulatory RNAs expressed in eukaryotes. Expression of many miRNAs is tissue or development stage specific and major changes in miRNA expression are observed in human pathologies. MiRNAs regulate gene expression post-transcriptionally, by imperfectly base-pairing to 3'UTR of mRNAs, what results in translational repression or mRNA degradation. Repressed mRNAs are localized to P-bodies, cellular structures involved in storage and degradation of mRNAs. Present data provided evidence that P-bodies function in storage of miRNA-repressed mRNAs and demonstrated that miRNA-mediated repression is a reversible process and may be controlled by extracellular cues. Deciphering the mechanism of miRNA-mediated gene regulation process in mammalian cells and identifying the regulators of miRNA expression and activities in animal cells is the primary research target of one research group.

A few genetic diseases that are common in India are being studied for identifying the underlying defects and the molecular basis of pathogenesis. These are eye disorders (primary open angle glaucoma, POAG & oculocutaneous albinism, OCA), neurological disorders (Wilson disease & Parkinson's disease), and bleeding disorder (Haemophilia). In addition the studies have also been undertaken to identify biomarkers related to arsenic toxicity using proteomic approaches.

Dr. S. Adhya & group

Delivery of large functional RNA to mitochondria

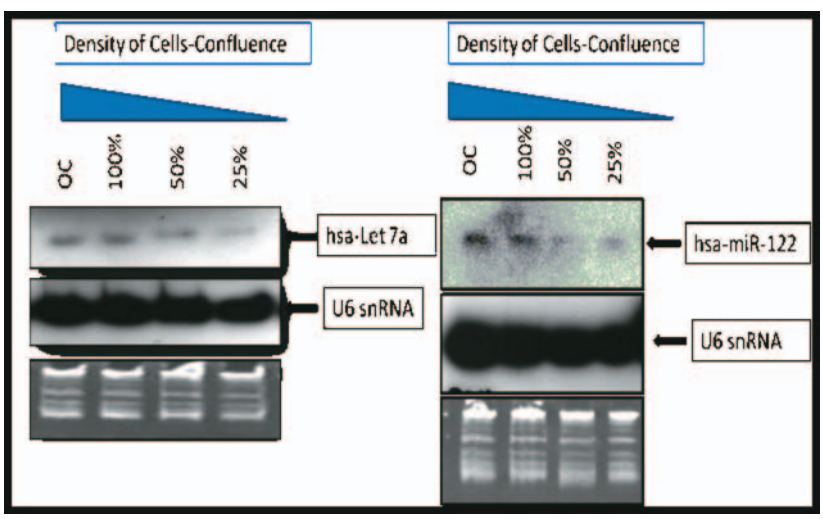
In the last year, we reported a major advance in the development of a novel protocol for mitochondrial gene therapy using a multi-subunit carrier complex. In 2009-10, the efficacy of the protocol in correcting the mitochondrial defect of cells with multiple mtDNA deletions was investigated. Many human diseases are associated with mutations and deletions in mitochondrial DNA (mtDNA). We have generated a cell line, EB delta1, with multiple mtDNA deletions, that is respiration-defective and generates high levels of superoxide, a reactive oxygen species. Treatment of EB delta1 with tagged polycistronic (pc) RNAs, encoding parts of the mitochondrial proteome, bound to a multi-subunit carrier complex, resulted in cellular uptake and transfer of the RNA to mitochondria, restoration of respiration, and suppression of superoxide levels by individual or combinations of pcRNAs. These findings have implications for correction of mitochondrial defects in age-related disorders due to mtDNA mutations.

Dr. S. N. Bhattacharyya & group

Mechanism of miRNA-mediated gene regulation in mammalian cells and effects of extracellular factors in controlling miRNA activities

Laboratory of Dr. Suvendra Nath Bhattacharyya is investigating the mechanism of miRNA-mediated gene regulation process by extracellular factors in mammalian cells. The cellular microenvironment is composed of an intricate blend of extracellular matrix components and numerous neighboring cell types, and influences cellular behavior and gene expression profile *in vivo*. However, the effect of cellular microenvironment on post-transcriptional regulation of gene expression has never been addressed in detail in metazoa. Multidimensional cell culture systems and arrays of microenvironments are being used for identification of extracellular factors regulating miRNA-dependent and miRNA-independent post-transcriptional gene regulation machineries in mammalian cells. The miRNA-122, a liver specific mRNA has found to be upregulated in cells maintained at high cell density and cell-cell contact **(Fig. 1A)**. Interestingly the upregulation of miRNA with cell density is a post-transcriptionally

A



regulated process. Number of P-bodies also differs in cells with different cellular microenvironment. We have documented that the changes of miRNA level was due to impaired miRNP loading and was not due to changes in miRNA stability in confluent cells. On contrary, we have observed that miRNA becoming more stable with cell density in a cell culture model. Additionally we observed that the increased miRNA level does not reflect higher miRNA activities in confluent cells. We speculate that the increased miRNA level is due to low turnover of miRNA engaged in translation repression in confluent cells. We have performed experiments to test the miRNA half life and data suggest that, in presence of transcription inhibitor, miRNA level showed a rapid decrease in non confluent cells than what in confluent cells. Interestingly localization of miRNP to P-bodies gets impaired in confluent cells with a reduction in P-body number in mammalian cells **(Fig. 1B)**. That can account for low efficiency of repression level in cells grown to higher confluence. A unique observation in HeLa

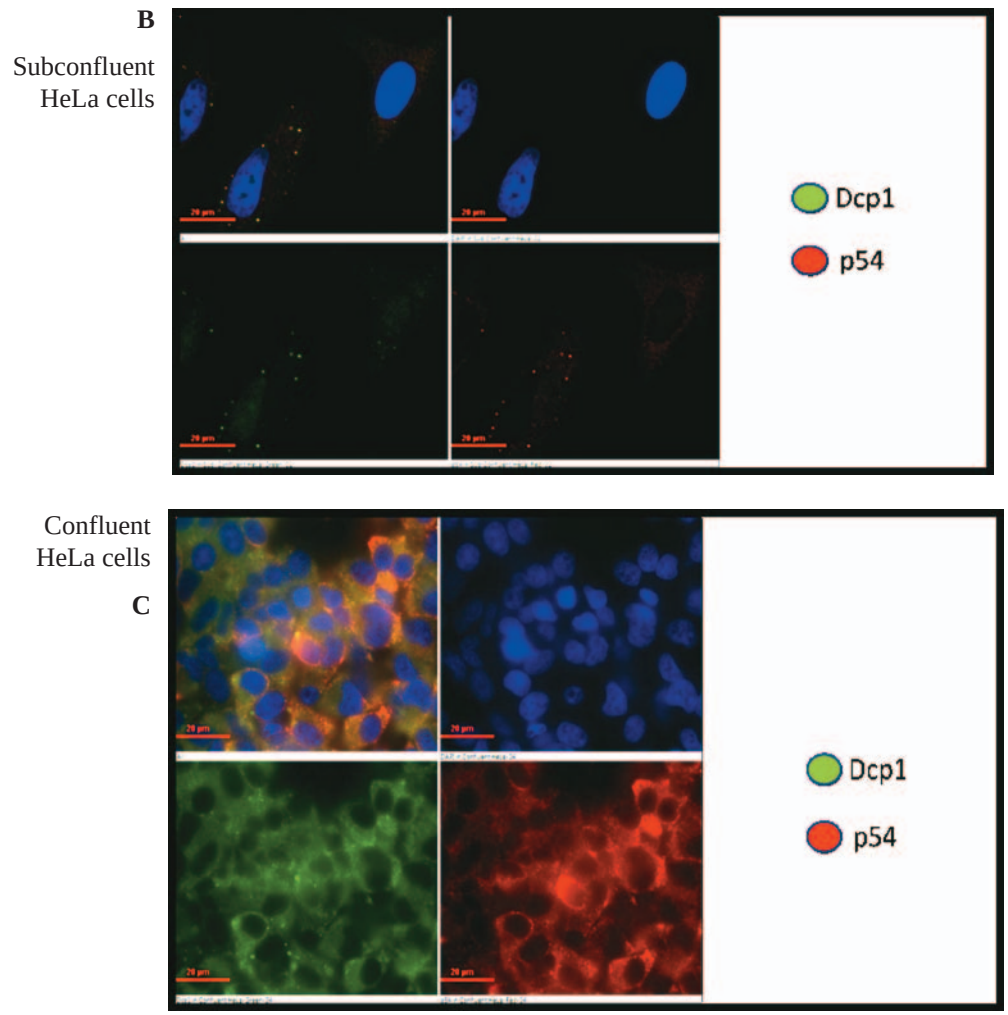


Fig. 1 : Effect of cell confluency on P-bodies and miRNA level in human cells. (A) Northern Blotting to check let7a and miRNA-122 miRNA levels in HeLa and Huh7 cells respectively. Upper Panels represent Northern blots of miRNAs isolated from cells cultured at different cell densities. Middle panels-showing northern blots for U6 snRNAs levels as a loading control; Lower Panel-EtBr staining of the gel used for microRNA analysis. **(B** and **C)** Reduced P-body localization of specific marker proteins like Dcp1a, and RCK/ p54 in confluent HeLa cells, whereas such structures are prominently observed and higher in number in HeLa cells grown at sub-confluent level. The endogenous proteins are visualized with specific antibodies against Dcp1a and DDX6/Rck/p54.

cells denoted that localization of Argonaute2 to P-bodies was impaired in HeLa cells grown to confluent levels. Nevertheless, in Sub Confluent HeLa cells, Ago2 was localized to P-bodies **(Fig. 1B** and **1C).** Currently we are investigating how the cell confluency controls miRNA turnover in mammalian cells.

Effect of Leishmania donovani infection on miRNA activity in mammalian macrophage

To study the effects of microenvironment composed of parasite infected macrophages on gene expression in neighboring mammalian cell, we have planned to use *Leishmania donovani* infection of macrophage as model system. *Leishmania donovani* is a protozoan parasite cause visceral Leishmaniasis in human. We have established the conditions of co-culture of infected macrophage with non-infected cells and doing subsequent isolation of RNA from non-infected cells to perform gene expression analysis and miRNA profiling. Interestingly after *Leishmania* infection miRNA let-7 showed increased level in Leishmania infected mammalian macrophage. The importance of miRNA activity changes in Leishmania infected macrophage is not apparent and we are currently investigating the mechanism and consequence of miRNA regulation in parasite infected macrophage cells.

Dr. Keya Chaudhuri and group

Biology of Vibrio cholerae: Association of cholera toxin with V. cholerae outer membrane vesicles

Cholera toxin (CT) is the major virulence factor of pathogenic *Vibrio cholerae*. The present study demonstrates that a fraction of CT is associated with the outer membrane vesicles (OMVs) released by *V. cholerae*. Atomic force microscopy (AFM) and also transmission electron microscopy (TEM) of purified OMVs from toxigenic *V. cholerae* O395 revealed spherical shaped vesicles of size range 20-200 nm. Immunoblotting of purified OMVs with polyclonal anti-CT antibody and GM1-ganglioside dependent ELISA suggest that CT is associated with OMVs. CHO cell assay indicated that OMV associated CT is physiologically active. OMVs labeled with fluorescent dye interacted with intestinal epithelial cells via the CT-receptor and were internalized increasing the cAMP level (Fig. 2). Thus OMVs may represent an important vehicle in delivering CT to epithelial cells.

Association of lysyl oxidase (Arg158Gly) polymorphism with zinc-vitamin A supplementation in oral submucous fibrosis

Genetic predisposition has been a strong contributing factor for susceptibility to habitual tobacco or areca nut associated oral carcinogenesis. The present study includes a case-series of Oral submucous fibrosis - a precancerous lesion, mainly due to areca nut usage and determination of the prevalence of Lysyl Oxidase G473A (*Arg* 158 *Gln*) polymorphism and its association with conventional Zn-Vitamin A therapy for management of the disease. One hundred newly diagnosed and histopathologically confirmed OSF patients and age-sex matched controls were included to observe the prevalence of Lysyl Oxidase (LOX) G473A polymorphism. Oral mucosal biopsies were obtained from seventy seven patients and seven control individuals to study the effect of G473A polymorphism upon Lysyl Oxidase protein expression as measured by active LOX: pro LOX expression. Among these, thirteen patients were monitored for observation of the effect of G473A upon conventional four month Zinc actetate -Vitamin A therapy.

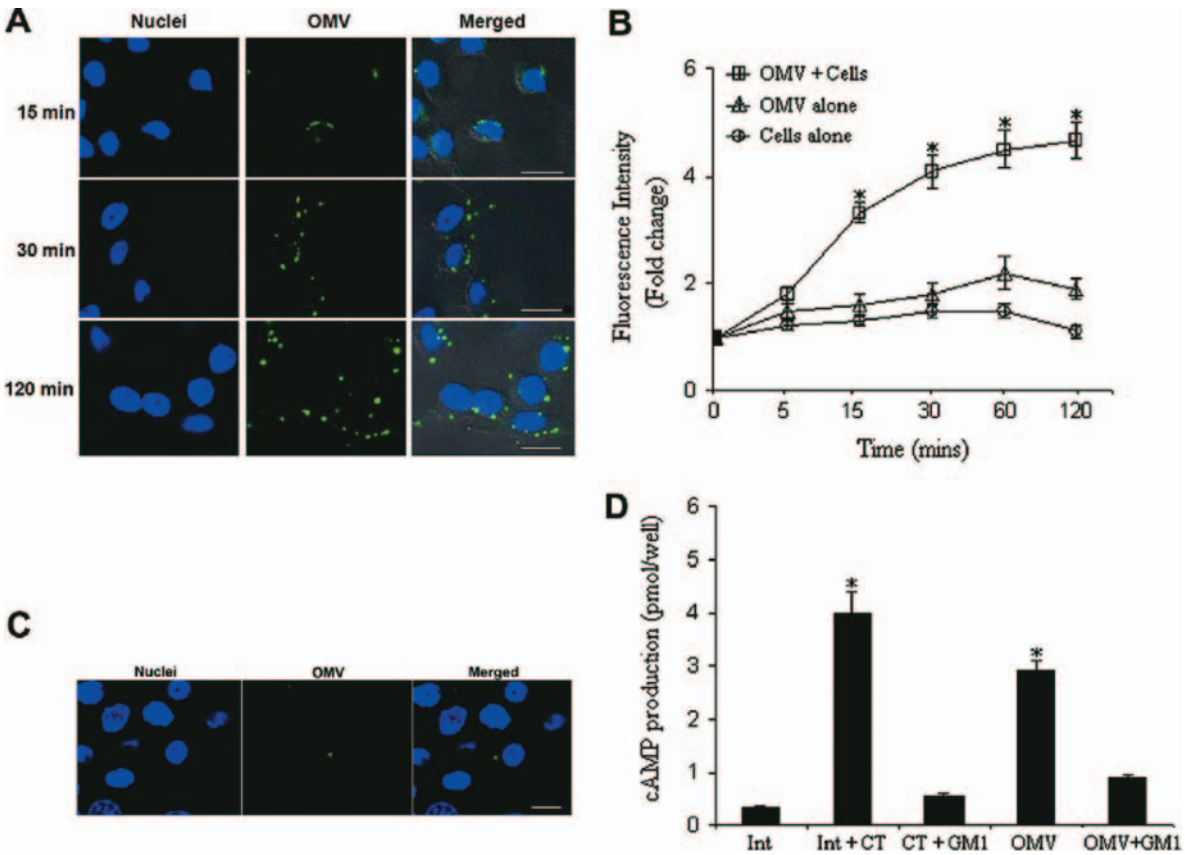


Fig. 2 : Internalization and cAMP production of *V. cholerae* OMVs into epithelial cells. (A) Int407 cells were incubated with FITC-labelled *V. cholerae* O395 OMVs (green, 20 lg/ml of protein concentration) for 15, 30 and 120 min at 37C. After incubation cells were washed, fixed in 2% paraformaldehyde. DAPI was used to stain the nuclei (blue) and localization of OMVs (green) within Int407 cells was examined by confocal microscopy (Scale bar = 20 lm). **(B)** FITC labeled vesicles were incubated with Int407 cells at 37C and fluorescence was measured over time as estimation of OMV fusion. Data are presented as mean fluorescence intensity. The error bars indicate the standard deviation, $P < 0.05$. **(C)** FITC labeled vesicles (green) pretreated with GM1 and incubated with Int407 cells for 2 h at 37C and visualized under confocal microscopy. DAPI was used to stain the nuclei (blue). Scale bar = 10 lm. **(D)** cAMP assay. Concentration of cAMP (pmol/well) produced by Int407 cells incubated for 4 h with CT, CT preincubated with GM1, O395 vesicles, or O395 vesicles preincubated with GM1. The error bars indicate the standard deviation, $P < 0.05$.

Heterozygous *Arg/Gln* genotype was found to be significantly higher [2.063 (95% CI =1.059-4.016) p=0.049] in OSF cases mainly among 26-40 years of age [4.375(95% CI=1.323-14.267) p=0.029] and in male cases [2.38 (95% CI= 1.107-5.121) p= 0.042]. Three fold increase in aLOX : pLOX expression was observed among grade I cases in comparison to controls (p = 0.05). A significant decrease in mean aLOX: pLOX ratio among heterozygous mutant (Arg/Gln) OSF cases were observed compared to wild type (Arg/Arg) OSF cases (p=0.05). Thirteen patients reported back after 4 months of Vitamin A and Zinc acetate supplementation with reduced symptoms and variable degree of improvement in mouth opening. It was found that out of seven wild genotypes, all except one case showed a decrease in aLOX: pLOX ratio. Four out of five heterozygous cases and one homozygous mutant case either showed an increased (about 60%) or minimal change (1.8% decrease) in the aLOX: pLOX ratio. A

significant decrease in aLOX : pLOX ratio suggested altered LOX expression among heterozygous OSF cases emphasizing some effect of the genotype on LOX expression. The cases having wild genotype responded well to supplementation with Vitamin A and Zinc acetate, whereas heterozygous and mutant carriers responded differentially to the treatment with almost no effect of the treatment on LOX expression.

Microscopic analysis of histological and immunohistochemical sections to differentiate normal, precancer and cancerous oral squamous epithelial tissues

Analysis of histopathological sections by image analysis software and Immunohistochemical localization for investigation of different protein expression patterns can be used as a valued tool for detection of progress of malignancy in oral cancer. The present study has applied microscopic analysis for different sections of oral precancerous conditions and lesions such as Oral Submucous Fibrosis, leukoplakia, as well as Oral squamous cell carcinoma in comparison to normal. Epithelial thickness, cellular area and roundness were analysed by image analysis software. Potent biomarkers for carcinogenesis such as VEGF, MMP2 & MMP9, shows a strong positivity in both precancerous and cancerous tissue sections when estimated immunohistochemically (Fig. 3). NQO1 expression was high in precancerous condition but decreased in OSCC revealing epithelial disintegration. Distribution of SOD was also observed as stress generated by ROS. Together all these can be used as a strong diagnostic approach for identification of different stages and severity of oral precancerous and cancerous conditions.

Arsenic-induced cell proliferation is associated with enhanced ROS generation, Erk signaling and CyclinA expression

Arsenic is a well-established human carcinogen; however molecular mechanisms to arsenic-induced carcinogenesis are complex and elusive. The present study identifies a potential biomarker of arsenic exposure, and redefines arsenic-induced signaling in stimulation of cell proliferation. The effect of arsenic exposure on gene expression was evaluated in PBMC of arsenic-exposed individuals selected from a severely affected district of West Bengal, India. A novel, un-documented biomarker of arsenic exposure, CyclinA was identified by microarray analysis from the study. Non-transformed cell lines HaCat and Int407 when exposed to clinically achievable arsenic concentration showed significant increase of CyclinA substantiating the clinical data. An associated increase in S phase population of cells in cell cycle, indicative of enhanced proliferation was also noticed. On further investigation of the pathway to arsenic-induced proliferation, we observed that arsenic resulted ROS generation; activated Erk signaling; stimulated AP-1 activity, including immediate early genes, c-Jun and c-Fos. N-Acetyl-L-cysteine, a ROS quencher, blocked the arsenic-induced effects.Our study underlines a previously undefined mechanism by which arsenic imparts its toxicity and results in uncontrolled cell proliferation.

Dr. Kunal Ray and group

Molecular Genetic Studies on Human Diseases

Eye Disorders: We are interested to understand the molecular bases of (a) primary open angle glaucoma (POAG), a major cause of restricted vision and blindness worldwide; and (b) Oculo-cutaneous

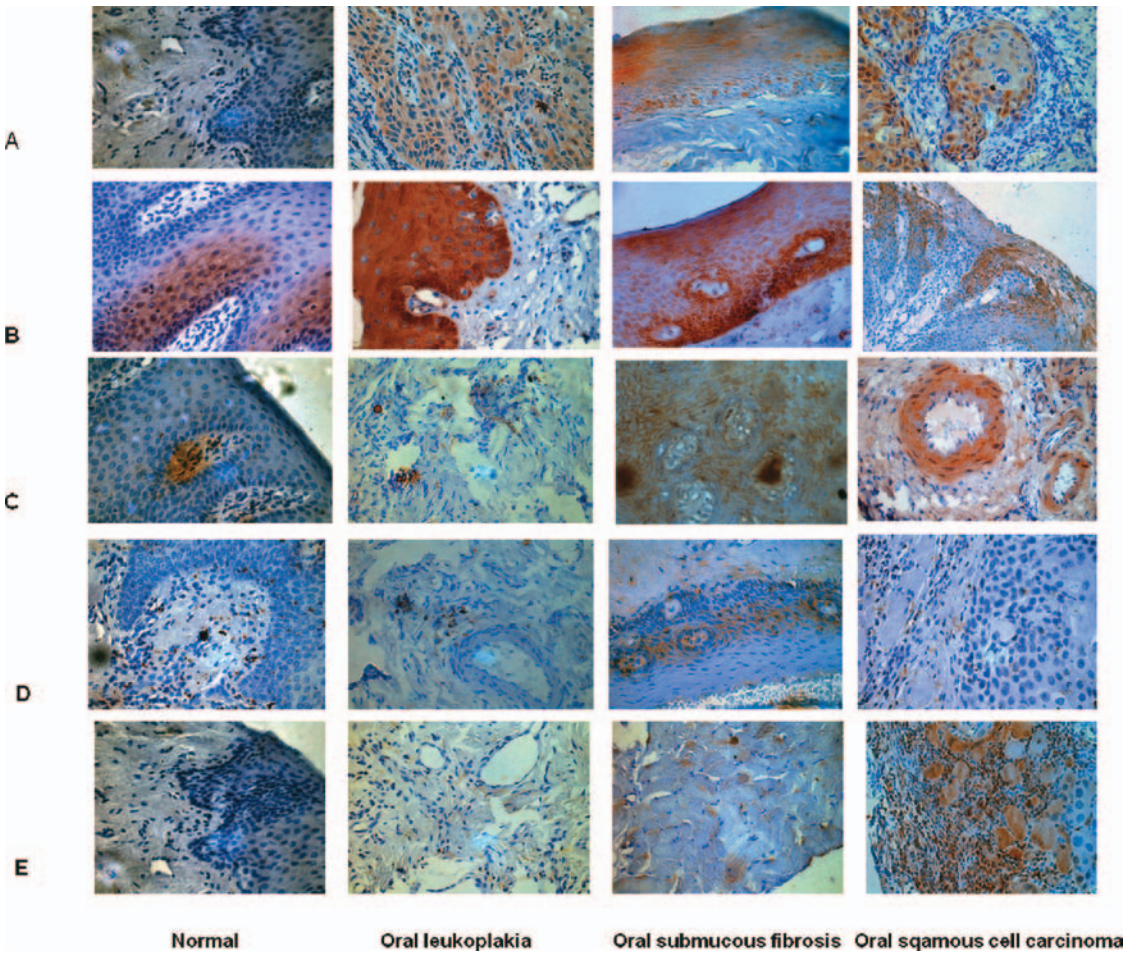


Fig. 3 : Comparative immunolocalization of tumor marker proteins in serial sections obtained from normal, oral leukoplakia, oral submucous fibrosis and oral squamous cell carcinoma. A, Vascular endothelial growth factor (VEGF); B, NADP(H) quinine oxidoreductase1; C, Matrix metalloproteinase 9; D, Matrix metalloproteinase 2; E, Superoxide dismutase.

albinism (OCA) an inherited disorder characterized by deficient synthesis of melanin pigment affecting skin, hair and eye.

(a) Recent studies suggest that glaucoma is a neurodegenerative disease in which secondary degenerative losses occur after primary insult by raised Intraocular pressure (IOP) or by other associated factors. It has been reported that polymorphisms in the *IL1A* and *IL1B* genes are associated with Primary Open Angle Glaucoma (POAG). The purpose of our study was to investigate the role of these polymorphisms in eastern Indian POAG patients. The study involved 315 unrelated POAG patients, consisting of 116 High Tension Glaucoma (HTG) patients with intra ocular pressure (IOP) > 21 mmHg and 199 non-HTG patients (presenting IOP < 20 mmHg), and 301 healthy controls from eastern India. Genotypes were determined for three single nucleotide polymorphisms (SNPs): *IL1A* (-889C/T; rs1800587), *IL1B* (-511C/T; rs16944) and *IL1B* (3953C/T; rs1143634). The study suggests that the genomic region containing the *IL1* gene cluster influences the POAG pathogenesis mostly in non-HTG patients in eastern India. A similar study in additional and larger cohorts of patients in other population groups is necessary to further substantiate the observation [*BMC Med Genet 11:99, 2010*].

(b) Oculocutaneous albinism (OCA) refers to a group of inherited disorders where the patients have little or no pigment in the eyes, skin and hair. Mutations in genes regulating multi-step melanin biosynthesis are the basis of four 'classical' OCA types with overlapping clinical features. We observed that defects in tyrosinase gene (*TYR*) were present in up to 61% of OCA cases among Indians and unlike the wild-type TYR, all the mutant proteins were immature ER-retained species [*J Invest Dermatol 131(1):260-262, Jan 2011*]. Next, we aimed to assess a comprehensive picture of the molecular genetic basis of OCA among Indians with no apparent mutations in TYR. For this purpose 24 affected pedigrees from 14 different ethnicities were analyzed for mutations in OCA2, TYRP1, SLC45A2 and SLC24A5. We identified 2 splice-site and 4 missense mutations in OCA2 in seven unrelated pedigrees, including four novel mutations. Haplotype analysis revealed a founder mutation (Ala787Thr) in two unrelated families of the same ethnicity. A patient homozygous for a novel SLC45A2 mutation also harbored a novel OCA2 defect. No mutation was detected in TYRP1 or SLC24A5. Our results suggest that an OCA2 gene defect is the second most prevalent type of OCA in India after TYR. The presence of homozygous mutations in the affected pedigrees underscores the lack of intermixing between the affected ethnicities [*Brit J Dermatol 163(3):487-94, 2010*]. Direct detection of the genetic lesions prevalent in specific ethnic groups could be used for carrier detection and genetic counseling to contain the disease.

Neurological Disorders: Among neurological disorders studies on (a) Wilson's disease (WD), (b) Parkinson's disease (PD) and (c) dystonia is being carried out. The focus of the study is to identify the molecular basis of the disease among Indians. The studies are conducted in collaboration with Bangur Institute of Neurology & Psychiatry for clinical areas of the study. While our group is focused primarily on Wilson disease, studies on PD and dystonia are done in collaboration with the Prof. Jharna Ray (SN Pradhan Centre of Neurosciences, Calcutta University). During the current year we examined a modifier genetic locus for WD which is described below.

WD results from accumulation of copper and caused due to mutations in ATP7B, a copper transporting ATPase. Besides regular hepatic and neurological symptoms, WD patients occasionally manifest atypical symptoms due to unknown cause. To understand the molecular etiology of atypical WD manifestations, we screened *COMMD1*, a gene implicated in canine copper toxicosis, in 109 WD patients including those with atypical symptoms. In a patient showing apoptotic symptoms and high urinary copper surpassing normal WD levels, we identified a novel, putative mutation in *COMMD1*. Two other changes were also identified in the gene. We have examined genotype-phenotype correlation between the detected changes and the atypical presentation of the WD patient.

Indian Genetic Disease Database: Indians, representing about one-sixth of the world population, consist of several thousands of endogamous groups with strong potential for excess of recessive diseases. However, no database is available on Indian population with comprehensive information on the diseases common in the country. To address this issue, Dr. Chitra Dutta and my groups joined endeavor resulted in Indian Genetic Disease Database (IGDD) release 1.0 (http://www.igdd.iicb.res.in)- an integrated and curated repository of growing number of mutation data on common genetic diseases afflicting the Indian populations. Currently the database covers 52 diseases with information on 5760 individuals carrying the mutant alleles of causal genes. Information on locus heterogeneity, type of mutation, clinical and biochemical data, geographical location and common mutations are furnished based on published literature. The database can be searched based on disease of interest, causal gene, type of mutation and geographical location of the patients or carriers. Provisions have been made for deposition of new data and logistics for regular updation of the database. The IGDD web portal is

freely available, contains user-friendly interfaces and is expected to be highly useful to the geneticists, clinicians, biologists and patient support groups of various genetic diseases [*Nucleic Acids Research, 39(Database issue):D933-8, Jan 2011*].

Dr. Susanta Roychoudhury and group

Transcriptional control of spindle assembly checkpoint genes

The Spindle Assembly Checkpoint (SAC) is one of the surveillance mechanisms that protect cells from genomic instability and prevents mis-segregation of chromosomes during mitosis and meiosis. It is executed by the Bub-Mad group of proteins which prevents ubiquitin (Ub)-mediated degradation of regulators of sister chromatid cohesion by Anaphase Promoting Complex (APC/C). This pathway involves the Mad1, Mad2, Mad3, Bub1, Bub3, BubR1, Cdc20 and Mps1 gene products. At molecular level the SAC is executed by the sequestration of Cdc20 by Bub-Mad group of proteins thereby inhibiting the ubiquitination activity of APC/C. Upon removal of SAC, Cdc20 activates E3 ubiquitin ligase APC/C which along with E2 ubiquitin conjugating enzyme, UbcH10, executes the ubiquitination of regulators of sister chromatid cohesion. Defects in the SAC are thought to be responsible for an increased rate of aneuploidization during tumorigenesis.

Thus, CDC20 is a critical molecule in the SAC. It activates the APC/C and helps a dividing cell to proceed towards Anaphase. Cdc20 is overexpressed in many tumor cells which cause chromosomal instability. However, the mechanism by which overexpressed Cdc20 causes the chromosomal instability is not known. We show that Cdc20 transcriptionally upregulates UbcH10 expression. The WD40 domain of Cdc20 is required for this activity. Physical interaction between Cdc20 and APC/C-CBP/p300 complex and its subsequent recruitment to the UBCH10 promoter is involved in this transactivation process. This transcription regulatory function of Cdc20 was observed to be cell cycle specific. We hypothesize that this co-regulated overexpression of both Cdc20 and UbcH10 contributes to chromosomal instability.

Deciphering host-susceptibility to Helicobacter pylori associated human diseases

Helicobacter pylori is a gastric pathogen that chronically infects more than half of the world's population. It is the major cause of neoplastic and inflammatory gastroduodenal diseases of the stomach. H. pylori infection and associated gastric diseases are common in developing countries, including India. The majority of infected individuals do not develop any clinically apparent disease, but there is compelling evidence that 6-20% of these infections result in duodenal ulceration, and a smaller proportion is associated with gastric cancer. A genetic predisposition to differential clinical outcomes upon H. pylori infection has been suspected for a long time. It has been speculated that IL-1 genes play a crucial role in the genetic predisposition to duodenal ulcer upon H. pylori infection by modulating the host immune response. *Helicobacter pylori* elicited IL1B is one of the various modulators responsible for perturbation of acid secretion in gut. We have earlier reported that IL1B activated NFkB down regulates gastrin, a major modulator of acid secretion. However, we hypothesized that the regulation of gastrin by IL1B would depend on the cells ability to integrate the input from multiple signaling pathways to generate the appropriate biological response. In this study, we report that IL1B induces Smad 7 expression by about 4.5 fold gastric carcinoma cell line, AGS. Smad 7 resulted in transcriptional repression of gastrin promoter by about 30 fold when co -transfected with

Smad 7 expression vector and gastrin-promoter luciferase in AGS cells. IL1B inhibited phosphorylation of Smad 3 and subsequently interfered with nuclear translocation of the positive Smad complex, thus occluding it off the gastrin promoter. *IL1B* promoter polymorphisms *(-511T/-31C IL1B)* are known to be associated with *H. pylori* associated gastro-duodenal ulcer. We observed that IL1B expressed from *-31T* promoter driven IL1B cDNA elicited 3.5 fold more Smad 7 than that expressed from the *IL1B-31C* variant in AGS cells. This differential activation of Smad 7 by IL1B promoter variants translated into differential down regulation of gastrin expression. We further analyzed Smad 7, NFkB, IL1B and gastrin expression in antral gut biopsy samples of patients with *H. pylori* associated duodenal ulcer and normal individuals. We observed that individuals with duodenal ulcer had significantly lower levels of IL1B, Smad 7, NFkB and corresponding higher level of gastrin expression. Pro-inflammatory cytokine IL1B repress gastrin expression by activating Smad 7 and subsequent inhibition of nuclear localization of Smad 3/4 complex. Polymorphic promoter variants of IL1B gene can modulate the IL1B expression which resulted in differential activation Smad 7 and consequent repression of gastrin expression, respectively. Analysis of *H.pylori* infected duodenal ulcer patient's gut biopsy samples also supported this observation.

Dr. Ashok K. Giri and group

Genetic variants responsibility for arsenic toxicity and susceptibility

In West Bengal, India, at present more than 26 million people are exposed to arsenic through drinking water. Among them only 15%-20% manifest arsenic induced non-cancerous, precancerous and cancerous skin lesions indicating that genetic variants play important role in arsenic susceptibility. Chronic arsenic exposure has been associated with impairment of immune systems in the exposed individuals. Since cytokines are important immune mediators so alteration in expression of these gene products may lead to arsenic specific disease manifestations. To investigate the probable association between the *TNF-a*-308 G>A (rs1800629) and *IL10* -3575T>A (rs1800890) polymorphisms and arsenic induced dermatological and non-dermatological health outcomes. A case-control study was conducted in West Bengal, India, involving 207 cases with arsenic induced skin lesions and 190 controls without skin lesions having similar arsenic exposure. The polymorphisms were determined using conventional PCR-sequencing method. ELISA was done to determine the serum levels of the two cytokines TNF-a and IL10. Attempts were also made to find out the association between the polymorphisms studied and non dermatological health effects in the study subjects. Individuals with GA/AA (-308*TNF-a*) and TA/AA (-3575*IL10*) genotypes were at higher risk of developing arsenic induced skin lesions, ocular and respiratory diseases. Also the -308*TNFA* allele corresponded to a higher production of TNF-a and -3575*IL10A* allele corresponded to a lower production of IL10. The polymorphisms studied impart significant risk towards development of arsenic induced dermatological and non-dermatological health effects in the chronically exposed population of West Bengal, India.

Evaluation of the serum catalase and myeloperoxidase activity in the chronic arsenic exposed individuals and concomitant cytogenetic damage

Chronic arsenic exposure is known to exert its toxic effects by a variety of mechanisms, of which generation of Reactive Oxygen Species (ROS) is one of the most important ones. High level of ROS, in turn, leads to DNA damage that might ultimately culminate in cancer. In order to keep the level of ROS in balance, an array of enzymes is present, of which catalase and myeloperoxidase are important

members. We have measured the activity levels of these two enzymes in the sera of individuals exposed to arsenic, and the correlation of activity with the level of DNA damage as monitored by chromosomal aberrations (CA) assay. Our results showed that individuals chronically exposed to arsenic have significantly higher activity levels of both the enzymes compared to unexposed controls. Also, the level of DNA damage was significantly higher in the former group compared to latter. We found moderate to strong positive correlations between enzyme activities, arsenic exposure in urine and water and induction of CA. These results suggest that individuals exposed chronically to arsenic have a higher amount of ROS in serum, which leads to a higher activity of the enzymes studied (Banerjee et al). 2010. We believe that the serum levels of these enzymes might be used as biomarkers of early arsenic exposure much before the classical dermatological symptoms of arsenicosis begin to appear.

Genetic damage induced by arsenic through rice

Arsenic in drinking water is a major problem now throughout the world. Very recently we have established that rice is a major source of arsenic exposure in humans. We report here for the time that rice alone can significantly induce genetic damage in human being. We recruited 302 individuals having various levels of arsenic exposure via rice and water sources and measured the level of arsenic in both drinking water and cooked rice. The corresponding genetic damage level for each study participant was measured using the sensitive micronucleus assay (MN) in urothelial cells. On the basis of arsenic content in rice and water the study population was divided into three study groups in which arsenic exposure was below the threshold from both rice and water, in one exposure was from cooked rice only and in the third, the exposure was both from water and rice. We did the same analyses taking different thresholds of rice arsenic content, viz., 150 µg/kg, 125 µg/kg and 100 µg/kg. Results from genotoxicity assays showed that arsenic solely from cooked rice could give rise to significant genetic damage if the threshold is 150 µg/kg or 125 µg/kg. The levels of genetic damage measured became comparable to basal damage induced only at a dosage of 100µg/kg. This study for the first time shows that chronic arsenic exposure from consumption of high arsenic containing rice on it own is sufficient to give rise to genetic damage at a dosage of more than100µg/kg.

Role of oxidation-triggered activation of JNK and p38 MAPKinases in black tea polyphenols induced apoptotic death of A375 cells

Theaflavins (TF) and thearubigins (TR) are the most exclusive polyphenols of black tea. We have studied the role of three most important mitogen activated protein kinases viz. extracellular-signal regulated kinase (ERK), c-Jun N-terminal kinase (JNK) and p38 in TF and TR induced apoptosis. TF and TR treatment on A375 cells led to sustained activation of JNK and p38 MAPKinases but not ERK, suggesting that JNK and p38 are the effector molecules in these two polyphenols-induced cell-death. This idea was further supported by subsequent studies in which JNK and p38 activation was inhibited by specific inhibitors. A significant inhibition was found in TF and TR treated A375 cells' death which was pretreated with JNK or p38 specific inhibitors only. Further we have found that TF and TR treatment induced time dependent increase in intracellular reactive oxygen species (ROS) generation in A375 cells. Interestingly, treatment with antioxidant N-Acetyl Cystein (NAC) inhibits TF and TR induced JNK and p38 activation as well as induction of cell death in A375 cells. Additionally we also provided evidences for demonstrating the critical role of ASK1 in TF and TR induced apoptosis in A375 cells. Taken together our results strongly suggest that TF and TR induce apoptotic death of

A375 cells through ASK1, map kinase kinase and JNK/p38 cascade, which is triggered by NAC intracellular oxidative stress.

Names of Technical staff

Tapas Chaudhury, Mahua Bhattacharya and Mr. Bhaskar Basu.

Names of Pool Officers, RA etc.

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Names of Junior and Senior Research Fellows and Project Assistants

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Summer Trainees

Madhurima Chowdhury, Sk. Md. Vassem, Anirban Roychoudhury, Upendra Soni, Neelava Das, Baidehi Basu, Sushma Reddy Paduru, Anuttoma Ray and Sanghati Roy Chowdhury.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Drs. Tarun Kumar Dhar, Anil Ghosh, Nirmalendu Das, Aparna Gomes, Pratap K. Das, Suman Khowala, Samir Kumar Dutta, Sharmila Chattopadhyay and Snehasikta Swarnakar

This group is involved in studies on bioactive compounds for improving health and quality of life, as also for promoting future economic growth through innovative research in the area of biotechnology. The major activity includes – isolation of lead bioactive compounds from plant, microbes and venom for useful pharmacological activity; mechanism of gastric ulceration; engineering plant genes for production of pharmaceuticals/nutraceuticales; protease inhibitors; biotransformation of plant secondary metabolites; improved method for rapid high throughput screening of mycotoxins; nanocapsulated drug delivery in combating acute liver toxicity and hepatocarcinoma; molecular mechanisms of trehalose metabolism and microbial gycosidase enzymes.

Dr. (Mrs.) Aparna Gomes and group

Development of drugs from plant materials, animal products and synthetic agents

Studies with Snake venom

A lethal cardiotoxic–cytotoxic protein (mol. wt. 6.76 kDa) has been purified from the Indian monocellate cobra (*Naja kaouthia*) venom by ion-exchange chromatography and HPLC (Fig. 1). CD spectra indicated the presence of 23% α helix, 19% β sheets and 35% coil (Fig. 2). Complete amino acid sequence was determined by MALDI, which showed similar homology with cardiotoxins/cytotoxins isolated from venom of other Naja species. Intraperitoneal LD50 was 2.5 mg kg^{-1} in BalbC male mice. In vitro cardiotoxicity studies on isolated guinea pig auricle showed that the molecule produced auricular blockade that was abolished after trypsin treatment. Cytotoxicity studies on human leukemic U937 and K562 cells showed that it significantly inhibited cell proliferation in a dose and time dependent manner, as observed by trypan blue exclusion method and tetrazolium bromide reduction assay. IC_{50} on U937 and K562 cells were 3.5 mg/ml and 1.1 mg/ml respectively. Morphometry and cell sorting studies indicated apoptosis induction in toxin treated leukemic cells (Fig. 3). Apoptosis was caspase 3 and 9 dependent and the treated leukemic cells were arrested in sub-G1 stage. There was an increase in Bax–Bcl2 ratio, decrease in HSP (Heat shock protein) 70 and HSP90 and induction of PARP cleavage after NK-CT1 treatment (Fig. 4). The toxin showed low cytotoxic effect on normal human leukocytes as compared with imatinib mesylate. Further detailed cytotoxic and cardiotoxic effects at the molecular level are in progress.

Various strains of cobra have already been explored for anticancer effect and following that trend we have tried to explore the venom of *Echis carinatus* for its effect on leukemic cell lines (U937 and K562).

Therefore the present investigation is a preliminary attempt to study the in vitro antileukemic effect of *Echis carinatus* venom (in human leukemic cell lines U937, K562).To begin with cytotoxicity of ECV was investigated in both normal lymphocytes and leukemic cell lines and compared. We have found that ECV showed significantly less cytotoxicity on normal lymphocytes when compared with U937 and K562 (Fig. 5). To study the morphological changes induced by ECV fluorescence microscopy

and confocal microscopy of both control and ECV treated (IC_{50}, 24 hrs) leukemic cells was performed and apoptotic changes were observed in treated cells. (Fig. 6)

Apoptogenic enzyme caspase-3 and caspase-9 activity was found to increase significantly in ECV treated (IC_{50}, 24 hrs) U937 and K562 cells when compared with control cells (0µg/ml) (Fig. 7). Analysis of DNA laddering pattern showed that DNA was fragmented in ECV treated (IC_{50}, 24 hrs)

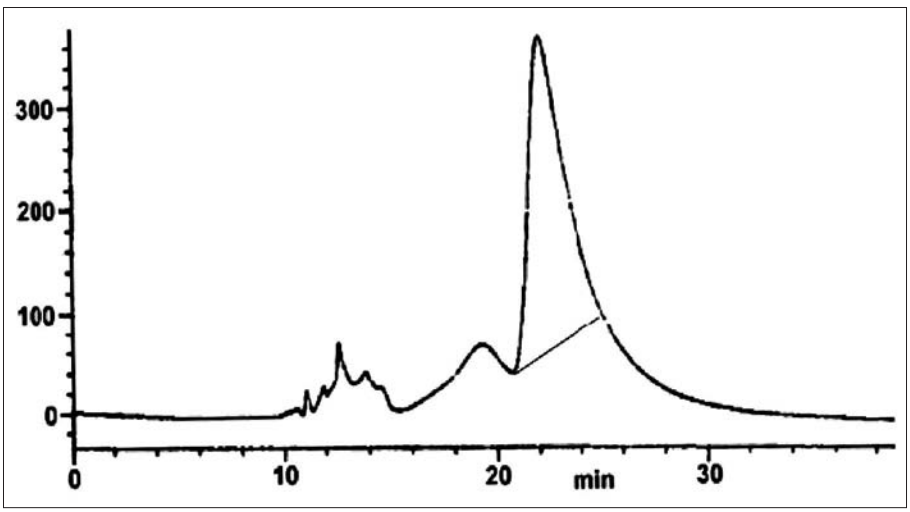


Fig. 1 : HPLC chromatogram of NK-CT1 on Protein Pak 60 column (7.8 x 300 mm). 200 µl of NK-CT1 (mg/ml) was applied. Elution was carried out at a flow rate of 0.8 ml min-1. A peak obtained having retention time of 22 min was eluted.

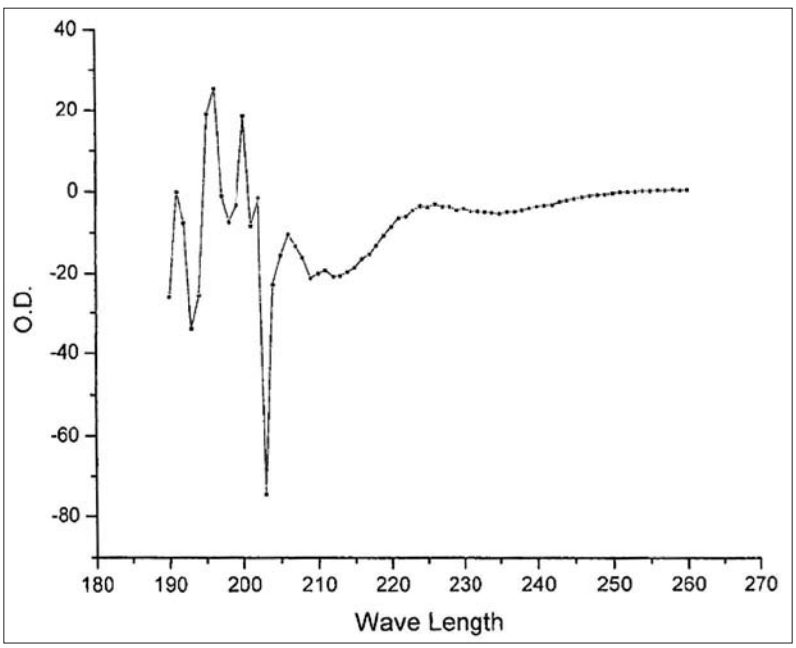


Fig. 2 : CD Spectra of NK-CT1

U937 and K562 cells indicated by the specific laddering pattern. Where as in control cells laddering of DNA were not observed. Expression of antiapoptotic protein Bcl-2 was found to reduce and proapoptotic protein Bax was found to increase when compared with control cells, analysed by western blot analysis.(Fig. 8).

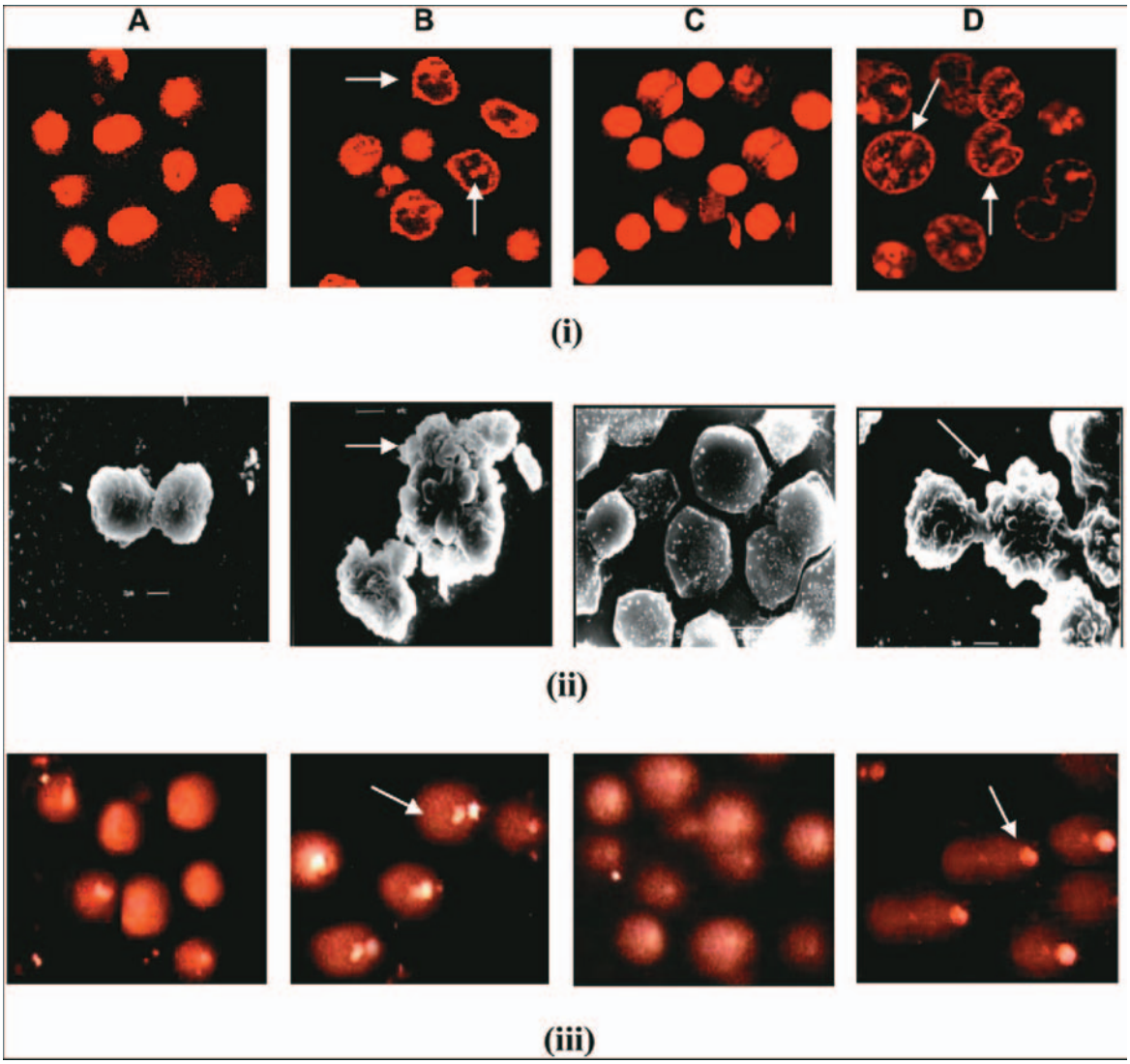


Fig. 3 : Morphological changes and comet assay of treated U937/K562 cells. (A and B) – U937 control and treated; (C and D)-K562 control and treated. Upper panel – Confocal microscopic photographs using Propidium iodide staining. Control cells show much integrated structures with intact nucleus taking homogenous stain whereas after NK-CT1 treated cells showed fragmented nucleus and heterogeneous staining indicated by arrow. Magnification (1000X). Middle panel – Scanning Electron Microscopic photographs of U937/K562 cells after NK-CT1 treatment. The control cells show intact plasma membrane, but the treated cells clearly show severe membrane blebbing, pore formation, apoptotic bodies as indicated by arrow. Magnification (3000X). Lower panel – Comet assay photographs. Control cells (A and C) showed no comet shaped structure but NK-CT1 treated cells (B and D) showed comet formations indicating DNA breakage. Magnification (100X).

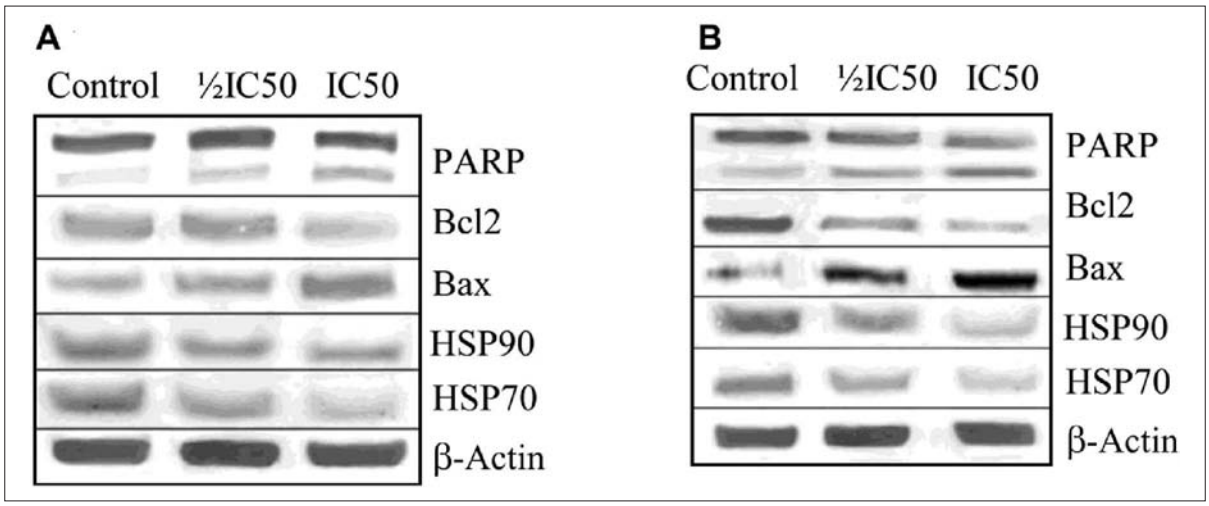


Fig. 4 : Effect of NK-CT1 on apoptosis associated proteins and cell proliferations. A – U937 and B – K562 cell lines. NK-CT1 treatment was done for 24 h in U937 cells at 3.7 and 1.85 mg/ml (IC_{50} and $^1/_2IC_{50}$) and K562 cells at 4.1 and 2.05 mg/ml (IC_{50} and $^1/_2IC_{50}$). Protein from the total cell lysate was subjected to SDS-PAGE and western blot using PARP, Bcl2, Bax, HSP70, HSP90 and β-actin antibody.

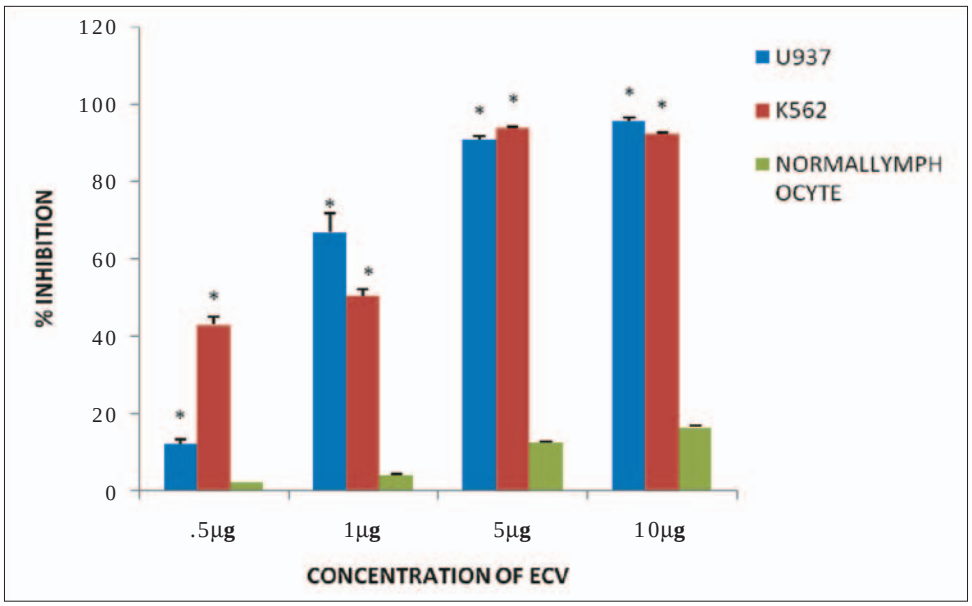


Fig. 5 : Percentage inhibition of ECV on viability of U937, K562 and normal lymphocytes at various concentrations (0.5µg/ml, 1µg/ml, 5µg/ml, 10µg/ml) when compared with untreated cells.

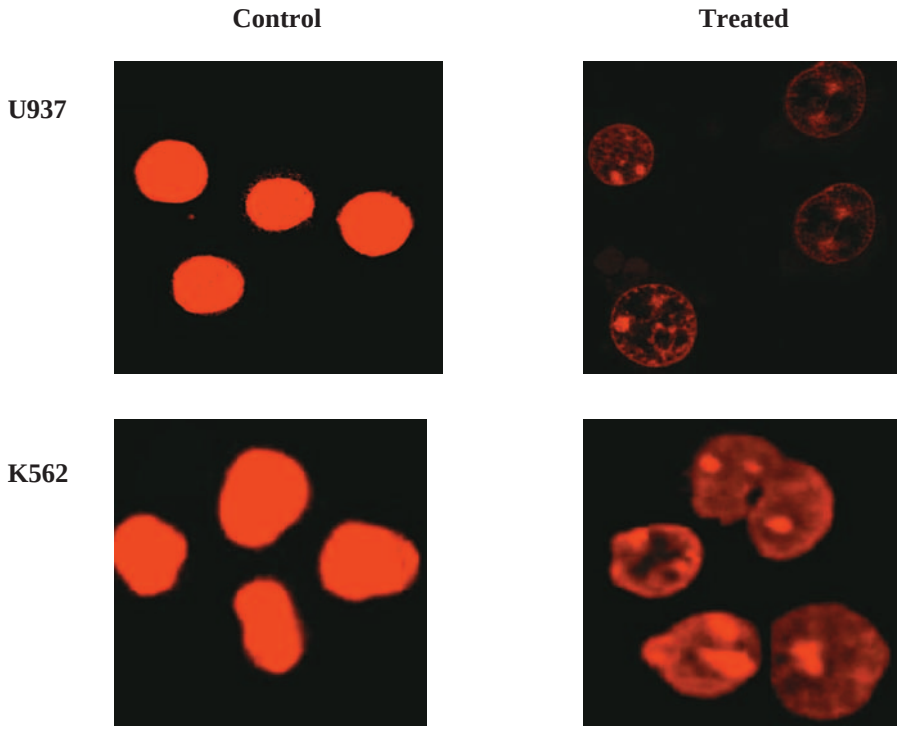


Fig. 6 : Confocal microscopy of ECV treated (IC_{50}, 24 hrs) leukemic cells: (A) Confocal microscopy of control U937, (B) Confocal microscopy of treated U937, (C) Confocal microscopy of control K562, (D) Confocal microscopy of treated K562.

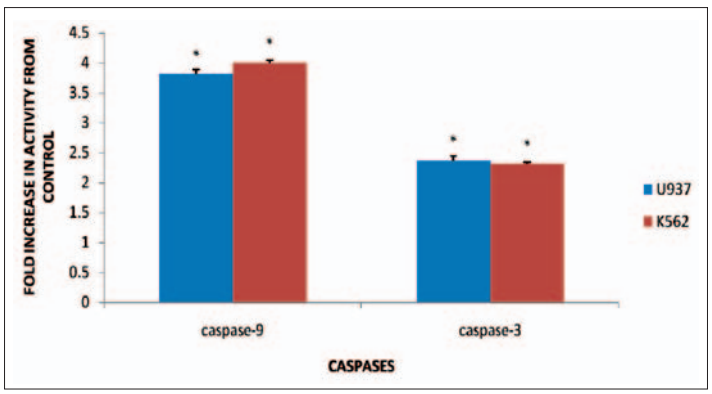


Fig. 7 : Fold increase in caspases activity in treated (IC_{50}, 24hrs) U937 & K562 when compared with control

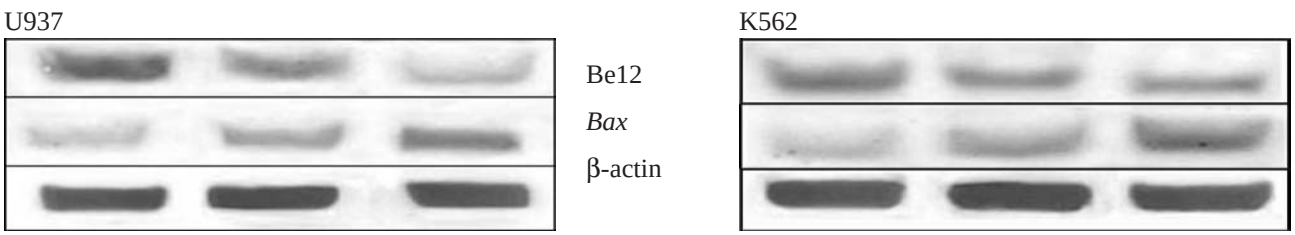


Fig. 8 : Antiapoptotic protein Bcl2 and proapoptotic protein Bax expression was measured by western blotting. ECV (IC_{50} & $^1/_2$ IC_{50}/ 24hrs) down regulated Bcl2 expression in both the treated U937 and K562 cells, along with an increase of Bax expression in comparison to control.

Dr. Pratap K. Das and group

Screening of Indian biodiversity and Indian Systems of medicine for anti gastric ulcer principle(s)

Revisiting Indian biodiversity and Indian Systems of Medicine in search of anti gastric ulcer principles through reverse pharmacology approach led to the identification and validation of a number of primary 'leads' that exhibited gastric antisecretory activity or anti *Helicobacter pylori* activity, two of the most strong etiologies of gastroduodenal ulcers. Methods and protocols for effective screening of crude extracts of plant and microbial origin against the above two targets were developed, validated and are being used extensively. During the period under consideration, we have screened about 1100 microbial samples and 900 plant samples for anti *H. pylori* activity, and could fish out three plant extracts as primary hit.

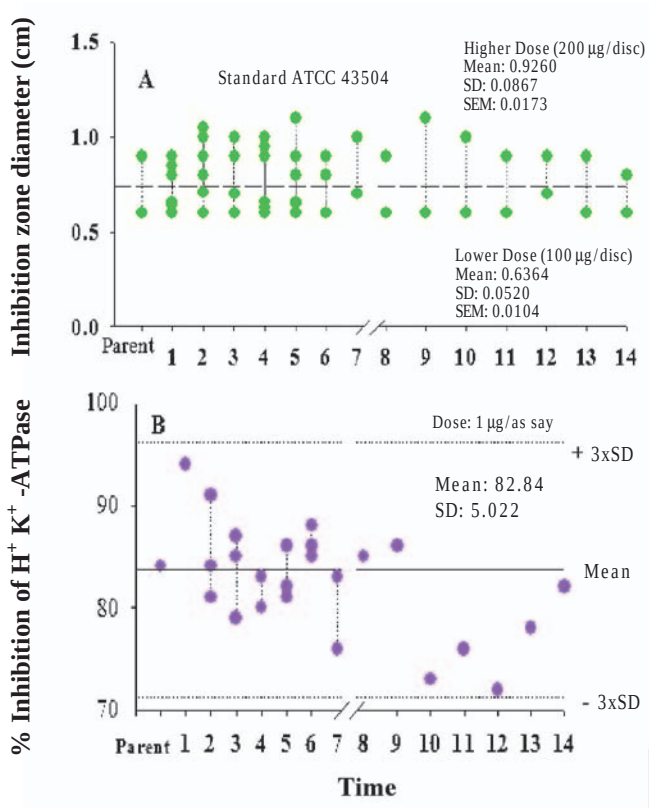
Screening thousands of such natural products helped delineate a mono-herbal extract for exhibiting both anti secretory and anti *H. pylori* activity, and therefore considered for further development towards drug discovery against peptic ulcer diseases. Recently, we have completed investigations around storage stability, mutagenicity, and phyto-sanity profile of the developed product, a hydro-alcoholic extract of the flowers of the plant *Woodfordia fruticosa*. The extract remained functionally stable during one year and found to be non-mutagenic (Fig. 9, panels A, B, C). The phyto-sanity analysis in terms of microbial load, aflatoxins level, solvent residues, heavy metal contamination and pesticide residues gave values within tolerance limit. Arrangement for clinical trial has now been finalized, with IND dossier and study protocol ready for submission to the regulatory authority. Meanwhile, the work on building structural analogues around the active principle, a monomeric ellagitannin, is in progress with Dr. GVM Sharma and group (IICT). Our attempt with gallic acid diversity was not successful but ellagic acid diversity generated encouraging hints (panels D & E). We are approaching towards total synthesis of the active principle with provision for diversity building.

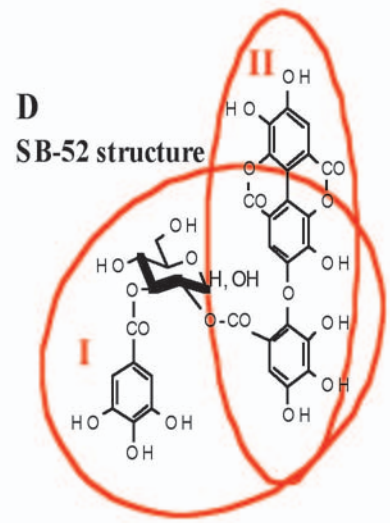
Under anti *H. pylori* lead discovery from microbial diversity including bacterial and fungal samples, we have recently initiated bioassay-guided fractionation of four identified and revalidated leads (one from IMT-Chandigarh and three from University Departments), obtained through screening of more than 17,000 microbial extracts. One gastric antisecretory lead (a plant sample IHB-630-P02-A001, IHBT-Palampur), identified and revalidated earlier, has now been further sub-fractionated from the n-hexane fraction which gave rise to four isolated molecules. All such sub-fractions and the isolated molecules were evaluated for gastric antisecretory activity in isolated frog chamber model and anti H+, K+-ATPase activity. One such molecule showed promising enzyme inhibitory activity.

Dr. Snehasikta Swarnakar and group

Role of Matrix Metalloproteinase-3 and -9 in Gastric Ulcer: Eradication of Helicobacter pylori Infection in Mice by Curcumin

Helicobacter pylori (Hp) has been implicated in the pathogenesis of most important gastroduodenal diseases including gastric carcinoma and defined as a Class I carcinogen. Hp can be subclassified into 'cag' pathogenicity island positive $(cag)^{+ve}$ and negative $(cag)^{-ve}$ strains based on the presence or absence of cagPAI, a 40-kb genome fragment containing 31 genes (Fig. 10). Currently, the most preferred Hp eradication therapy (triple-therapy) employ, one proton pump inhibitor and two antibiotics. However, such multiple therapy regimens have not been very successful in clinical practice, since the





C Mutagenic potential of ICB-A002 and active principle SB-52

Background	A002 1/10/100 µg/ml	SB-52 0.1/1/10 µg/ml
6	6/10/6	5/4/12

E

Inhibition of gastric H^+pump activity

Molecular formula & Mol Wt	% Inhibition at 10/50 µM
$C_{27}H_{28}O_{10}$ (512)	7/12
$C_{20}H_{22}O_{10}$ (422)	0/8
$C_{33}H_{32}O_{10}$ (588)	17/18
$C_{20}H_{22}O_9$ (406)	8/9
$C_{14}H_{18}O_6$ (282)	0/2
$C_{34}H_{38}O_{15}$ (686)	10/27
$C_{34}H_{38}O_{15}$ (686)	22/25
$C_{54}H_{58}O_{24}$ (1090)	17/47
$C_{44}H_{48}O_{19}$ (880)	18/25
$C_{14}H_{18}O_6$ (282)	0/18
$C_{54}H_{58}NO_{24}$ (1090)	15/40

Fig. 9 : Developmental studies with one lead extract ICB-A002 and its active principle SB-52. Accelerated storage stability study (40ºC and 75% RH) was carried out with the parent extract. The anti *H. pylori* and gastric anti H+ pump activity were evaluated over one year (panels A and B). The term 'parent' indicates control values of the extract kept at 4ºC on 0-week till 14th week, and expressed as mean ± SD. Panel C represents evaluation of mutagenic potential of the extract and the active molecule by AMES test. With background scoring of 6/96, the sample is considered mutagenic if the score is > 13–21. Sodium azide (5 µg/ml) was used as standard mutagen showing a score of 74/96 ($p < 0.0001$). Panel D shows an approach towards total synthesis of the molecule along with its structural analogues from two different start-point (I & II). Panel E represents anti proton pump activity of few such analogues towards synthesis of part I as shown in panel D.

overuse or rather misuse of antibacterial agents have resulted in the emergence of antibiotic-resistant strains which is the prime cause of treatment failure apart from potential side effects. Increasing complications in the conventional triple-therapy (TT) stimulate an urgent need to develop new non-antibiotic antibacterial agents against Hp-infection that are safe, highly effective and have specific cellular targets.

Since, matrix metalloproteinase (MMP)-3 and -9 are inflammatory molecules associated to the pathogenesis of Hp-infection, we investigated the role of curcumin on inflammatory MMPs. Curcumin (diferuloylmethane) the principle yellow pigment present in the rhizome of turmeric *(Curcuma longa)*, has a wide array of pharmacological and biological activities. Curcumin dose dependently suppressed MMP-3 and -9 expression in Hp infected human gastric epithelial (AGS) cells. Consistently, Hp-eradication by curcumin-therapy involved significant downregulation of MMP-3 and -9 activities and expression in both cytotoxic associated gene (cag)$^{+ve}$ and cag^{-ve} Hp-infected mouse gastric tissues. Moreover, we demonstrate that the conventional triple therapy (TT) alleviated MMP-3 and -9 activities less efficiently than curcumin. To our knowledge, this study is the first to document the biochemical changes at the level of MMPs brought about by curcumin as well as TT treatments in Hp infected mice (Fig. 11).

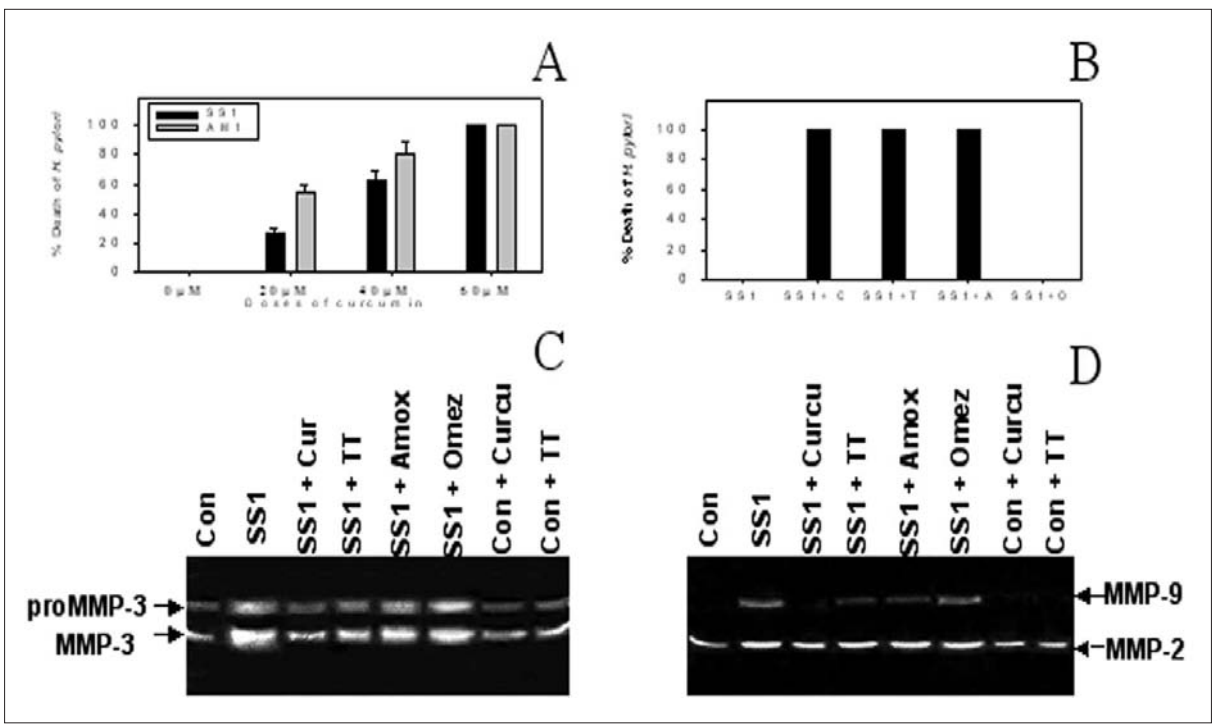


Fig. 10 : Curcumin downregulates increased MMPs in cag^{+ve} Hp-infected mice more efficiently than either TT or antibiotics during Hp eradication. Two weeks SS1 (cag^{+ve} Hp) infected mice groups were treated with different doses of curcumin or TT or only-antibiotics for 7-days. Histographic representation of colonization of SS1 strain, obtained by quantitative culture, in mouse and the effect of varying doses of curcumin (A) or TT (B) thereon. The activities of MMP-3 and gelatinases in the PBS extracts of respective mouse gastric tissues were analyzed by casein (C) and gelatin (D) zymograms respectively.

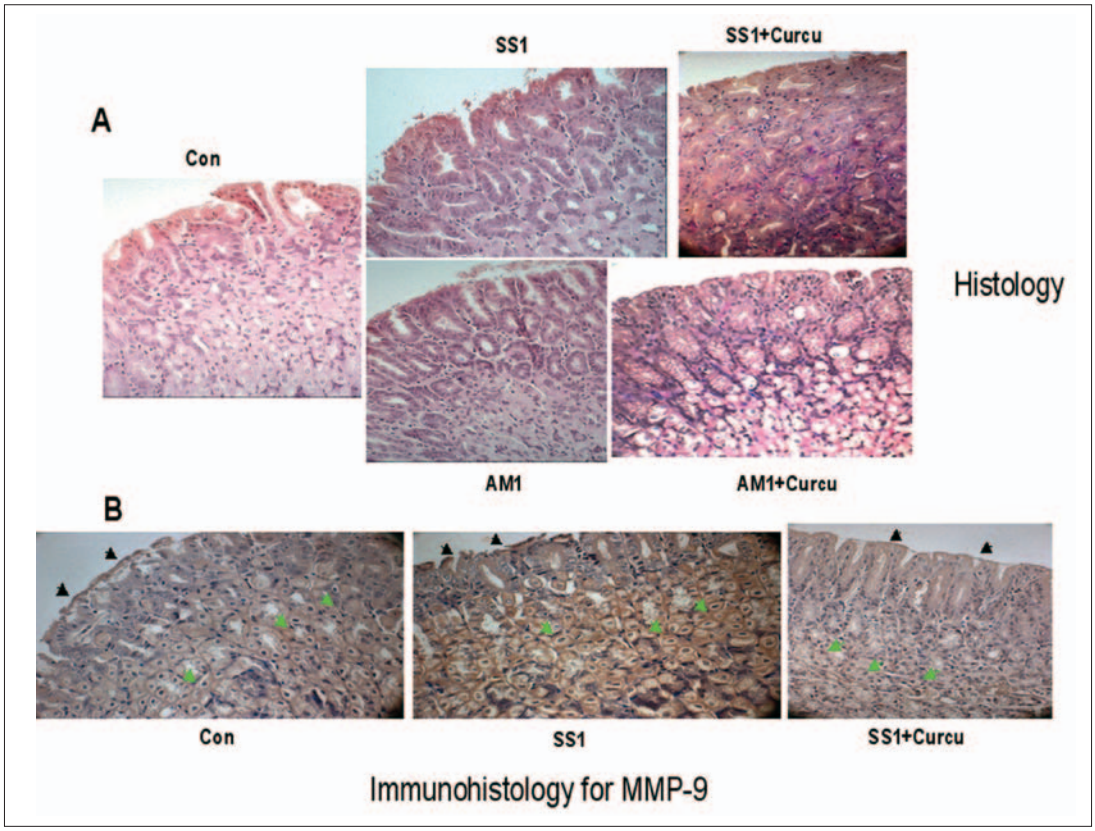


Fig. 11 : Histology and immunohistochemistry of mouse gastric tissues after Hp-infection and eradication; MMP-9 suppression by curcumin. Two weeks SS1 (cag^{+ve} Hp) or AM1 (cag^{-ve} Hp) infected mice were orally fed with 25 mg/kg b w curcumin for 7 consecutive days. Mice were sacrificed and antral biopsy specimens were processed for histological analysis. The expression of MMP-9 in gastric mucosa was analyzed by immunohistochemistry. Histological section of gastric tissues were stained with hematoxylin and eosin and photographs were taken at 40X magnification respectively (A). Immunohistology of gastric tissues probed with anti-MMP9 antibody (B). Epithelial layer and parietal cells were marked by black and green arrows respectively.

Polymorphisms in the MMP-3 gene promoter and their haplotypes are linked to gastric cancer risk in the eastern Indian population

No report is available on the association between the MMP-3 gene promoter single nucleotide polymorphisms (SNP)s and the development of gastric cancer in Indian population. A hospital-based case control study was conducted to explore variants of MMP3 promoter SNPs and resultant haplotypes in the development of gastric cancer in the eastern Indian population. A total of 218 gastric cancer patients and 175 healthy controls were studied. Genotyping for the two variants MMP3-707 and A/G MMP3-375 C/G (rs522616, rs617819) were performed using direct DNA sequencing in ABI3130 platform. MMP3-1612 5A/6A (rs3025058) genotyping were carried out by PCR-RFLP using Tth111I enzyme and 10% rechecked by sequencing (Fig. 12). In cancer patients, MMP3-1612 5A/6A genotype (P= 0.026, OR= 1.756, CI= 1.070-2.883) and combination of 5A5A and 5A6A genotype (P= 0.015, OR= 1.791, CI= 1.122-2.858), and the MMP3-707 GG genotype (P = <0.0001; OR = 9.424;

95% CI = 2.877-30.867) and combination of GG and AG genotype (P = 0.006, OR= 2.114, CI= 1.238-3.610) are conferring significant risk for gastric cancer development (Table 1).

Also the 5A allele (P= 0.002, OR= 1.75, CI= 1.21-2.53) and G allele (P= <0.0001, OR=2.09, CI= 1.444-3.023) accounted for significant risk development for gastric cancer occurrence. The genotypic combinations of all three MMP3 polymorphisms and their haplotypes showed a trend in increase in risk for developing gastric cancer (Fig. 13). The analyses suggested that the MMP3 promoter polymorphisms and their haplotypes are independent predictors of gastric cancer risk development.

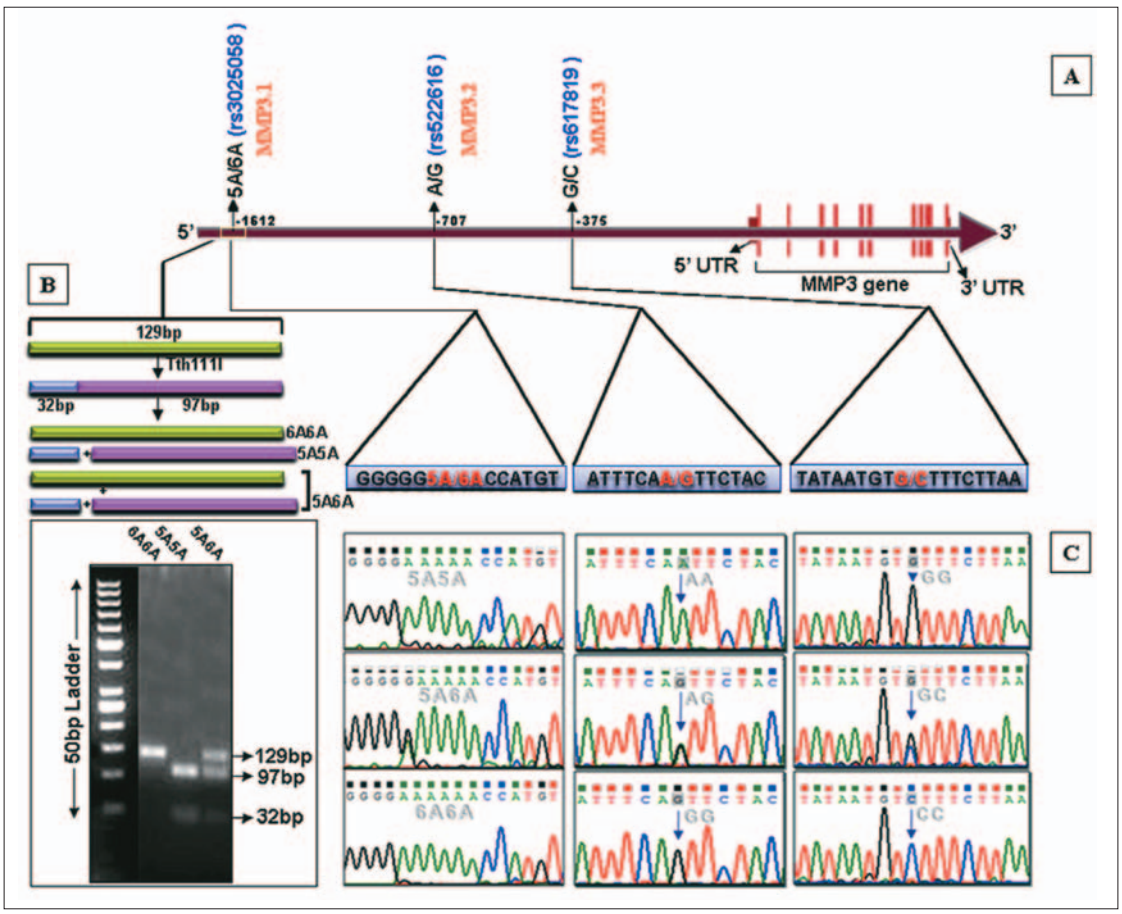


Fig. 12 : Genotyping of the MMP3 polymorphisms. (A) Schematic representation of MMP3 promoter polymorphisms. Location of the polymorphic sites within MMP3 promoter and the nature of the polymorphisms are shown. The promoter region is not in scale. **(B)** Schematic representation of MMP3.1 RFLP analysis and representative PCR-RFLP analysis of MMP3.1 polymorphism 129bp target region of MMP3 gene promoter is PCR-amplified and digested with Tth111I, which cleaved the 5A allele to two fragments of 97bp and 32bp but not 6A allele. Heterozygous allele showed three bands of 129bp, 97bp and 32bp; **(C)** Representative chromatogram of DNA sequences for each genotype for the MMP3 polymorphisms with their flanking regions. Arrows indicate the position of polymorphism in the chromatogram.

Table 1 : Analysis of association between MMP3 SNPs and gastric cancer risk in population group

Genotype	GC Patient (n)		Controls (n)		OR	95% CI	*P* Value
MMP3.1(-1612 1G/2G)	218	%	175 (A)	%			
5A5A	16	7.3	7	4	1.962	0.742-5.189	0.175
5A6A	70	32.1	38	21.7	**1.756**	**1.070-2.883**	0.026
6A6A	132	60.6	130	74.3	1 (Ref)		
MMP3.2 (-707 A/G)	159		121 (B)				
AA	58	36.5	66	54.5	1 (Ref)		
AG	74	46.5	51	42.1	**1.582**	**0.905-2.766**	0.107
GG	27	17	4	3.3	**9.424**	**2.877-30.867**	<0.0001
MMP3.3 (-375 G/C)	150		120 (C)				
GG	17	11.3	8	6.7	1.599	0.562-4.548	0.379
GC	64	42.7	61	50.8	0.85	0.483-1.496	0.573
CC	69	46	51	42.5	1 (Ref)		

Adjusted OR calculated by binary logistic regression model using SPSS v16.0 software.

P value is for χ^2 test showing the significance of difference in the distributions of the genotypes between patients and controls. Values in bold indicate positive significance. OR= Odds ratio, CI= Confidence Interval, Ref= Reference genotype or allele to calculate OR.

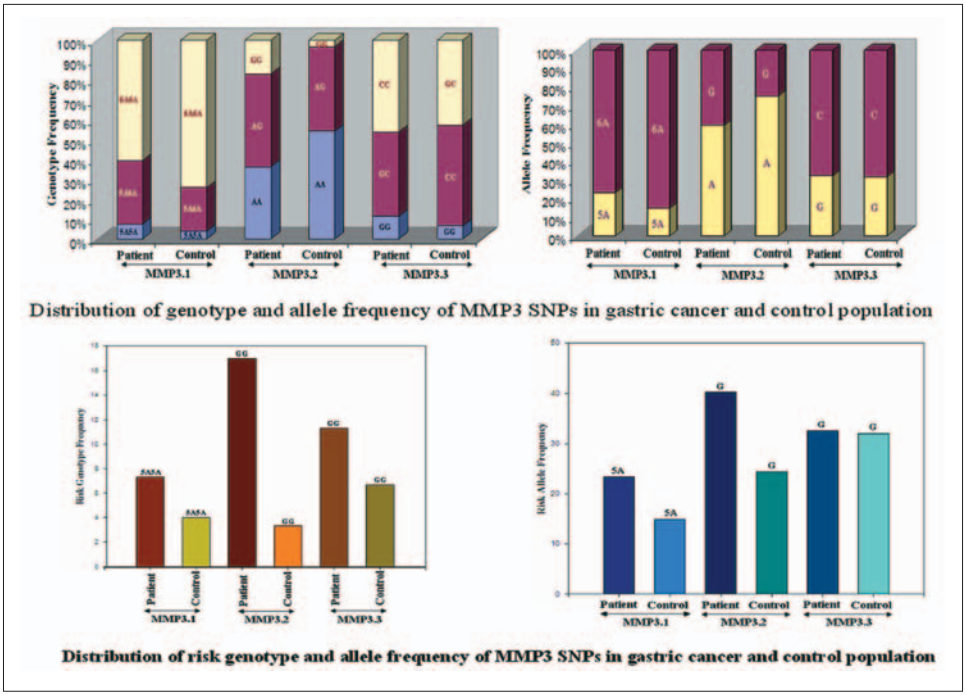


Fig. 13 : Association of individual SNPs of MMP3 in gastric cancer and control subjects

Dr. T. K. Dhar and group

Membrane-based ELISA in Microtitre plate Format

Since its discovery the microtitre plates is widely used as a solid-phase in the enzyme linked immunosorbent assays (ELISA) for the detection and quantification of various substances. However, the ELISA method involves time-consuming (multi-step) operations, which usually involve multiple incubation and washing steps (among antibody, antigen and immunological reagents).

A simple-to-operate analytical device for performing rapid ELISA for monitoring of Aflatoxin B_1 (AFB_1) has been developed. The device consists of a rectangular membrane sheet with 96-antibody immobilized zones having the same layout and dimension as plastic microtitre plates; a filter paper containing channels is attached to a semi-rigid polyethylene card below the membrane. The channels were created by straight row-wise cutting of the filter paper at a position just below the 96-spotted zones of the membrane, using a sharp blade and ruler. During the assay, the spotted membrane, placed in intimate contact over the moist adsorbent body, forms an aqueous network of capillary channels between them. This allows faster transfer of the applied fluid over spotted zones of the membrane to the adsorbent body within few seconds. The assay procedure involves sequential addition of standards or sample, AFB_1–horseradish peroxidase (HRP) conjugate, and substrate solution over anti-AFB_1 antibody-spotted zones of the membrane surface. Semiquantitative results were obtained by visual comparison of the colour intensity of a sample spot with those of reference standards. Quantitative estimation is possible by densitometric analysis (Fig. 14).

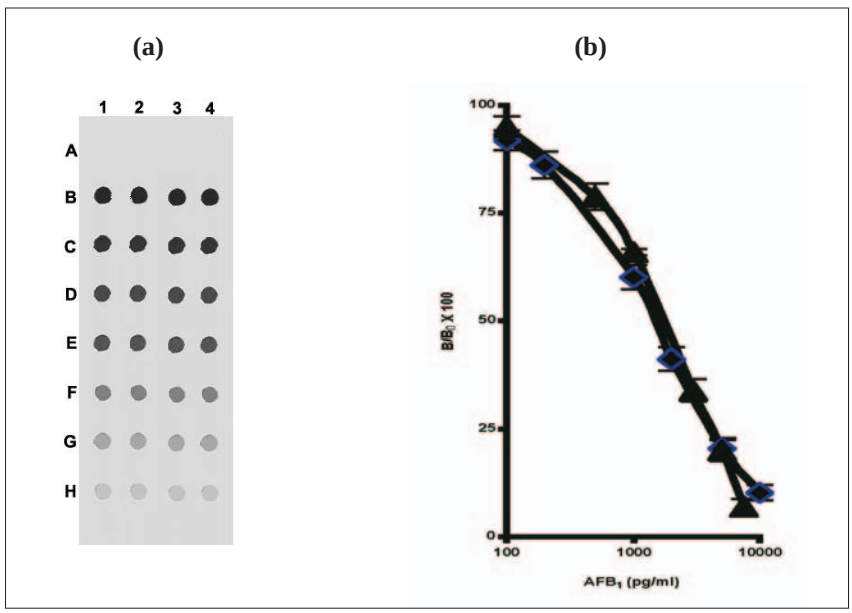


Fig. 14 : (a) Competitive ELISA of AFB_1 in assay buffer. The AFB_1 standards used in each column (1 to 4) were (A) control (without immobilized antibody); (B) 0; (C) 100; (D) 500; (E) 1000; (F) 3000; (G) 5000; and (H) 7500 pg/ml.

(b) Dose-response curve of AFB_1. The present ELISA method (- s -); conventional ELISA (- u -). Each point represents the mean and standard deviation of four measurements.

The AFB1 dose-response curve obtained using the present device was compared to those obtained by conventional ELISA under optimized conditions using the same reagents. The results showed that the detection limit of AFB_1 and the range and slope of both curves were slightly different. The lower limit of detection (distinguishable from blank by twice SD) by the present method and the conventional ELISA was 100 pg/ml, corresponding to B/B_0 values of 95+1.5% and 93+2.5 % respectively. The corresponding AFB_1 concentration required to achieve 50% inhibition was 1800 ng/ml and 1200 pg/ml, respectively. It may be pointed out that inspite of total incubation time of 4 min by the present method compared to 45 min in conventional ELISA; the sensitivities obtained by both the methods were similar. This can be attributed to the focused rapid filtration of the applied solution over the antibody-immobilized membrane surface, which overcomes the diffusion limit and improves the overall reaction kinetics.

The method allows rapid detection of AFB_1 in corn samples with a detection limit of 1µg/kg with accuracy and precision. A batch of 88 extracted samples can be analyzed in presence of reference standards in a single test card. The matrix interference was eliminated by 4-fold dilution of the aqueous methanol extract. Average recoveries from different infected corn samples spiked with AFB_1 at concentrations from 5 to15 µg/kg were between 77 and 115%. The method is rapid and cost-effective and combines the sensitivity and specificity of plastic plate ELISA with the convenience and ease-of-use of a membrane-based test device platform. The main advantages over conventional ELISA are: (i) it is more rapid and user-friendly; (ii) it utilizes simple equipment; (iii) the small volume of reagent distributed using multi-channel pipette during each step ensures time and labour saving, good precision, and accuracy; (iv) the consumption of reagents, washing buffer and substrate solution is markedly reduced; and (v) it is highly suitable for initial cost-effective screening of samples under field conditions.

Dr. Nirmalendu Das and group

Synergistic combination of nanocapsulated Quercetin with meso 2, 3-Dimercaptosuccinic acid in combating chronic arsenic induced ROS mediated hepatic and neuronal mitochondrial dysfunction and p53 activation in rats

Oxygen free radicals generated during chronic arsenic exposure distorts intracellular pro-oxidant antioxidant balance and causes mitochondrial dysfunction. In practice chelation therapy with *meso* 2,3-Dimercaptosuccinic acid (DMSA) is used to reduce metalloid burden but membrane impermeability restricts its application. Quercetin (QC) exhibits strong free radical scavenging property, but its clinical application against the toxicant is complicated by its lipophilicity. Nanocapsules have emerged as potent drug delivery system and have the feasibility to incorporate both hydrophilic and lipophilic compounds. Nanoencapsulated formulations with QC (NQC) or DMSA (NDMSA) or a coencapsulated form of both [N(QC+DMSA)] intercalated in polylactide co-glycolide were made to explore their therapeutic applicability in combating chronic $NaAsO_2$ mediated rat neuronal and hepatocellular mitochondrial oxidative damage. Reactive oxygen species mediated damage incurred on mitochondrial membrane lipids and the associated bulk properties alter the mitochondrial membrane potential leading to cell damage and death. We demonstrate that N(QC+DMSA) is most effective in comparison with other formulations and also acts synergistically in reducing the As burden in liver and brain, protect cells from ROS induced damage, restored mitochondrial integrity and downregulated ROS induced signalling pathway that lead the cells towards p53 dependent apoptosis.

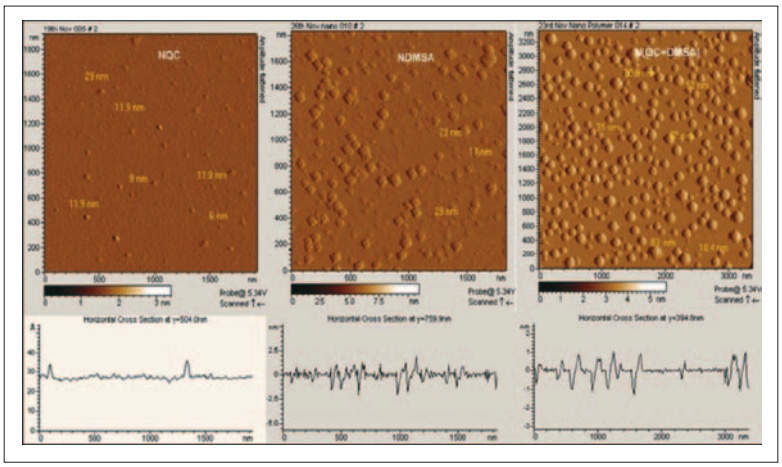


Fig. 15 : AFM images of nanocapsules obtained 2 min after deposition on mica support. Amplitude flattened view of NQC, NDMSA and N(QC+DMSA). Horizontal cross sections indicate height of nanocapsules from the substratum i.e. the mica sheet.

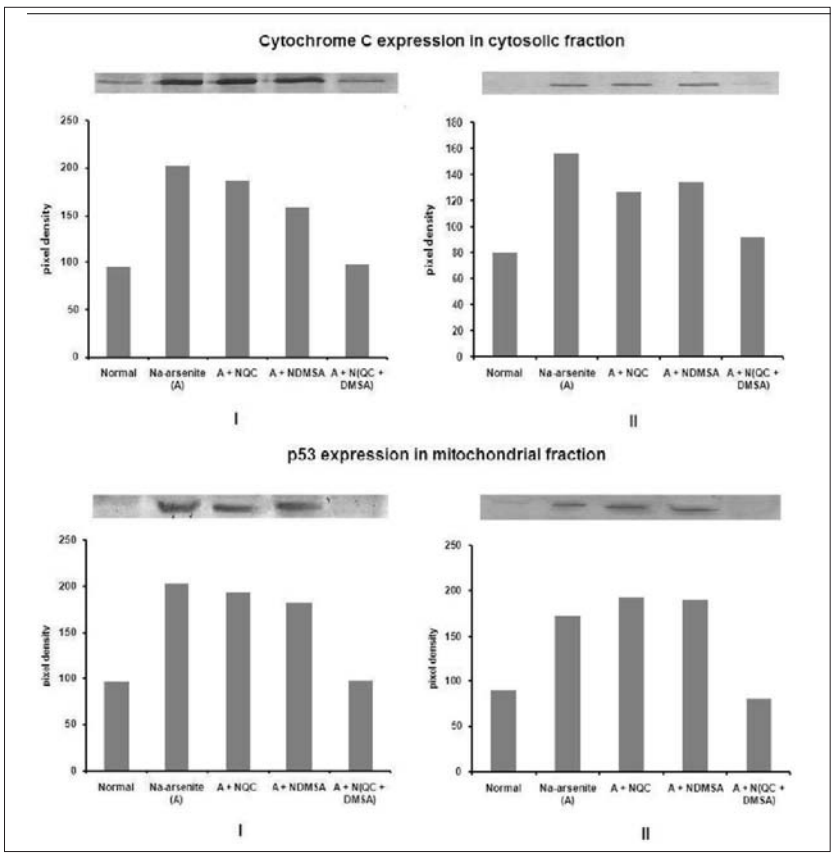


Fig. 16 : Western Blot analysis of cytochrome c protein expression in cytosolic fraction and p53 expression in mitochondrial fraction of liver (I) and brain (II) tissues of experimental rats: Histogram showing representative pixel intensities (arbitrary units of densitometric analysis using Image J software) of the immunoblot performed with different individual rats.

Oral Nanocapsulated Curcumin in combating Hepatocellular Carcinoma in rat model

Toxic outcome of chemical therapeutics and multidrug resistance are the two serious causes for their inacceptance for cancer chemotherapy. Flavonoids like curcumin (Cur) have gained immential importance for their excellent anticarcinogenic activities and minimum toxic manifestations in biological system. However, Cur is lipophilic and thus following oral administration it hardly appears in blood which comprises its potential therapeutic uses and is a major challenge in cancer therapy. The theme of work was to evaluate effectiveness in oral route of polylactide co-glycolide (PLGA) Nanocapsulated Curcumin (Nano Cur) against hepatocellular carcinoma (HCC) in rat. Size, encapsulation efficiency, Fourier Transform Infrared (FTIR) analysis of Nano Cur were done. Antitumor efficacy of those Nano Cur were monitored by an increase in liver weight, liver toxicity tests, reactive oxygen species generation (ROS), changes in membrane fluidity, lipid peroxidation, antioxidant enzyme status and by histopathological and histochemical analysis. Nano Cur of average diameter 14nm and encapsulation efficiency of 78% was prepared. FTIR analysis revealed that there is no chemical interaction between drug and the polymer. Nano Cur treatment in Diethylnitrosamine (DEN) induced HCC rats significantly exhibited protection against HCC. Nanocapsulated Cur caused massive cancer cell apoptosis and it was monitored by Apo-BrdU analysis. Nano Cur provided a significant protection in oral route against DEN induced hepatocellular carcinoma in rat whereas identical amount of free Cur was found almost ineffective.

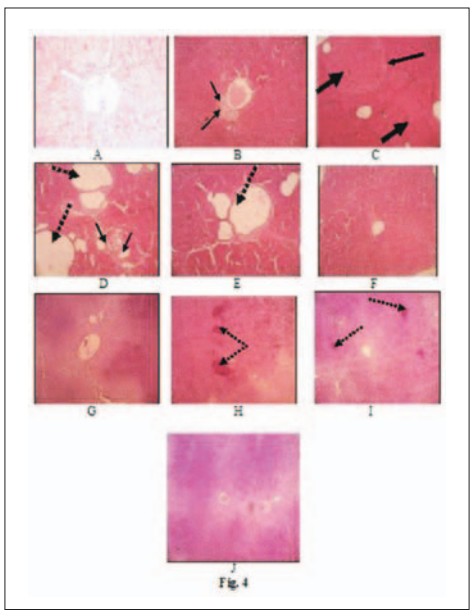


Fig. 17 : Histopathological examination of eosin-hematoxylin stained liver section of normal and experimental rats with magnification x 10. (A) Normal, (B-D) DEN-treated, (E) DEN +Free Cur treated, (F) DEN + Nano Cur treated. Histochemical examination of P.A.S. stained liver section of normal and experimental rats with magnification x 10. (G) Normal, (H) DEN-treated, (I) DEN+ Free Cur treated, (J) DEN+Nano Cur treated, Prenioplastic hyperplasia, Hepatocellular carcinoma (HCC), with distinct “nodule in nodule” appearance; Preneoplastic lesions; Hyperplastic nodules; PAS positive cells.

Mixture of dietary curcumin and quercetin in a polylactide nanocapsule drug delivery system: effect on hepatocellular carcinoma in a rat model

Drug toxicity is the prime obstacle for chemotherapy of hepatocellular carcinoma. Herb origin dietary flavonoids like Quercetin (QC) and Curcumin (Cur) are known to inhibit carcinogenesis by affecting the molecular events in the initiation, promotion and progression stages. Therapeutical potential of those promising molecules is hindered by their poor solubility, short biological half life and low bioavailability. The theme of our study was to optimize the therapeutic efficacy of a mixture of QC and Cur in polylactide nanocapsule drug delivery system in combating Diethylnirosamine (DEN) induced hepatocellular carcinoma in rat model. Rats developed hyperplastic nodules with preneoplastic lesions in liver after 18 weeks of DEN injection Nanocapsulated mixture of QC and Cur (0.679 mg QC, 2.47 mg Cur /kg b. wt, molar ratio 1:3 and 1.359 mg QC, 1.649 mg Cur /kg b. wt, molar ratio 1:1) were administered orally once in a week for 16 weeks. The former composition induces an apoptosis with a release of Cytochrome C from mitochondria and provides a complete protection from DEN induced development of hyperplastic nodules as well as preneoplastic lesions in liver and it was

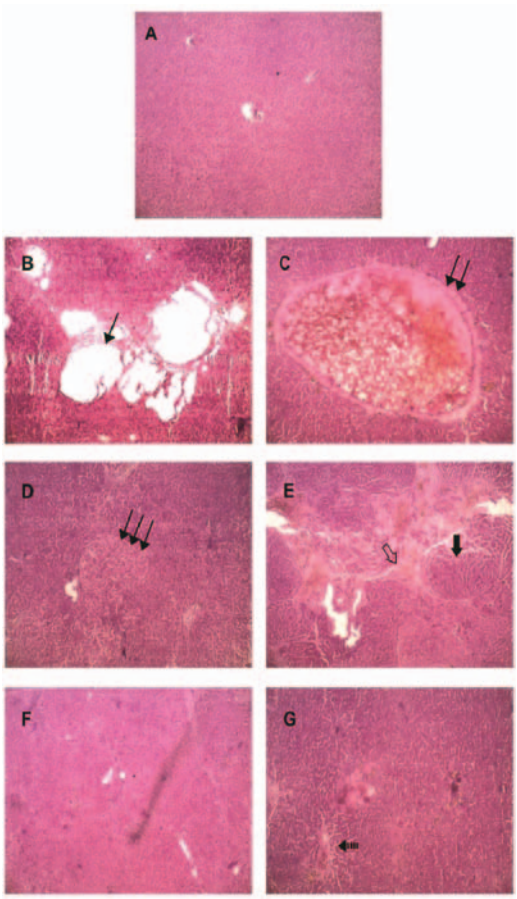


Fig. 18 : Histopathological examination Eosin-Hematoxylin stained liver section of Normal and experimental rats with magnification x 400. A] Olive oil treated Normal; B and C] DEN treated; D] DEN+ Free QC with Cur [at 1:3 molar ratio] treated; E] DEN+ Free QC with Cur [at 1:1 molar ratio] treated; F] DEN + Nanocapsulated QC with Cur [at 1:3 molar ratio] treated; G] DEN + Nanocapsulated QC with Cur [at 1:1 molar ratio] treated indicates hyperplastic nodules, indicates necrosis, indicates focal nodular hyperplasia, indicates fatty metamorphosis, indicates hyperplasia, which is compressing the large vessel from contiguous periportal area, indicates loss of architecture.

reconfirmed by our histopathological and histochemical analysis. Application of polylactide nanocapsulated mixture of QC and Cur may be a potential therapeutic approach against chemical carcinogen induced hepatocellular carcinoma.

Dr. Anil K. Ghosh and group

Arginine mediated purification of trehalose-6-phosphate synthase (TPS) from Candida utilis: its characterization and regulation

Trehalose is the most important multifunctional, non- reducing disaccharide found in nature. It is synthesized in yeast by an enzyme complex: trehalose-6-phosphate synthase (TPS) and trehalose-6-phosphate phosphatase (TPP). In the present study TPS is purified using a new methodology from *Candida utilis* cells by inclusion of 100 mM L-Arginine during cell lysis and in the mobile phase of high performance gel filtration liquid chromatography (HPGFLC). Electrophoretically homogenous TPS purified was 60 kDa protein with 22.1 fold purification having specific activity of 2.03 U/mg. Alignment of the N-terminal sequence with TPS from *Saccharomyces cerevisiae* confirmed the 60 kDa protein to be TPS. Optimum activity of TPS was observed at protein concentration of 1 µg, temperature of 37°C and pH 8.5. Aggregation mediated enzyme regulation was indicated. Metal cofactors, especially $MnCl_2$, $MgCl_2$ and $ZnSO_4$, acted as stimulators. Metal chelators like CDTA and EGTA stimulated enzyme activity. Among the four glucosyl donors, highest V_{max} and lowest K_m values were calculated as 2.96 U/mg and 1.36 mM when ADPG was used as substrate. Among the glucosyl acceptors, glucose-6-phosphate (G-6-P) showed maximum activity followed by fructose-6-phosphate (F-6-P). Polyanions heparin and chondroitin sulphate were seen to stimulate TPS activity with different glucosyl donors. Substrate specificity, V_{max} and K_m values provided an insight into an altered trehalose metabolic pathway in the *Candida utilis* strain where ADPG is the preferred substrate rather than the usual substrate UDPG.

Purification and Characterization of Neutral Trehalase - Invertase, a Dual Substrate Specific Enzyme from Candida utilis.

Trehalose and sucrose, two most important anti-stress non-reducing disaccharides found in nature are catabolized by neutral trehalase (NT) and invertase (INV). An enzyme active against both substrates was purified to electrophoretic homogeneity from wild type *Candida utilis*. Physicochemical characterization was performed to investigate the dual activity of the protein. A 175 kDa protein was purified and found to be composed of three identical 57 kDa monomers. Substrate specificity assay and activity staining revealed the enzyme to be dual substrate specific for sucrose and trehalose. Ratio between invertase and trehalase activity was found to be constant at 1:3.5. 40 fold purification and 30% yield for both activities were achieved at the final step of purification. Common enzyme inhibitors, thermal and pH stress had analogous effect on both activities. K_m values for two activities were similar while V_{max} and K_{cat} differed by a factor of 3.5. Competition plot and end products analysis for both substrates revealed the two activities to be occurring at a single active site. N-terminal sequencing and MALDI-TOF data analysis confirmed the purified protein to be a neutral trehalase rather than an invertase. Purification table and physicochemical characteristics confirm the presence of a single protein displaying both NT and INV activities. Earlier workers mentioned the independent purification of NT or INV from different sources; however, the present study reports the purification of a single protein showing dual activity from *C. utilis*.

Dr. Suman Khowala and group

Molecular mechanisms regulating production and secretion of carbohydrases in the fungus Termitomyces clypeatus

The main objective of the project is to study the regulatory mechanisms of production, secretion and properties of cellobiase from filamentous fungus *Termitomyces clypeatus* influenced by intracellular processing and translocation of the enzymes by post-translational modification in presence of glycosylation inhibitors.

Evidence of an alternative route of cellobiase secretion in presence of Brefeldin A in the filamentous fungus Termitomyces clypeatus

The target of Brefeldin A (BFA), a fungal macrocyclic lactone, which is a potent inhibitor of protein trafficking through the endomembrane system of mammalian cells, is a subset of Sec-7 like GTP exchange factors that catalyze the activation of a small GTPase called Arf-1p. Arf-1p is responsible for recruitment of coatomer proteins (COP I) as well as clathrin via adaptor complex AP-1 to membranes, and results in the formation of transport vesicles. Arf-1p and BFA sensitive guanidine exchange factors (GEFs) are localized to the Golgi apparatus of mammalian and yeast cells. Till now, little is known about the subcellular effects of BFA in filamentous fungi. Our study focused on the effects of BFA on the filamentous fungus *Termitomyces clypeatus* where, unlike other fungi, secretion of proteins is under the regulation of catabolite repression and glycosylation. Secretion of cellobiase, the model enzyme, occurred in a BFA uninhibited manner in the filamentous fungus *Termitomyces clypeatus*. Fluorescence Confocal Microscopy revealed that application of the drug at a concentration of 50 µg ml^{-1} caused arrest of Spitzenkorper assembly at the hyphal tip (Fig.19). This resulted in greater than 30% inhibition of total protein secretion in the culture medium. However, cellobiase titer increased by 17% and an additional 13% was localized in vacuolar fraction *en route* secretion. The secretory vacuoles formed in presence of the drug were also found to be bigger (68 nm) than those in the control cultures (40 nm). The enzyme secreted in presence and absence of BFA revealed a single activity band in both cases in native PAGE and had similar molecular weights (approx. 120 kDa) in SDS-PAGE. In presence of BFA, secretion of cellobiase induced by 2-deoxy glucose (DG) did not change significantly (4% decrease) (Fig. 20a). However, extracellular protein secretion was arrested by 44% (Fig. 20b). This observation supported the observed inhibitory action of BFA in protein secretion. DG is known to inhibit O-linked glycosylation of filamentous fungal glycoproteins. Cellobiase synthesized and secreted in presence of DG was found to retain about 22 % of normal glycosylation.

In presence of BFA, residual glycosylation increased to 33.74 %. This indicated that the targets of DG in the conventional route were different from those in presence of BFA. In *T. clypeatus*, Tunicamycin (TN) reduced the titer of extracellular cellobiase to 51% (in comparison to 82.3%) which clearly demonstrated its inhibitory action on secretion of cellobiase (Fig. 20a). Net glycosylation of the enzyme also reduced to 51%. However protein secretion was not inhibited (Fig. 20b).

In order to attain a commercial status for use in industries, an enzyme needs to be stable besides being secreted in high titer. Cellobiase secreted in presence of BFA retained 72% of native glycosylation. It also showed better stabilities over wider temperature (Fig. 21a) and pH (Fig. 21b) ranges, retaining 98% activity at 50°C compared to 68% residual activity of the control enzyme and 93.3% residual activity at pH 9 compared to 75% for control. The enzyme was also more resistant (63% residual

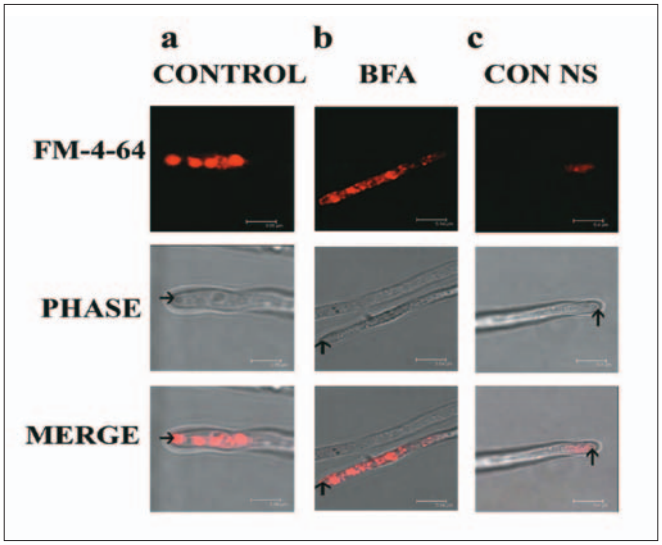
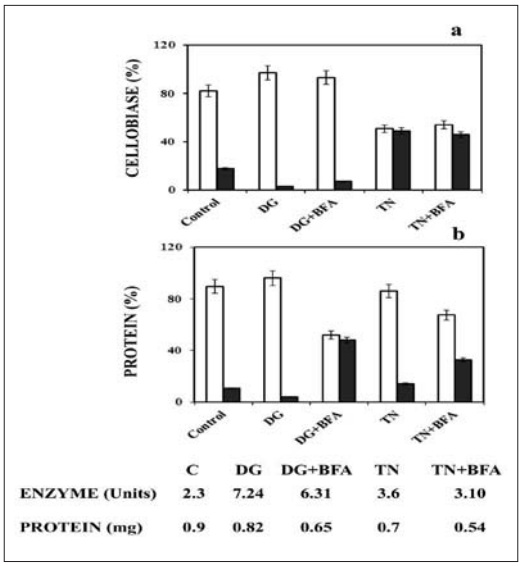


Fig. 19 : Fluorescence confocal microscopy with FM 4-64 showed intact "*Spitzenkorper*" represented by the dense vesicle cluster. (a) CONTROL hyphal tip (marked by arrowheads), (b) absent in presence of BFA (c) CON NS (mycelia grown under non secreting conditions where vesicle turnover is minimal) ensured FM 4-64 uptake was only confined at the hyphal tip and not random throughout the hyphal surface. Scale bar, as mentioned in figures.



	C	DG	DG+BFA	TN	TN+BFA
ENZYME (Units)	2.3	7.24	6.31	3.6	3.10
PROTEIN (mg)	0.9	0.82	0.65	0.7	0.54

Fig. 20 : Relative distribution of (a) total cellobiase units and (b) total protein in extracellular (E) and intracellular (I) fractions. Control, DG, DG+BFA, TN and TN+BFA labeled 4th day cultures expressed as percent of total cellobiase (U) and total protein (mg) respectively (mentioned below the figures).

activity) to the denaturing effects of the chaotropic salt guanidium hydrochloride (1 M) as compared to control (35% residual activity) (Fig. 21c). This enhanced stability may be attributable to altered glycosylation of the enzyme by virtue of secretion through a different route. Cellobiase secreted in the BFA mediated traffic also demonstrated better glucose tolerance retaining 50% activity at sugar concentration of 10 mg ml^{-1} compared to only 20% activity observed for the native enzyme (Fig. 21d). The observations collectively aimed at the operation of an alternative secretory pathway, distinct from the target of Brefeldin A, which bypassed the Golgi apparatus, but still was able to deliver the cargo to the vacuoles for secretion. This can be utilized in selectively enhancing the yield and stability of glycosidases for a successful industrial recipe.

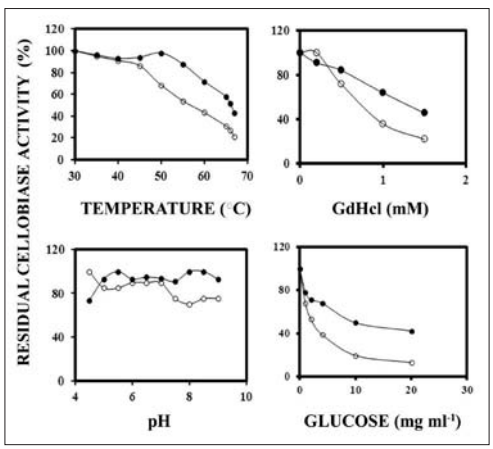


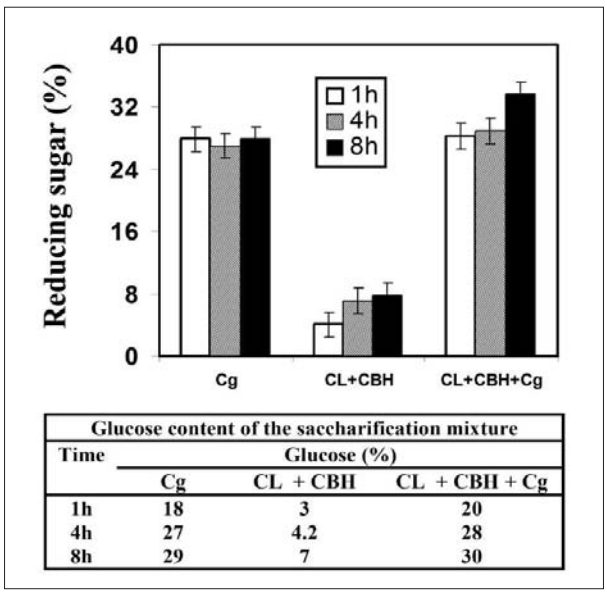
Fig. 21 : Stability of the partially purified enzyme. Control (◦) and BFA (ı) treated culture filtrates were assayed for a) temperature b) pH and c) chaotropic agent (Guanidium hydrochloride).

Regulation of enzyme by glycosylation: Improved production and properties of β-glucosidase influenced by 2-deoxy-D-glucose in the culture medium of T. clypeatus

Increased production, secretion and activity of β-glucosidase in the filamentous fungus *Termitomyces clypeatus* up to 143.8 U/mL of the enzyme was achieved in presence of the glycosylation inhibitor 2-deoxy-D-glucose (0.05%, w/v) in the growth medium in submerged fermentation. Enzyme activity increased to 163 U/mL by adding mannose (2 mg/mL) in the medium. Such high enzyme activity is not known so far without mutation or genetic manipulation. K_m and V_{max} of the enzyme in culture medium were determined as 0.092 mM and 35.54 U/mg respectively with p-nitrophenyl β-D-glucopyranoside as substrate confirming its high catalytic activity, which showed that catalytic efficiency of underglycosylated glucosidase was 5.5 times higher than the control enzyme with increased substrate affinity (2.66 times) and reaction velocity (2.06 times). Presence of DG in the growth medium of *Termitomyces clypeatus* led to significant increase in β-glucosidase activity which was much higher than reported so far from any source by submerged fermentation or solid state fermentation, even the β-glucosidase from mutant strain of *Trichoderma atroviride*. The enzyme from *T. clypeatus* showed better stability in temperature range of 45-60ºC than the control enzyme. Apart from increase in β-glucosidase, activities of other enzymes like CMCase, FPase, sucrase and xylosidase

also increased by 2.1, 1.2, 3.6 and 7.6 times in presence of DG in the fungus. Catalytic activity of the crude enzyme was 3205 times higher than the purified enzyme due to lowering of V_{max} values on purification. The purified enzyme was also observed to be less stable towards temperature, pH and chemical agents compared to the culture filtrate enzyme. These properties render the crude enzyme more suitable to use for application purposes.

Comparing the hydrolytic efficiencies of the enzyme preparations, the culture filtrate preparation of *Termitomyces clypeatus* (Cg) was roughly equivalent to that of its mixture with two commercial enzymes cellulase and exo-glucanase (Cg+CL+CBH) (Fig. 22). Considering the above facts the culture filtrate enzyme would be more potent for industrial applications as it can directly be added to any saccharification mixture without further downstream processing like concentration or partial purification.



Glucose content of the saccharification mixture

Time	Glucose (%)		
	Cg	CL + CBH	CL + CBH + Cg
1h	18	3	20
4h	27	4.2	28
8h	29	7	30

Fig. 22 : Extent of carboxymethyl cellulose saccharification was expressed as initial sugar taken as 100%. Control experiments with enzyme, substrate and heat inactivated enzymes were also run in parallel. β-glucosidase (DG-500 µg/mL) from *T. clypeatus* (Cg), commercial cellulase (CL) and exo-glucanase (CBH) were added in saccharification digests. Total reducing sugar was taken as 100.

Bioremediation of hexavalent chromium by heat inactivated fungal biomass of Termitomyces clypeatus: surface characterization and mechanism of biosorption

The existence of heavy metals in the environment represents a significant and long-term environmental hazard including humans. Chromium is a contaminant that is a known mutagen, teratogen and carcinogen. Hexavalent chromium, Cr(VI) present in wastewaters produced by industrial processes are traditionally removed by electrochemical treatment, chemical precipitation, membrane process, reverse osmosis, ion exchange, liquid extraction, electro dialysis, evaporation and sorption. However, the applications of these treatment processes are expensive and eco-friendly. We have developed an improved process for the preparation of inactivated/dead biomass of *T. clypeatus* for the removal of

Cr(VI). Chemical pretreatment of the fungal biomass by acid and $CaCl_2$ showed improvement of Cr(VI) removal rate at pH 5.0 and 7.0 while reverse was true for alkali and NaCl treatments (Fig. 23). The mass loss recorded after each chemical pretreatment due to cleaning of the cell wall of the biomass, which indicated that degradation and solubilization of the biomass caused by the alkali treatment and thereby exhibited negative effect on Cr(VI) biosorption. The active sites involved in the sequestration of Cr(VI) was identified by using biochemical techniques like potentiometric titration, PZC, modification of functional groups and instrumental analysis like FTIR and SEM-EDX analysis (Fig. 24). The acidic and alkaline functional groups, carboxylic, imidazole, phosphate, amine, sulfhydryl and hydroxyl were present on the cell wall of the biomass as inferred from their pk_α values derived from potentiometric titration curve. Total acidic sites estimated on the cell wall of the biomass were higher than the basic sites suggesting that the surface of the biomass was acidic. Cell surface sorption for Cr(VI) removal by the heat inactivated fungal biomass showed involvement of more than one mechanisms such as physical adsorption, ion exchange, complexation and electrostatic attraction. The study showed that low pH and acid treatment rendered the biomass surface more positive and showed faster the removal rate of Cr(VI) in the aqueous phase, since the binding of anionic Cr(VI) ion species with positively charged groups was enhanced. Amino, carboxyl and phosphate groups were involved in Cr(VI) biosorption process, as established after chemical modification of those functional groups. FTIR analysis confirmed the involvement of amino, carboxylic, phosphate, sulfonyl and carbonyl groups in Cr(VI) biosorption by heat inactivated biomass of *Termitomyces clypeatus*. The roles played by functional groups in chromium biosorption were found to be in the order: carboxyl>phosphates>lipids >sulfhydryl>amines. Integrative analyses of kinetic studies, surface chemistry, the effect of pH values on adsorption behavior of Cr(VI) and the results of FTIR showed that the biosorption of Cr(VI) followed two subsequent steps, biosorption of $Cr_2O_7^{2-}$ by electrostatic force at the protonated active sites (amino, carboxyl and phosphate groups) and reduction of Cr(VI) to Cr(III) by reductive groups (hydroxyl and carbonyl groups) on the surface of the biomass. These findings would contribute to a better understanding of biosorption and aid in the development of potential biosorption that possess almost complete removal efficiency for Cr(VI) from aqueous environment.

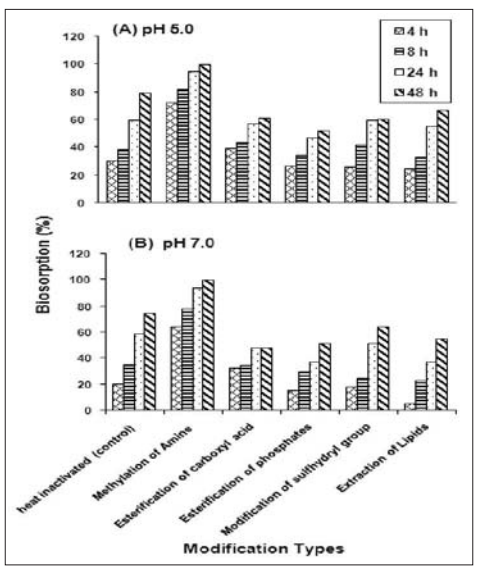


Fig. 23 : Initial Cr(VI) conc.; 100mg/L, Biomass dose 0.2g/25 mL, Agitation speed; 150 rpm, Temp; 30°C.

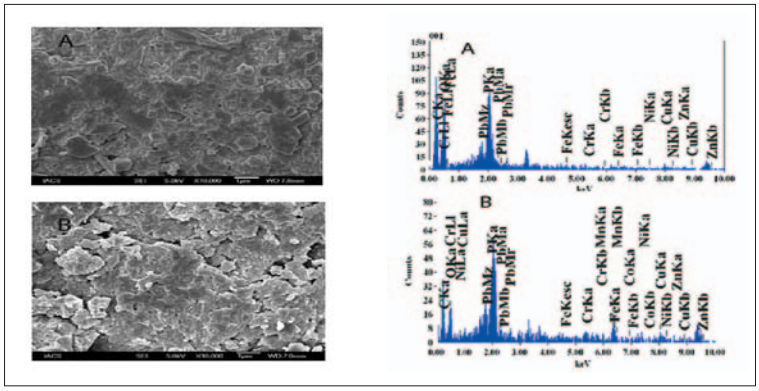


Fig. 24 : SEM micrograph and EDX spectra of heat treated *T. clypeatus biomass* (A) heat treated (B) Cr(VI) loaded.

Dr. Sharmila Chattopadhyay and group

Medicinal plants and metabolic engineering

The main objective of this work is to unravel the dynamic mechanism through which plants cope up with one of the disastrous environmental hazards like microbial invasion; to explore the phytoceuticals, plant secondary metabolites of medicinal interest, at genomics and proteomics level; and bioactivity screening of natural resource/s with a view to identify herbs with antioxidant potential.

To obtain an in depth insight into the mechanism through which GSH is involved in the crosstalk with established signaling molecules to mitigate biotic stress, transgenic *Nicotiana tabacum* overexpressing *Lycopersicon esculentum* gammaglutamylcysteine synthetase (*LeECS*) gene (*NtGB* lines) were generated with enhanced level of GSH in comparison with wild-type plants exhibiting resistance to pathogenesis as well (Fig. 25). The expression levels of non-expressor of pathogenesis-related genes1(NPR1)-dependent genes like pathogenesis-related gene 1 (*NtPR1*), mitogen-activated protein kinase kinase (*NtMAPKK*), glutamine synthetase (*NtGLS*) were significantly enhanced alongwith NtNPR1. However, the expression levels of NPR1-independent genes like NtPR2, NtPR5 and short-chain dehydrogenase/ reductase family protein (*NtSDRLP*) were either insignificant or were downregulated (Fig. 26). Additionally, increase in expression of thioredoxin (*NtTRXh*), S-itrosoglutathione reductase1 (*NtGSNOR1*) and suppression of isochorismate synthase 1 (*NtICS1*) was noted. Comprehensive analysis of GSH-fed tobacco BY2 cell line in a time-dependent manner reciprocated the *in planta* results. Better tolerance of NtGB lines against biotrophic *Pseudomonas syringae* pv. *tabaci* was noted as compared to necrotrophic *Alternaria alternata*. Through two-dimensional gel electrophoresis (2-DE) and image analysis, 48 differentially expressed spots were identified and through identification as well as functional categorization, ten proteins were found to be SA-related. Hence, it can be concluded safely that GSH, being a member of the signaling network participates actively in the cross-communication with other established molecules to mitigate biotic stress *in planta* through NPR1-dependent SA-mediated pathway.

Plant pathogenic fungi cause important yield losses in crops. To identify the proteins up accumulated because of microbial invasion, a model was established using an economically important crop like pudina infected with a fungal strain. Finally, a proteomic approach was used to study the changes in the leaf proteome profile of the plant *Mentha arvensis* infected with a necrotrophic fungus, *Alternaria*

alternata (Fig. 27a). High-resolution 2-DE followed by colloidal Coomassie staining and mass spectrometric analysis was used to identify highly abundant proteins differentially expressed in response to fungal infection. From a total of 210 reproducibly detected and analyzed spots, the intensity of sixty-seven spots was altered, and forty-five of them were successfully identified by matrix assisted laser desorption/ionization time of flight-mass spectrometry (MALDI TOF/TOF MS/MS). Fifty-six percent of the identified proteins belonged to energy and metabolism whereas 29% were stress and defense related (Fig. 27b). In conclusion, an initial defense response, not strong enough to overcome the pathogenesis, which may be similar to other susceptible plant–pathogen interactions; however, cross-talks between various defense pathways, regulatory networks and physiological conditions are other important aspects to be considered.

Podophyllotoxin, a plant secondary metabolite of therapeutic interest, belongs to the diarylnapthelene group of lignan, is the predominating compound and the active ingredient used as the starting compound for the chemical synthesis of etoposide (VP-16-213), and teniposide (VM-26) and ethophos that are used for the treatment of lung and testicular cancers. Presently podophyllotoxin is collected from a critically endangered Himalayan plant *Podophyllum hexandrum* and that also from wild to meet the ever-increasing demand of the drug in modern medicine. Hence, synthetic biology may be explored to address the demanding situation. For that, pathway engineering of podophyllotoxin, has been targeted with an aim to identify and characterize the genes/enzymes of podophyllotoxin biosynthetic pathway through the application of cutting edge 'omics' techniques. Initially, calli was induced from leaves of *P. hexandrum* and cell suspension culture was established which was further elicited with Methyl Jasmonate (MeJA) to obtain enhanced accumulation of podophyllotoxin, the molecule of interest. HPLC analysis confirmed the enhanced content of podophyllotoxin in MeJA elicited cell suspension culture of *P. hexandrum*. Further work is in progress.

There is increasing recognition that many of today's diseases are due to the "oxidative stress" that results from an imbalance between the formation and neutralization of reactive molecules such as reactive oxygen species (ROS) and reactive nitrogen species (RNS), which can be removed with the help of antioxidants. Antioxidant activity of several plants routinely used in the Unani system of medicine were screened for radical scavenging activity, and ten, that showed promising results were selected for further evaluation. IC_{50} values for scavenging $DPPH^{\cdot}$, $ABTS^{\cdot+}$, NO, $^{\cdot}OH$, $O2^{\cdot-}$ and $ONOO^{-}$ were in the ranges 0.007±0.0001 - 2.006±0.002 mg/ml, 2.54±0.04 - 156.94±5.28 µg/ml, 152.23 ±3.51 - 286.59±3.89 µg/ml, 18.23±0.03 - 50.13 ±0.04 µg/ml, 28.85±0.23 - 537.87±93 µg/ml and 0.532± 0.015 - 3.39±0.032 mg/ml, respectively (Table 2). The total phenolic, flavonoid and ascorbic acid contents were in the ranges of 62.89±0.43 - 166.13±0.56 mg gallic acid equivalent (GAE)/g extract, 38.89±0.52 - 172.23±0.08 mg quercetin equivalent (QEE)/g extract and 0.14±0.09 - 0.98±0.21 mg AA/g extract with quercetin as standard.

Correlation of phenolics content and antioxidant activity of three plant extracts showed that the correlation coefficients of total phenolics and flavonoid contents of *Cleome icosandra* were greater than 0.9 (R = 0.9995; R =0.9919 respectively), the same of *Rosa damascena* (R = 0.9830; R = 0.9848) and *Cyperus scariosus* (R = 0.9604; R = 0.9910) was comparative as shown in Fig. 28.

The Fenton reaction is a major physiological source of ·OH, which is produced near DNA molecules in the presence of transition metal ions such as iron and copper. The Fenton reaction is prevented by hydroxyl radical-scavenging flavonoids. Here, the capacities of ten plant extracts to protect against oxidative DNA damage were checked against DNA strand scission by ·OH generated in Fenton

reactions on pBluescript II SK (–) DNA and the activities against oxidative DNA damage were noted in the range 0.13-1.60 µg/ml, confirmed by densitometric analysis (Fig. 29, a, b & c). Finally, significant oxidative DNA damage preventive activity and antioxidant potential was noted with three plants extracts namely *C. icosandra, R. damascena* and *C. scariosus* with no cytotoxic activity against U937 cells (Table 3). In conclusion, results obtained from this investigation explain its life-long use in the Unani system of medicine and possible health benefits. These routinely used plants can be explored further as potential sources of natural antioxidants.

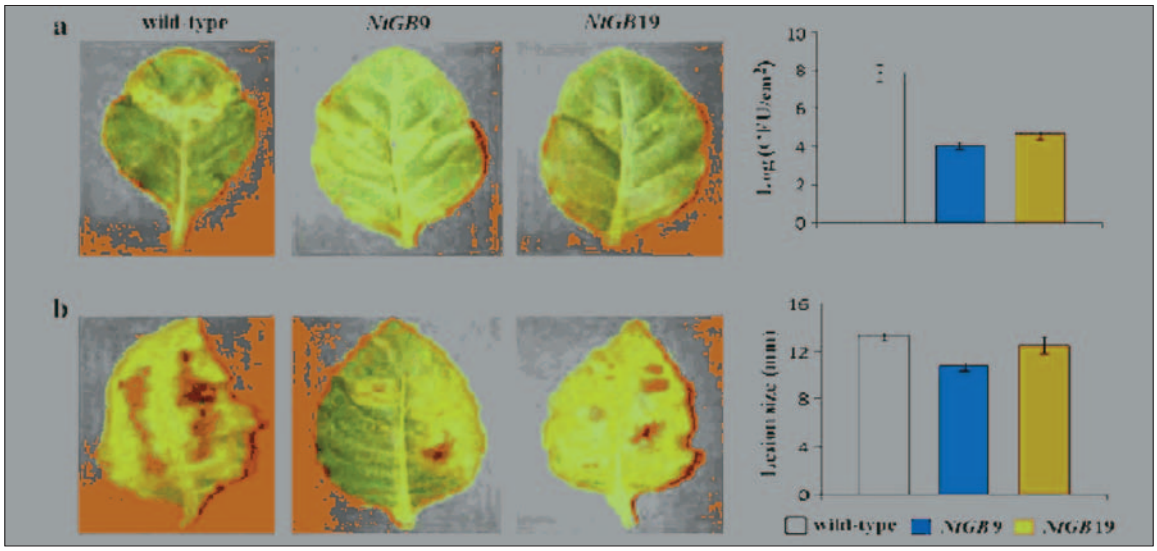


Fig. 25 : Disease resistance analysis of *NtGB* lines against the biotrophic and necrotrophic pathogens, *P. syringae pv. tabaci* and *A. alternata.* (a) Reduction of *P. syringae pv. tabaci* infection in whole plants and (b) *A. alternata* infection in detached leaves of NtGB lines as compared to wild-type.

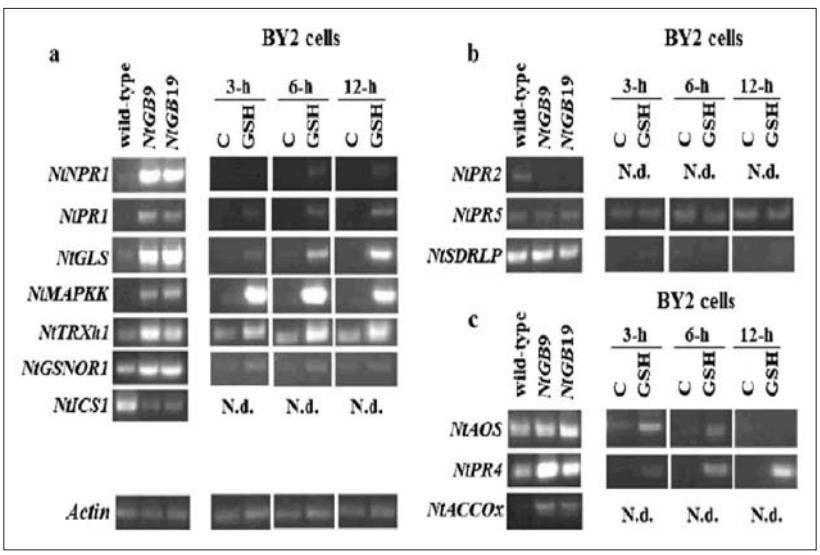


Fig. 26 : Changes in the transcript levels of NPR1-dependent and -independent SA-mediated pathway, alongwith JA and ET pathway genes by the overexpression of *LeECS* and in GSH-fed tobacco BY2 cells.

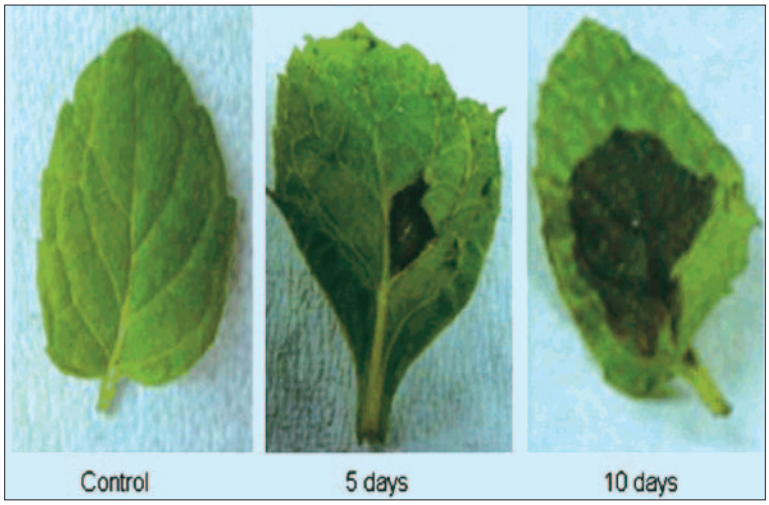


Fig. 27a : *Mentha arvensis–Alternaria alternata* pathosystem. Leaves of *Mentha arvensis* infected with *Alternaria alternata* 5 and 10 days after inoculation.

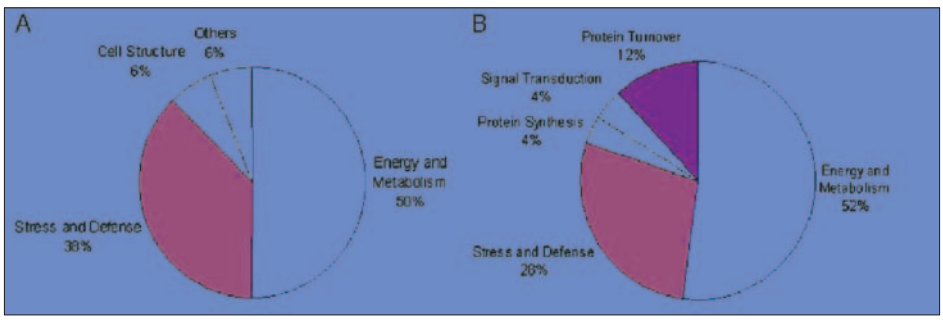


Fig. 27b : Functional classification of identified proteins from *Mentha arvensis*. Pie chart of proteins identified as up-accumulated (A) and down-accumulated (B) in *Mentha arvensis* in response to *Alternaria alternata* infection.

(a) **(b)**

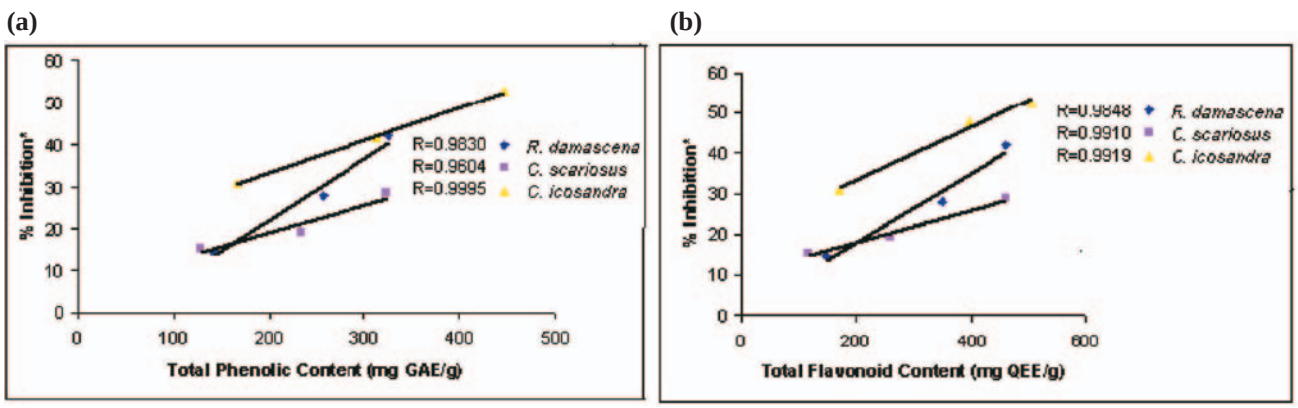
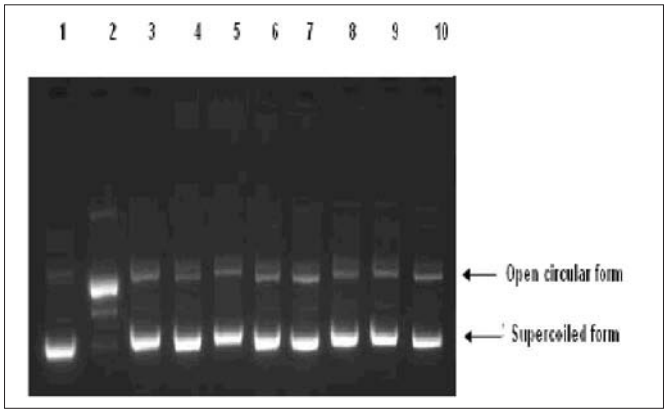
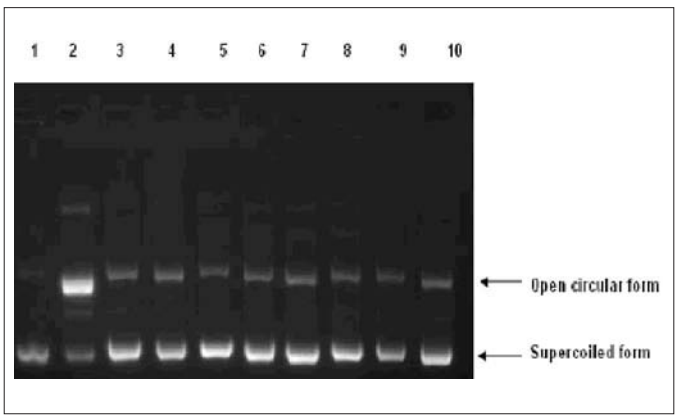


Fig. 28 : Correlation of % inhibition with Phenolic and Flavonoid contents. The relationship between (a) total phenolics content or (b) total flavonoid content in *R. damascena, C. scariosus, C. icosandra* and their antioxidant activity. The correlation analysis was described as linear correlation coefficient (R). The differences were considered statistically significant if $p < 0.05$.% Inhibition* = freeradical scavenging activity as determined by ABTS assay.

(a)



(b)



(c)

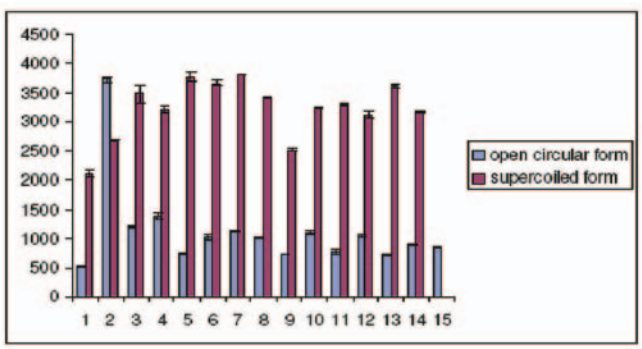


Fig. 29 : Electrophoresis patterns of pBluescript II SK (–) DNA breaks by ·OH generated from the Fenton reaction and prevented by different plant extracts. (a & b) Lane 1: treated control DNA (250 ng); lane 2: $FeSO_4$ (0.5 mM) + H_2O_2 (25 mM) + DNA (250 ng); lane 3: only H_2O_2 (25 mM) + DNA (250 ng); lane 4: only $FeSO_4$ (0.5 mM) + DNA (250 ng); lanes 5–10: $FeSO_4$ (0.5 mM) + H_2O_2 (25 mM) + DNA (250 ng) in the presence of quercetin (1 mM), (n = 3). **(c)** Confirmation of the data by densitometric analysis.

Table 2: IC_{50} values of selected plant extracts (μg/ml)

Activity assays	Selected plants			Standards used	
	Cleome icosandra	*Rosa damascena*	*Cyperus scariosus*	*Quercetin*	*Gallic acid*
DPPH•	7.28 ± 0.37**	10.36 ± 0.02***	11.10 ± 0.37**	3.21 ± 0.11	–
ABTS•+	2.54 ± 0.04***	3.57 ± 0.11**	6.27 ± 0.44**	1.34 ± 0.08	–
•OH	20.13 ± 0.01***	23.01 ± 0.03**	18.23 ± 0.038***	7.42 ± 0.32	–
NO	152.23 ± 3.51***	273.18 ± 3.52***	240.31 ± 4.28***	18.23 ± 0.42	–
$O_2^{\cdot-}$	30.96 ± 0.98***	42.10 ± 0.82^{NS}	28.85 ± 0.23***	41.98 ± 0.95	–
$ONOO^-$	532.85 ± 15.93*	637.57 ± 52.93**	590.23 ± 2.37**	–	820.12 ± 27.34

Results are mean ± SD (n = 3), each set in triplicate
Units of IC_{50}: $(mg/ml)^1$ * $p < 0.05$; ** $p < 0.01$;*** $p < 0.001$; NS = Non significant

Table 3: Cytotoxic activity of best three plant extracts

Time	*Rosa damascena*		*Cyperus scariosus*		*Cleome icosandra*		*Doxorubicin*
	0.2μg/ml	2μg/ml	0.2μg/ml	2μg/ml	0.2μg/ml	2μg/ml	25μg/ml
0h	100%	100%	100%	100%	100%	100%	100%
24h	97.5%	95.8%	96.4%	96.5%	99.7%	96.8%	42%
48h	97.6%	96.9%	96.2%	96.1%	99.4%	97.0%	0%
72h	97.4%	97.1%	96.6%	96.1%	98.8%	96.7%	0%

[1]Results are mean from three sets of experiments, each set in five replicates.

Dr. Samir K Dutta and Group

Cloning, expression, and characterization of Plant Protease Inhibitors–plausible biotechnological application and Biotransformation of Plant Secondary Products for value addition

We have cloned, expressed and mutated an inhibitor from ragi *(Eleusine coracana)* that can inhibit both amylase and trypsin simultaneously by forming a ternary complex. It is one of the very rare inhibitors that can affect both carbohydrate and protein metabolism. It is known as ragi amylase/ trypsin bi-functional inhibitor (RATI/ RBI). We clone it for the first time (GenBank Accession No. DQ494211) using matured inflorescence of ragi plants grown at our garden. The inhibitor consists of 122 amino acids with five disulfide bonds. From the published primary sequence, degenerate primers containing inosine were designed and used for RT-PCR cloning. Subsequently, the PCR product of ~ 366bp size was purified and the DNA sequence verified (Fig. 30). The product was again amplified with primers containing Nco1 and HindIII sites in the forward and reverse directions respectively. The PCR product was purified and ligated to pET-22b(+) expression vector, digested with Nco1 and HindIII. The ligated product (pET-22b(+)-RBI) was used to transform *E. coli* Novablue competent cells from Novagen. Positive transformants were screened by colony hybridization using α-32P-dATP labelled probe. Initially clones were identified from the autoradiogram, which were then confirmed from PCR and RE digestion of DNAs isolated from the clones. For expression and proper

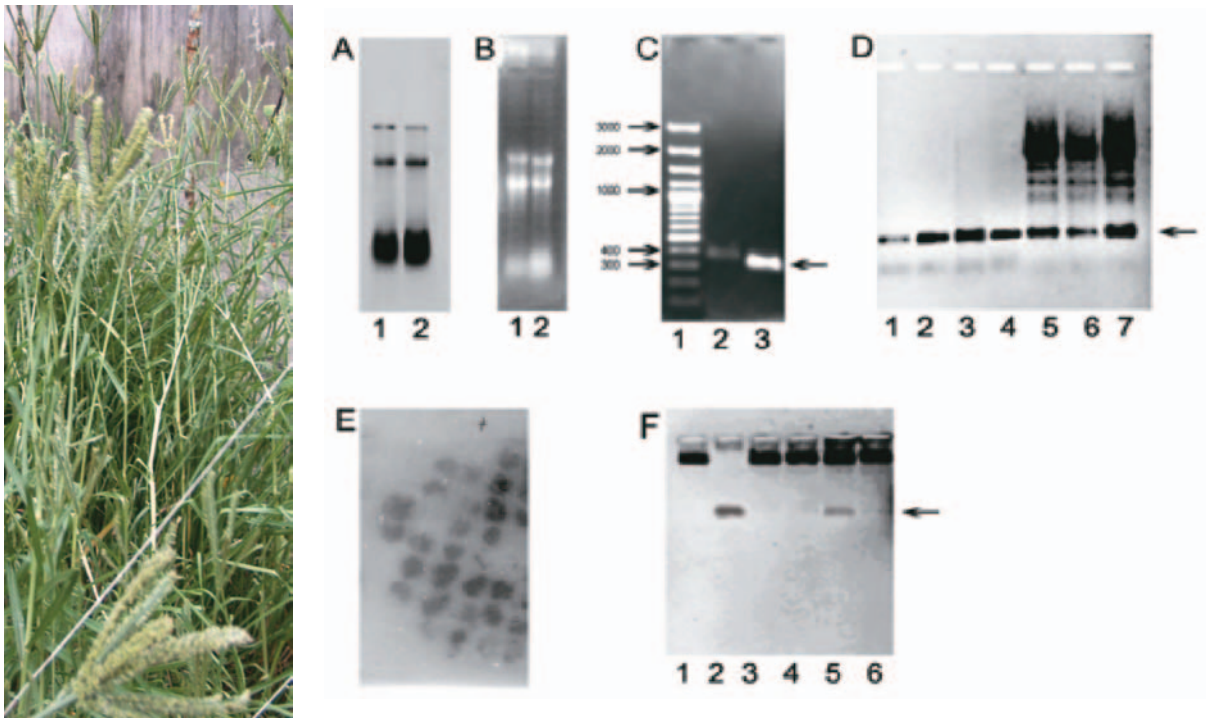


Fig. 30 : Cloning of RBI from *Eleusine coracana* Gaertn. (Ragi) seeds from plants grown at IICB garden.
A. Agarose gel electrophoresis (0.8%) of genomic DNA isolated from Ragi seeds (lanes 1 & 2), **B.** Formaldehyde RNA Agarose (1%) gel electrophoresis of total RNA (lanes 1 & 2) extracted from Ragi seeds, **C.** Size determination of the PCR product. DNA ladder (100 bp, Fermentas) (lane 1), PCR product of RBI (~366 bp) obtained from cDNA using inosine containing gene-specific primers and Taq DNA polymerase recombinant (Fermentas) (lacking proof-reading activity) (lane2). **D.** Standardization of PCR reaction with ragi cDNA as template, proof-reading proficient Taq DNA polymerase and gene specific primers containing RE sites. Agarose gel electrophoresis (1.2%) of RBI PCR product (~366 bp) obtained by 2-step PCR (with varying amount of cDNA template) (lanes 1-3), RBI PCR product (~366 bp) obtained from previous reaction as marker (lane 4), Agarose gel electrophoresis of RBI PCR products (~366 bp) obtained by 3-step PCR (with varying amounts of cDNA template) (lanes 5-7). **E.** Screening of Novablue cells transformed with pET-22b(+)RBI vector by colony hybridization with α^{32}P-dATP laleled probe, transformants grown on nytran membrane, treated with denaturing, nertralizing solution, SSPE buffer, hybridized with radiolabeled probe, washed, dried and exposed to X-ray film and autoradiogram developed. F. Screening of transformed Rosetta2 (DE3) cells. Plasmid DNA of pET-22b(+) vector digested with NcoI and HindIII (lane 1), RBI PCR product obtained from previous reaction (lane 3), plasmid DNAs extracted from transformed colonies and digested with NcoI and HindIII to release the insert (lanes 3-6). Arrows indicate the DNAs representing RBI.

folding of the recombinant RBI (for five disulfide bonds), the recombinant pET-22b(+) RBI plasmid was transformed in Rosetta2 (DE3) competent cells. DNA was extracted from positive clones and checked by RE digestion and finally confirmed from sequence analysis (Fig. 31).

For recombinant protein isolation, the clones were grown at 37ºC, induced with IPTG for 24hrs. The cells were pelleted down and resuspended in $MgSO_4$ for release of the periplasmic protein. Shocked cells were pelleted again and the supernatant fraction was concentrated using molecular cut off membranes. This fraction was used for initial assay for trypsin and a-amylase inhibition. For purification of r-RBI, His-bind resin from Novagen was used. For the presence of His-tag with r-RBI, it was eluted out from the column in presence of imidazole containing buffer.

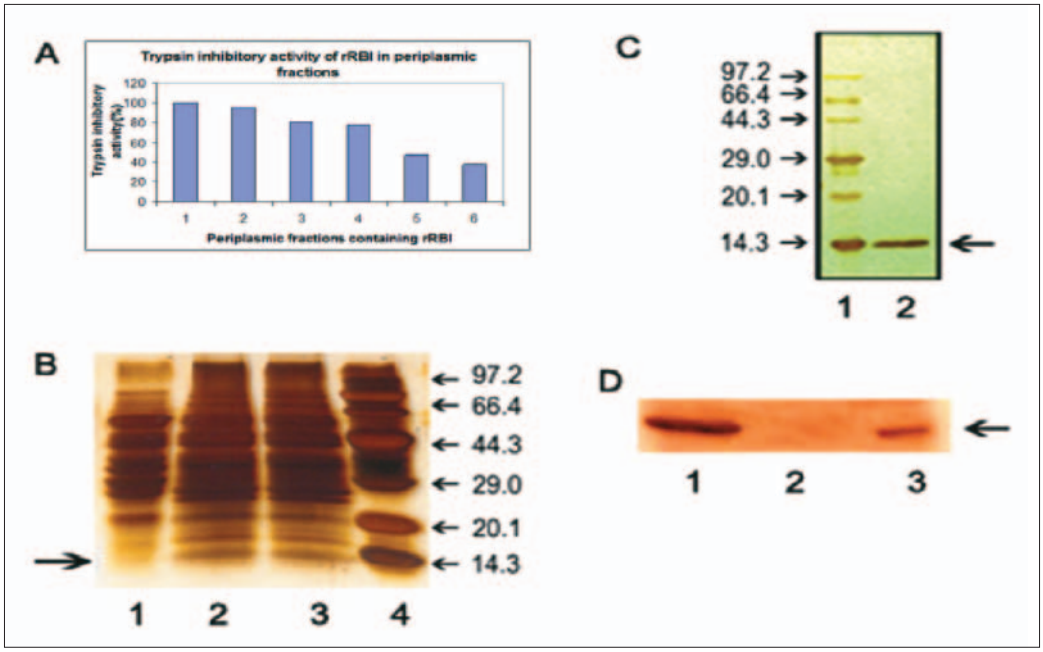


Fig. 31 : Expression pattern of rRBI in the periplasmic space of transformed Rosetta2(DE3) at different temperatures. **A.** Protein expressed in the periplasm after growth at 37 °C and induction with 1mM and 1.5 mM IPTG at 16 °C (lanes 1 & 2), Protein expressed in the periplasm after growth at 16 °C and induction with 1mM and1.5 mM IPTG at 16 °C (lanes 3 & 4), Protein expressed in the periplasm without IPTG at 16 °C after growth at 37 °C and 16 °C (lanes 5 & 6). **B.** SDS-PAGE (15%) analysis (Silver staining) of RBI protein expression in *E.coli* Rosetta2(DE3). Periplasmic fraction of *E.coli* Rosetta2 (DE3) cells containing the empty vector pET22b(+) without induction (lane 1), Periplasmic fraction of Rosetta2 (DE3) cells containing pET22b (+)RBI after 24 h induction with 1 mM and 1.5 mM IPTG (lanes 2 & 3). Protein molecular weight marker (Takara) (lane 4). **C.** SDS-PAGE (15%) analysis (Silver staining) of molecular weight determination of recombinant RBI protein. Protein molecular weight marker (Takara) (lane 1). From periplasmic fraction of Rosetta2(DE3) cells containing pET22b (+)RBI after IPFG induction, recombinant RBI protein purified by His-Bind resin column (lane 2). **D.**Western blot analysis with Anti-His antibody. Periplasmic fraction of Rosetta2(DE3) containing pET22b(+)RBI (lane 1), Negative control i.e, periplasmic fraction of Rosetta2(DE3) containing pET22b(+) vector alone (lane 2), rRBI purified from Rosetta2 (DE3) cells containing pET22b(+)RBI by His-Bind resin column and concentrated (lane 3). Arrows in the figures indicate the RBI protein.

The purity and size of the recombinant RBI (r-RBI) was determined from 15% SDS-PAGE using silver staining. For western blot analysis, proteins transferred on PVDF membranes was incubated with primary His-tag antibody, which was cross reacted with polyclonal goat anti-mouse immunoglobulin conjugated with alkaline phosphatase (AP) from Navagen and finally developed with NBT-BCIP solution for detecting r-RBI bands (Fig. 31).

α-amylase inhibition was performed using p-nitrophenyl-α-d-maltoside (NPM) as the substrate from Sigma. Alternatively, soluble starch and dinitro salicylic acid were used as per the published procedure. Hydrolysis was measured from the increase in absorbance at 405nm (A 405nm ε ~ 8200 $M^{-1}CM^{-1}$). Decrease in hydrolysis in presence of r-RBI was considered as the amount of inhibition in presence of a control. Trypsin inhibition was measured from the decrease in hydrolysis of BAPNA in presence of varying amount of r-RBI. Changes at A 410nm were monitored in this case (Fig. 31).

Finally, site directed mutagenesis was carried out to confirm the P1 residue responsible for trypsin inhibition using Stratagene quick-change site-directed mutagenesis kit as per vendor's instruction.

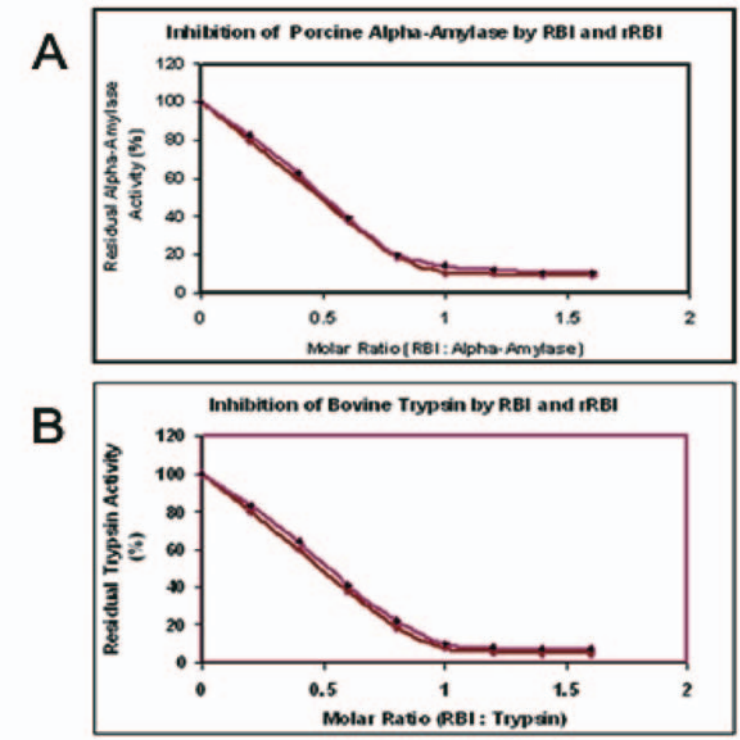


Fig. 32 : Inhibition of alpha-amylase and trypsin by purified RBI and rRBI. **A.** Alpha-amylase inhibitory activity showing residual alpha-amylase activity in percent as function of the inhibitor concentration at a fixed enzyme concentration using NPM as substrate. **B.** Trypsin inhibitory activity in percent as function of the inhibitor concentration at a fixed trypsin concentration using BAPNA as substrate. All experiments were done three times and averaged.

The mutated clone identified when checked for activity failed to inhibit trypsin, which confirmed 34th Arg as the P1 residue that was so far a prediction only.

Biotransformation of plant secondary metabolites viz., andrographolite and betulinic acid has been taken up recently to increase their water solubility, since the Plant Secondary Metabolites (PSM), being non-polar in nature, are water insoluble. This solubility problem has restricted their pharmaceutical formulations, even after their tremendous potential as drugs in many life threatening diseases. Interestingly, many such non-polar molecules become relatively polar after various transformations, viz., acetylation, esterification, glycosylation and so on. Assuming very limited quantity of such glucosyl transferases, development of affinity matrices/ techniques have been initiated as the potential tool for the identification and isolation of enzymes responsible for glycosylation of such PSM. We are very hopeful about identifying such a transferase, but for technical reasons, we are not describing it further.

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CHEMISTRY

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Chemistry department is a vital hub of this institute with deep historic roots, and a ready grasp and focus on the future. The department intensively pursues interdisciplinary research activities in the fields of synthetic and natural product chemistry, carbohydrate chemistry and biophysical chemistry. Chemistry in biological systems addresses the synthesis, isolation, characterization and application of chemical species and molecules of high relevance to biological processes and biomedical applications in human health like in the treatment of cholera, leishmaniasis Parkinson disease etc. The division is thus engaged in active collaboration with the biologists of this institute and in other CSIR laboratories, utilizing their expertise in chemical synthesis, isolation and characterization of natural products, and studying their efficacy for the development of functional molecular materials for potential applications in biology and medicine. Furthermore, the mandate of the division is also focused in human resource development by taking up active teaching and research guidance at both MSc and PhD levels.

SYNTHETIC CHEMISTRY

Dr. S. B. Mandal and group

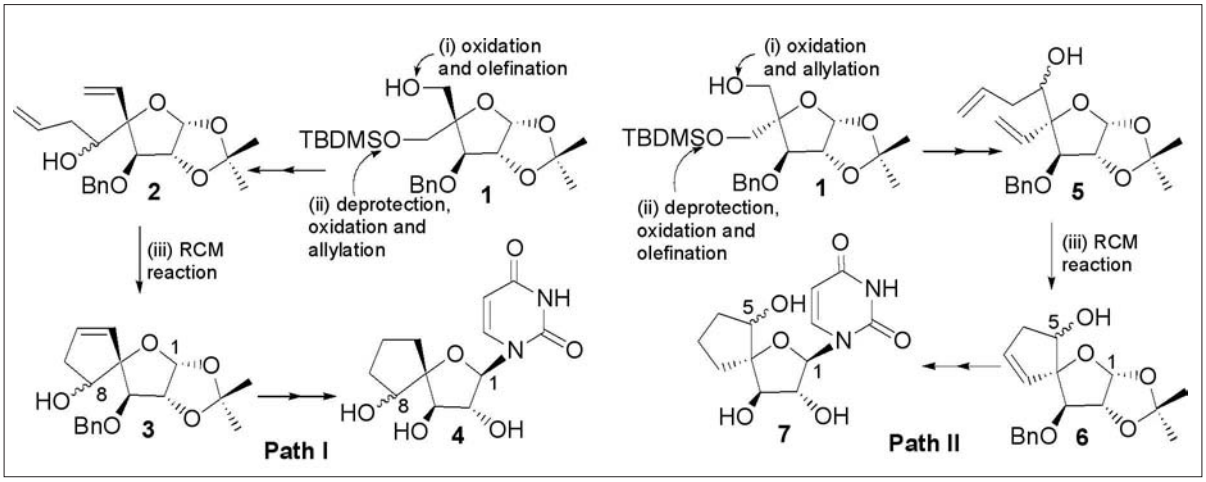
Synthetic approaches to structurally novel nucleosides and analogues from D-glucose

Conformations of the ribose ring in natural nucleosides equilibrate in solution between the C-3′-endo (N-type) and the C-2′-endo (S-type) due to low energy barriers; restriction of this conformational flipping could provide nucleoside analogues with greater selectivity and less toxicity for the treatment of viral diseases. Paquette subsequently introduced the concept of spirocyclic restriction in nucleosides through insertion of a carbocyclic ring at C-4′ of furanose/thiofuranose rings. The free radical-induced degradation of the ribose ring of nucleosides by C-4′-H abstraction can thus be precluded, resulting in enhanced metabolic stability as well as conformational rigidity in the furanose ring and the products would be expected to play a different role in the biochemical reactions improving the binding properties and the base pairing preference when inserted in oligonucleotides. Considerable attention has thereafter been given on structural modifications of nucleosides and syntheses of a number of spiro derivatives including C-1′-spiro, C-2′-spiro, C-3′-spiro, and C-4′- spironucleosides as conformationally restricted/biased analogues have appeared in the literature.

Based on the above observations, the objective of the subproject was fixed to develop synthetic routes to structurally unique and conformationally locked spirocyclic nucleosides derived from carbohydrate precursors.

To fulfill the above objective our perceived synthetic scheme was based on the utilisation of the known starting material **1** (Fig. 1) having a 4, 4-disubstituted furanose ring. The free CH_2OH group was to be elaborated through oxidation followed by methylenation (Path I) or Barbier allylation (Path-II). The silyl protected primary alcohol group in **1** could then be deprotected and subjected to oxidation

followed by allylation (Path I) or methylenation (Path-II) to produce **2** and **3** respectively. RCM reaction of the two olefin bearing substituents at C-4 of the furanose ring was thereafter expected to provide spiro rings in **3** and **6** for further elaboration. Deprotection of the acetonide group followed by peracetylation, nucleoside base introduction via Vorbrüggen reaction, hydrogenation and final deprotection resulted in the generation of the desired nucleoside analogues **4** and **7** (Scheme 1).



Scheme 1

The scope of the strategy to synthesize other ring systems from carbohydrates could be investigated and the work is in progress.

Dr. Partha Chattopadhyay & group

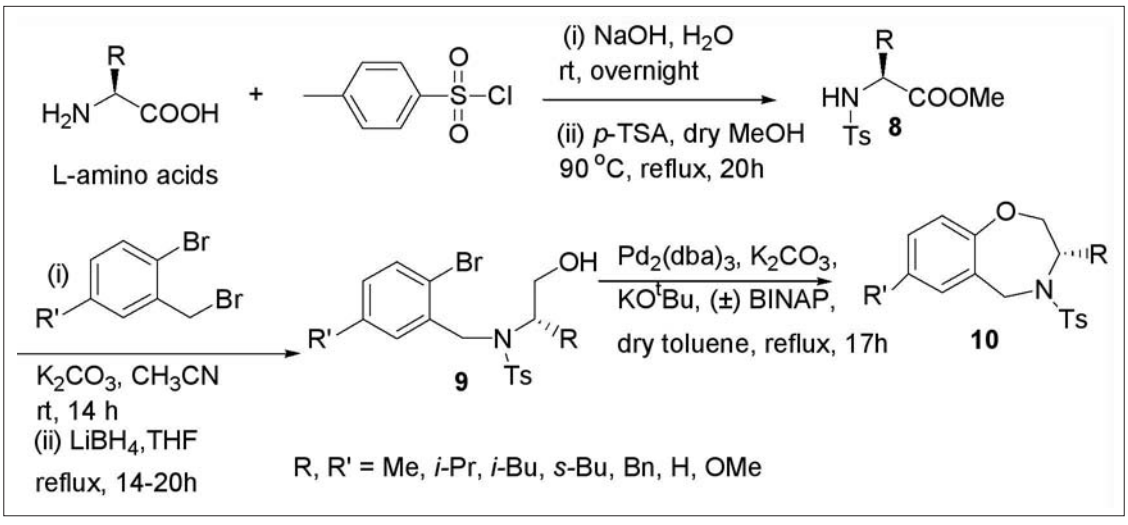
Synthesis of annulated medium ring heterocycles

The principal objective of the subproject is to develop synthetic methodologies for medium ring heterocycles possessing diverse biological properties.

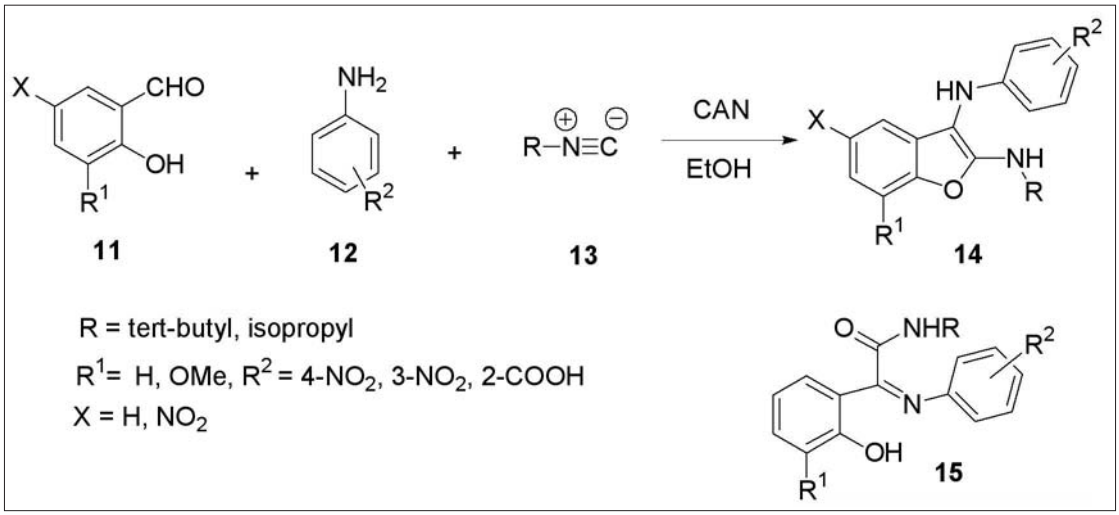
Synthesis of optically pure benzoxazepines from aminoacid precursors. 1, 4-benzoxazepines are well known for their anti-inflammatory, antitumor and antithrombotic activities. Here, we have developed an easy improved synthesis of enantiomerically pure 1,4-benzoxazepines from naturally abundant L-amino acid derivatives using Pd-catalyzed intramolecular arylether ification reaction in the presence of bulky binaphthylphosphane ligand. Towards this, different L-amino acids were converted via N-tosyl esters **8** to the corresponding alcohols **9**, which were transformed to **10** (Scheme 2).

Application of various spectroscopic methods on the synthesized compounds and X-ray analysis of benzoxazepine were used to assign the structure and stereochemistry of the products. Some compounds showed promising *in-vitro* anticancer activity against human cancer cell lines of varied tissue origin.

Lewis acid catalyzed one pot selective synthesis of amino benzo[b]furans. An efficient one-pot reaction between isocyanides, anilines and salicylaldehydes in presence of Lewis acid proceeded smoothly at room temperature within short time interval affording amino benzo[*b*]furans derivatives in high yield. With the optimized reaction conditions, salicylaldehydes **11**, aniline derivatives containing strong electron withdrawing substituents **2** and isocyanides **13** were reacted in presence of CAN to produce benzofuran derivatives **14** (Scheme 3). However, similar reaction of **12** (*o*- and *p*-haloanilines) with



Scheme 2



Scheme 3

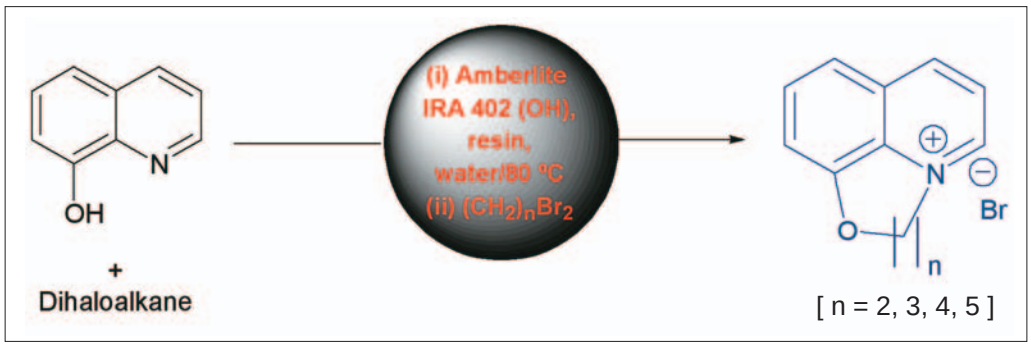
11 (X = H) and **13** produced unusual adducts, *N*-alkyl-2-arylimino-2-arylacetamide derivatives **15**, the structure of one such compound was supported by x-ray analysis.

Dr. Nirup Bikash Mondal, Dr. Sukdeb Bandyopadhyay and group

Synthesis of structurally unique bioactive heterocycles

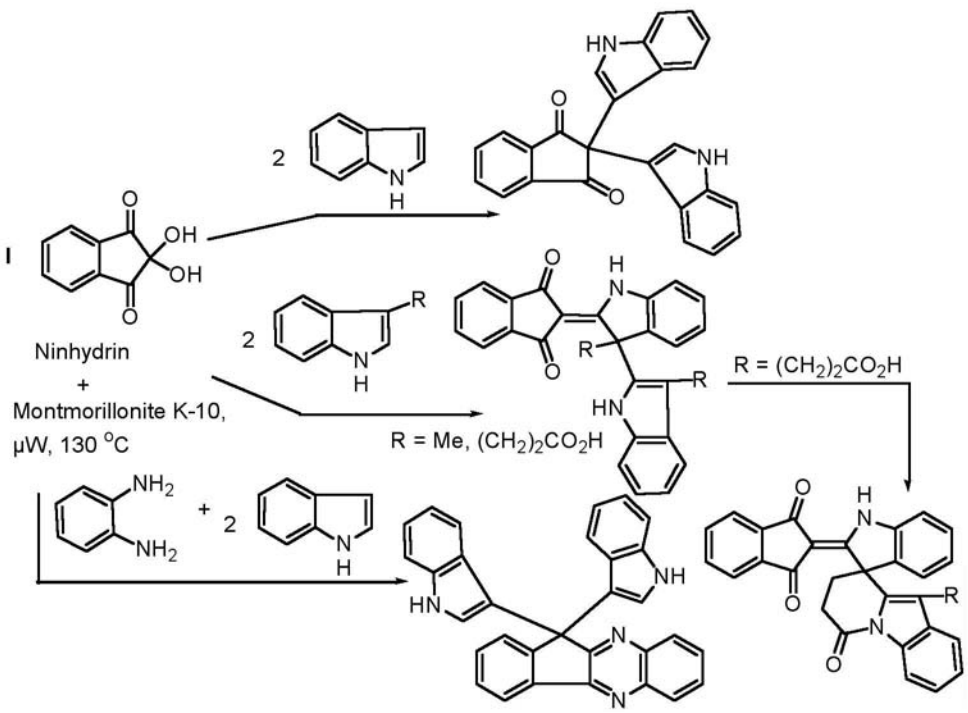
The objective of the research work is to synthesize structurally unique and biologically active heterocyclic compounds.

Main findings. (a) A high yielding green protocol for the synthesis of tricyclic oxazaquinolinium salts has been developed using Amberlite IRA 402(OH) in water (Scheme 4). This method is more effective compared to previously reported phase-transfer catalytic (PTC) condition in terms of yield of the product, reaction time and ease of separation.

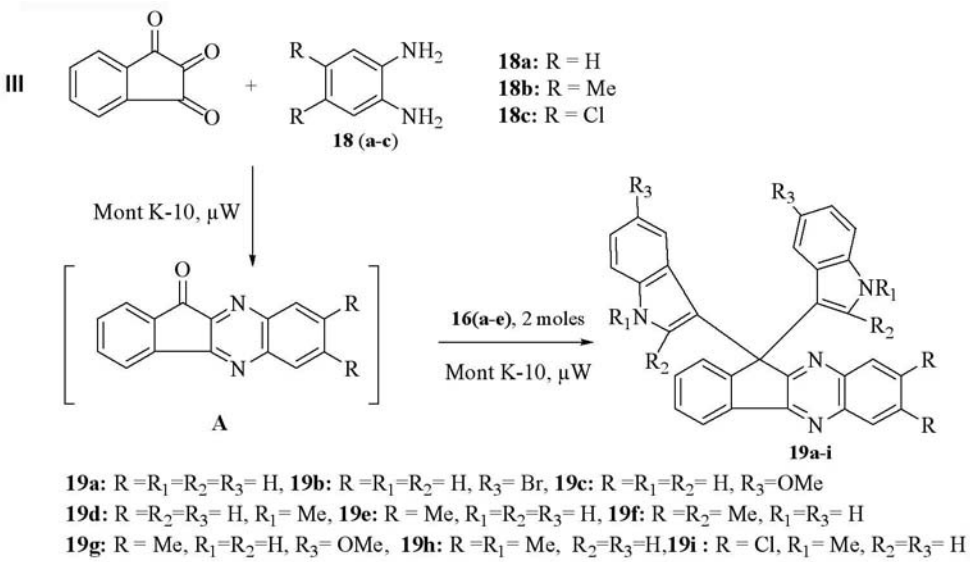


Scheme 4

(b) An environmentally benign protocol has been described for the synthesis of novel 2-(1',3'-dihydro-1H-[2,3']biindolyl-2'-ylidene)-indan-1,3-diones/bis indolyl indane-1,3-diones from ninhydrin and 3-substituted/ unsubstituted indoles in presence of montmorillonite K-10 as catalyst in a solvent-free condition under microwave irradiation (Scheme 5). The method has also been used for the synthesis



16a/17a: $R^1 = R^2 = R^3 = H$, **16b/17b**: $R^1 = R^2 = H$, $R^3 = Br$, **16c/17c**: $R^1 = R^3 = H$, $R^2 = Me$
16d/17d: $R^1 = R^2 = H$, $R^3 = OMe$, **16e/17e**: $R^1 = Me$, $R^2 = R^3 = H$



Scheme 5

of bisindolylindeno[1,2-*b*]quinoxaline derivatives. The structures of the representative products were confirmed by x-ray analyses (Figs. 1 and 2).

(c) Efficient syntheses of 6,6,8,6,6-pentacyclic naphthofused oxazocinoquinolinones and 6,6,8,6,6,6-hexacyclic benzo[*g*]quinoxalino-fused oxazocinoquinolinones were realised in one-pot sequences. The generation of libraries of their diaryl- and alkynyl-substituted analogues via Suzuki–Miyaura and Sonogashira cross-coupling reactions respectively, were also achieved (Scheme 6). The structure of the product (**A**) was confirmed by x-ray analysis (Fig. 3).

(d) A high yielding environmentally benign protocol has been developed for the synthesis of pyrrolo [2,1-*a*] isoquinoline using chromone-3-carboxaldehyde, isoquinoline and phenacyl bromide/bromoacetic acid ester as reagents in aqueous micellar medium (Scheme 7). The method is operationally simple and more effective compared to the previous methods in terms of the yield of the products as well as the reaction time.

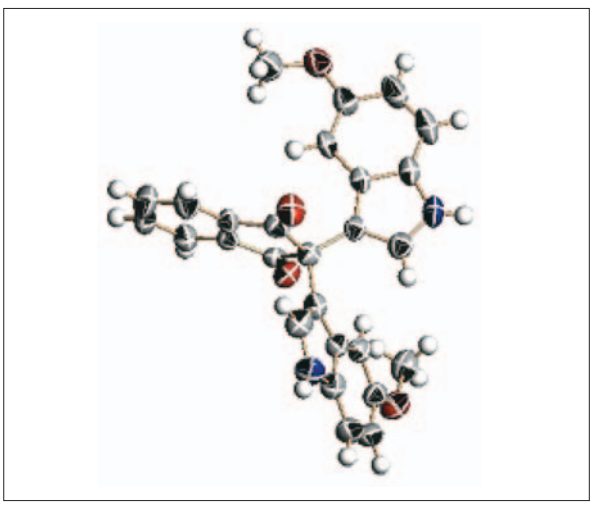


Fig. 1 : ORTEP representation of 17d

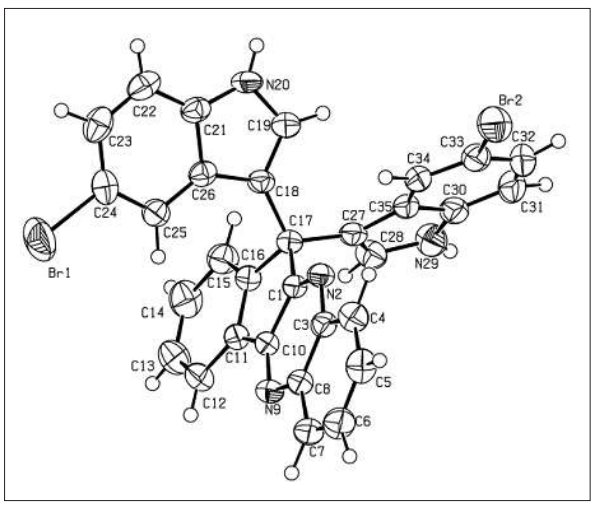
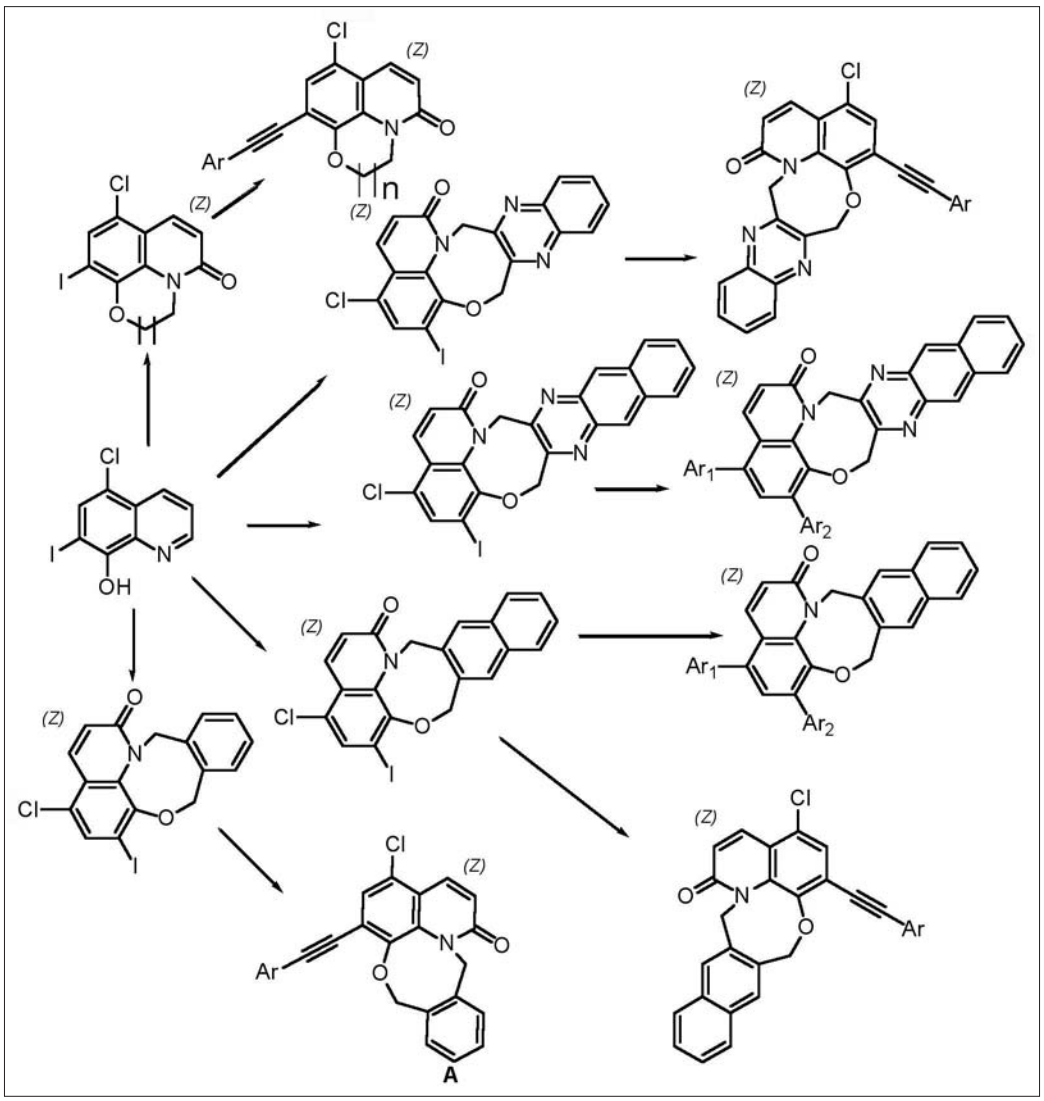


Fig. 2 : ORTEP representation of 19b



Scheme 6

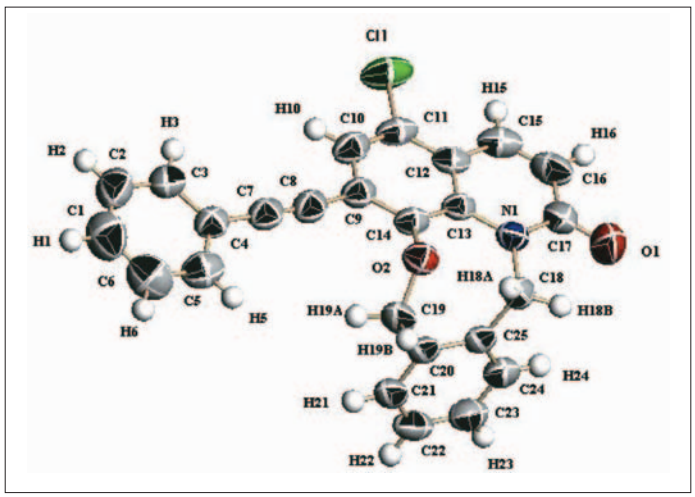
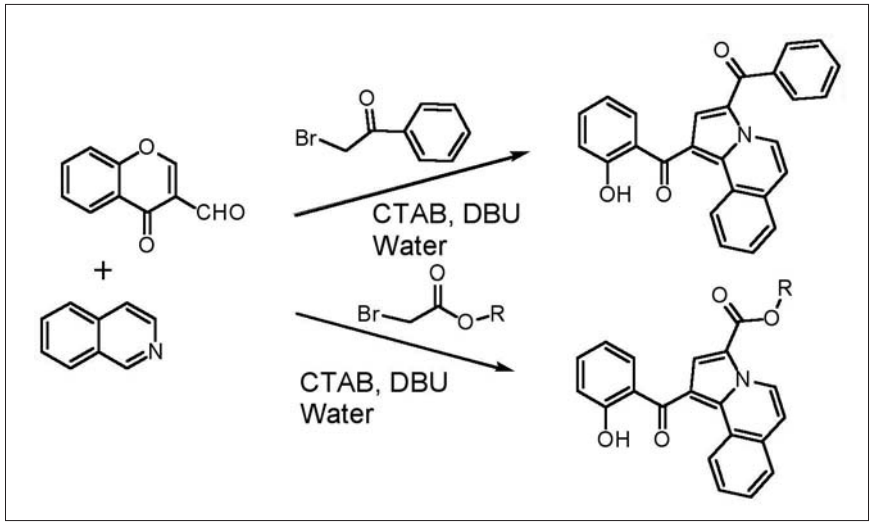


Fig. 3 : ORTEP representation of compound (A)



Scheme 7

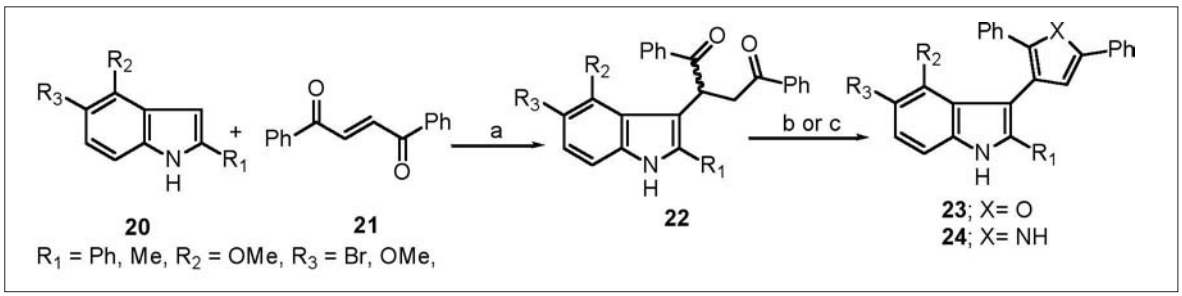
Dr. Parasuraman Jaisankar and group

Synthetic studies in heterocyclic chemistry using catalysts

The aim of the subproject is to generate new heterocycles (chiral and achiral forms) due to their wide applications in drugs/pharmaceuticals used for various diseases. The use of catalysts might result in unexpected and completely new compounds having specific and desired skeletons.

Facile synthesis of bioactive indolo-furan and indolo-pyrrole. Our initiative towards synthesizing new biologically active heterocyclic compounds has resulted in the observation that bioactive 3-(furan-3-yl)-1H-indole (**23**), 3-(pyrrole-3-yl)-1H-indole (**24**) derivatives could be synthesized starting from indoles **20** in presence of either p-TsOH or ammonium acetate respectively (Scheme 8). The structure of the 3-(furan-3-yl)-1H-indole derivative was confirmed by X-ray analysis (Fig. 4). Some 3-(furan-3-yl)-1H-indole derivatives (**23**) have shown good to moderate cytotoxic activity against human leukemic cell line U937 with IC_{50} 5-15 μM.

Catalytic dehydrative s-allylation of cysteine containing peptides in aqueous media toward lipopeptide chemistry. Thiol-containing peptides and cysteine have been successfully S-allylated with various allyl alcohols in aqueous medium containing a catalytic amount of [CpRu-(η3-C_3H_5)(2-quinolinecarboxylato)]PF6. A quick and easy installation of 2-propen-l-ol having a long-chain alkyl



Scheme 8 : Synthesis of indolo-furans **23** and pyrroles **24**

Reagent and Conditions : (a) $InCl_3$ (20 mol%), DCM, stir, rt, 20 h; (b) *p*-TsOH (0.8 equiv.), DCM, 50 °C, 1-2 h (for X = O); (c) NH_4 OAc (20 equiv.), DCM, 50 °C, 24 h (for X = NH)

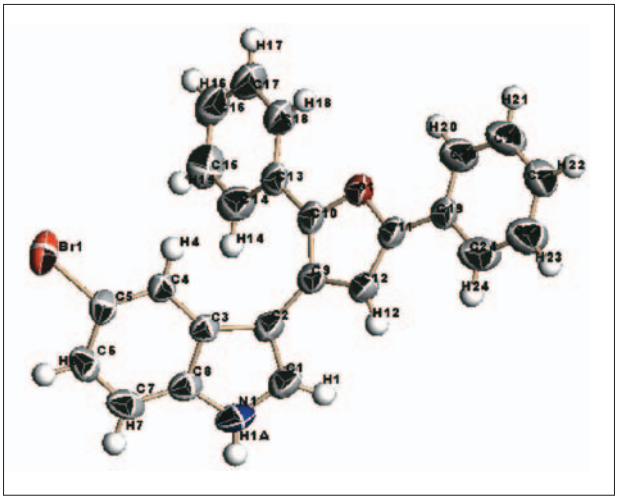
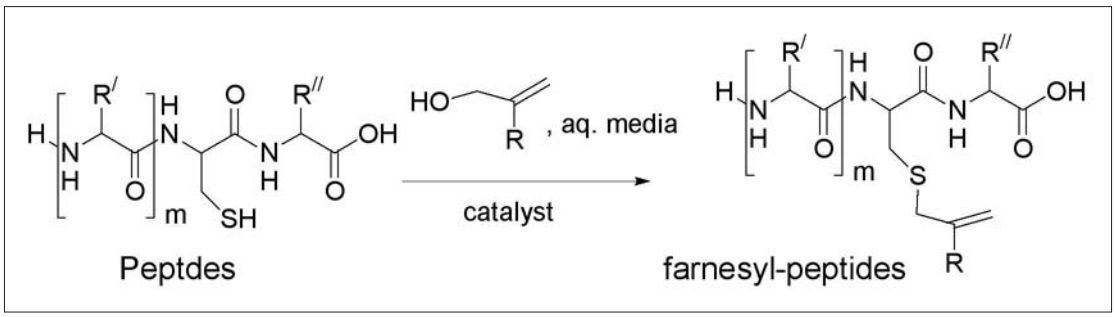


Fig. 4 : X-ray structure of 5-bromo-3-(2,5-diphenyl-furan-3-yl)-1H-indole

group at C (2) facilitates the synthesis of a new series of artificial lipopeptides, indicating a potential application to synthetic biology (Scheme 9).



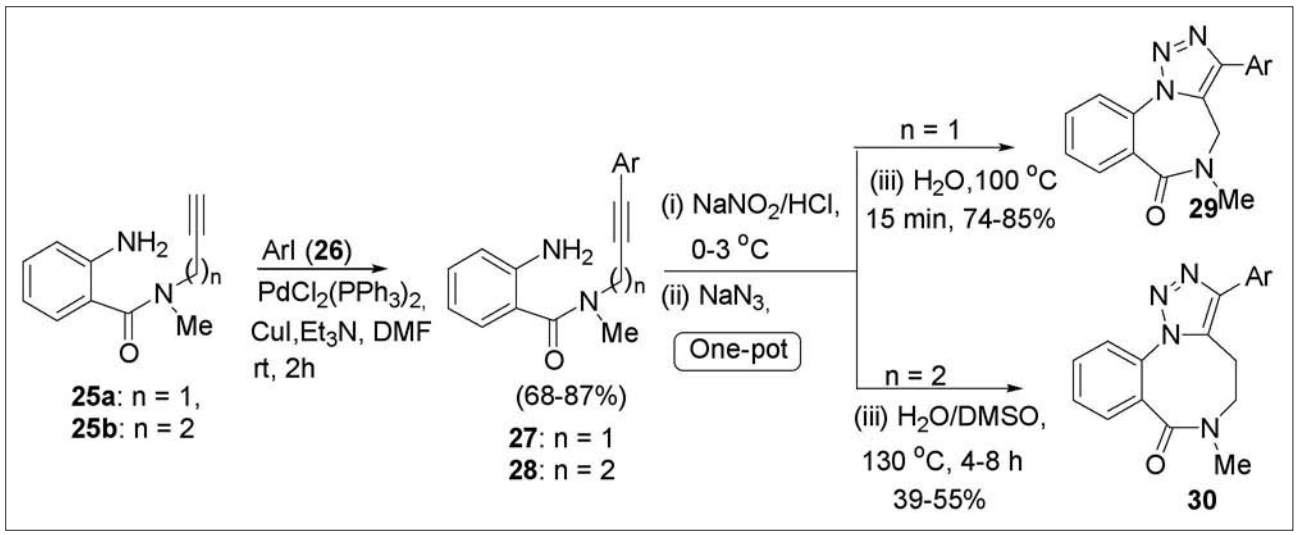
Scheme 9

Dr. Chinmay Chowdhury and group

Development of elegant methods for the synthesis of heterocycles of biological interests

Seven, eight and larger-membered rings are generally more difficult to prepare due to their torsional, transannular and large-angle strain combined with enthalpic and entropic constraints for ring closure and thus pose tremendous synthetic challenge in organic chemistry. Among the large varieties of heterocycles, 1,4-benzodiazepines have been integral parts of many drugs and therapeutic leads. More importantly, the spectrum of these therapeutic activities has been enhanced significantly by developing scaffolds made through the fusion of 1,4-benzodiazepinone moieties with some specific heterocycles (e.g. pyrrole, imidazole, triazole, and oxazole). In view of the immense biological activities of these classes of compounds, we became interested in the general synthesis of 1,2,3-triazolo[1,5-*a*][1,4]benzodiazepin-6-ones **29** and 1,2,3-triazolo[1,5-*a*][1,5]benzo- diazocin-7-ones **30**.

Towards the approach, the reactions of **25a** with aryl iodides **26** were carried out under very mild conditions by stirring the mixture at room temperature for 2 h in the presence of palladium-copper catalysis (Scheme 10). Subsequent one-pot diazotisation/azidation followed by cycloaddition reaction afforded the desired seven-membered 1,2,3-triazolo[1,5-*a*][1,4]benzodiazepin-6-ones **29** within 15 min upon heating at 100 °C. We next applied the aforesaid protocol for the synthesis of 1,2,3-



Scheme 10 : Synthesis of 1, 2, 3-triazolo [1, 5-*a*][1, 4] benzodiazepin-6-ones **29** and 1,2,3-triazolo [1,5-*a*] [1,5] benzodiazocin-7-ones **30.**

triazolo[1,5-*a*][1,5]benzodiazocin-7-ones **30**. However, the cycloaddition reaction for the synthesis of the latter compound required a small amount of DMSO to the reaction mixture followed by heating at 130 °C for few hours, but with somewhat lower yield compared to their seven-membered analogues **29**. When the products **29** and **30** were treated with lithium aluminium hydride (LAH) in dry THF under reflux for 2 h, reduction of the amide functionality of products took place smoothly affording the corresponding amine derivatives with moderate to good yields. Final structural confirmation came from X-ray diffraction analysis of the products **29** and **30** (Fig. 5).

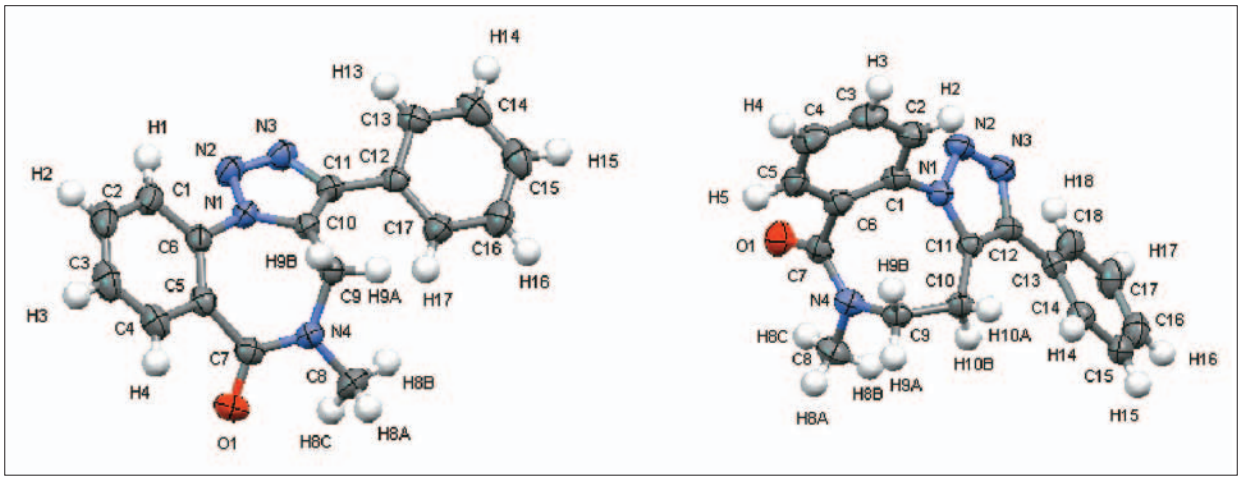


Fig. 5 : ORTEP representations of product 29 and 30

Dr. Asish Kr. Banerjee and group

Novel synthetic routes for natural products and their analogues: enantioselective approaches and radical cyclization strategies

The sub-project aims at establishing novel strategies for the synthesis of natural products, development of stereoselective synthetic methodologies, and application of regioselective radical reactions for the construction of condensed carbo- and heterocyclic ring systems.

Spiro[pyrrolidine-3,3-oxindole] heterocycles are found in a range of bioactive entities with both synthetic and natural origin.They are found to be present as an important motif in a number of naturally occurring alkaloids like, rhynchophylline, formosanine, horsfiline, elacomine, spirotryprostatin A & B (Fig. 6) and are known to possess moderate to high biological activities. Apart from these, some spirooxindole analogues are also well known for showing inhibitory activities against poliovirus / rhinovirus 3C - proteinase and aldose reductase.

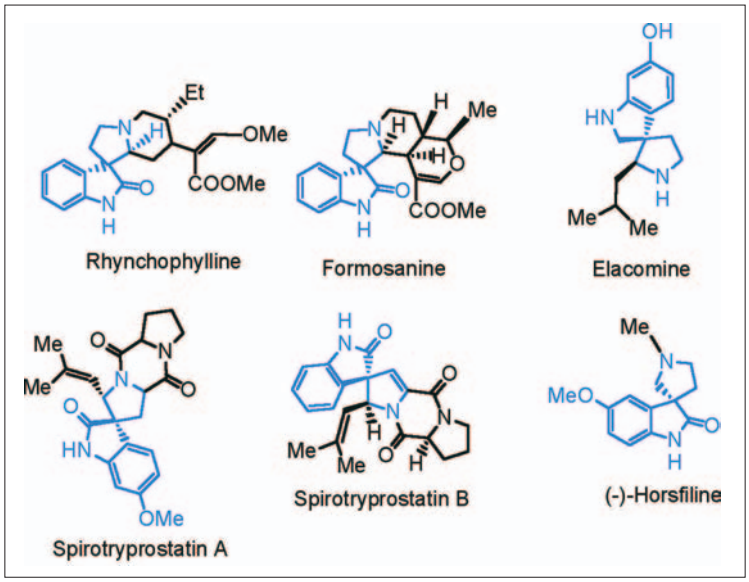
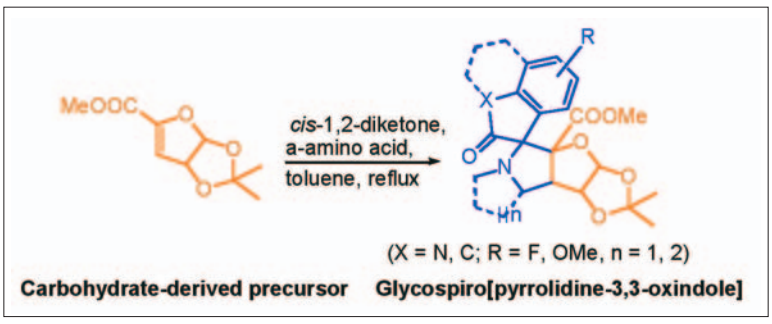


Fig. 6.

Being prompted by the structural features and biological activity reports of these molecules, we contemplated to fuse such structurally unique spiro[pyrrolidine-3,3-oxindole] motif with a properly functionalized glycoside derivative, assuming that the outcome of this fusion may lead to the identification of a new class of carbohydrate-based heterocycles with potential biological impact. Towards this end, we have synthesized for the first time a new series of sugar-fused spirooxindole derivatives, using secondary α-amino acids (sarcosine, proline and pipecolinic acid) and 1,2-diketones (isatin and acenaphthoquinone) as the generators of the azomethine ylides and the sugar derived precursor (Scheme 11).



Scheme 11 : Synthesis of some novel fused glycospiro heterocycles

Dr. Biswadip Banerji and group

Design, synthesis and biological activities of structurally novel heterocycles as new chemical entities

The group has initiated various organic synthetic efforts in diverse fields at the interface of chemistry and biology starting from the synthesis of enzyme inhibitors, novel organic methodologies, peptide based nano-particle synthesis and their characterization, biophysical studies of small bioactive peptides to elucidate their structure etc.

Design, synthesis and protection studies of potent inhibitors of cell division cycle 25A (Cdc25A) on neuronal apoptosis (in collaboration with Dr. S. C. Biswas). The cell division cycle 25 (Cdc25) family of proteins are highly conserved dual specificity phosphatatse that play a key role in cell-cycle progression by activating cyclin-dependent kinases (CDKs). In mammalians three isoforms have been identified so far: Cdc25A, Cdc25B and Cdc25C. Aberrant activation of CDKs are also reported in neurons in response to apoptotic stimuli. For example, neuronally differentiated PC12 cells undergo apoptosis in response to nerve growth factor (NGF) deprivation. In the NGF-deprived neuronal cells, the cell cycle molecules get activated. The first step of this cascade is the rapid activation of G1/S kinase CDK4 by the activation of Cdc25A molecule. This in turn kick starts a series of signals leading to neuronal apoptosis. Therefore, inhibiting the activity of Cdc25A will have pronounced effect on the neuronal protection from apoptosis. With this aim, a series of Cdc25A inhibitors (namely BB01 to BB15) have been synthesized and tested. Among them, the preliminary result shows good neuro-protection by BB07 and BB08 compound (see the graph and the cell-morphology picture in Fig. 7).

Ag(I) catalyzed synthesis of novel triazol-heterocycle via one pot sequential Sonogashira coupling, diazotization, azidation and [3+2] cycloaddition reactions. Highly nitrogen rich seven/eight member medium sized heterocyclic rings are important scaffolds in drug discovery. Thus synthesis and biological properties of triazole-fused medium sized heterocycles are of current synthetic interests. Recently we have developed a methodology to show that azides and alkynes undergo [3+2] cycloaddition reaction in presence of Ag(I) catalyst (Fig. 8).

Extending this methodology the group has successfully synthesized a series of novel triazole-fused seven member heterocyclic rings by a one-pot sequential four different organic reactions as depicted in the above Fig. 2. The structure of the triazole-heterocycles was further verified by single X-ray crystallography (see the ORTEP diagram in the Fig. 9).

Design & synthesis of novel peptide based self-assembly : their characterisation. It is well established in the literature that small peptides with varied chain length and side-chain functionality tend to self-assemble and produce different structures. We have synthesized few small peptides by the usual amide coupling protocols and tried to make self- assembly out of it. Thus the peptide was dissolved in 20% MeOH:H_2O mixture and its structure was studied by atomic force microscopy (AFM), tunnelling electron microscopy (TEM) as well as scanning electron microscopy (SEM). The AFM images show the presence of candle-shaped structure (top view), whereas the SEM & TEM images confirm the presence of rod-shaped structure (Fig. 10). The detailed study is still currently underway.

Synthesis of magnetic iron oxide nano-particle and its application in drug delivery. Magnetic iron oxide (IO) nanoparticles with long blood retention time, biodegradability and low toxicity have emerged as one of the important nanomaterial for biomedical applications. Here we plan to use iron oxide nano-particles as a drug delivery vehicle for MRI-monitored magnetic targeting of cancerous tumors. We

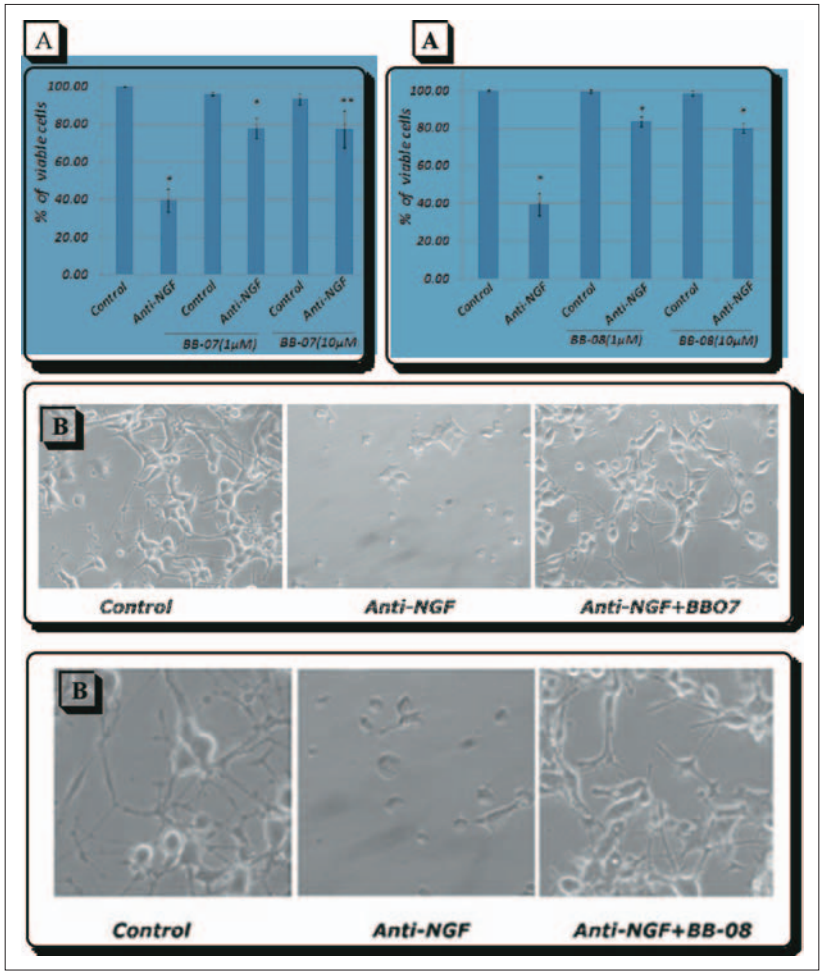


Fig. 7 : BB-07 protects differentiated PC12 cells against NGF deprivation. Differentiated PC12 cells (5DIV) were subjected to NGF deprivation for 18 h in presence and absence of BB-07 at doses 1 and 10μM. A: Graphical representation of percentage of viable cells in presence and absence of BB-07 following NGF deprivation. *p<0.001, **p<0.03. B: Representative phase contrast images of differentiated PC12 cells in absence and presence of BB07 following NGF deprivation. BB-08 protects differentiated PC12 cells against NGF deprivation. Differentiated PC12 cells (5DIV) were subjected to NGF deprivation for 18 h in presence and absence of BB-08 at doses 1 and 10μM. A: Graphical representation of percentage of viable cells in presence and absence of BB-08 following NGF deprivation. *p<0.001. B: Representative phase contrast images of differentiated PC12 cells in absence and presence of BB08 following NGF deprivation.

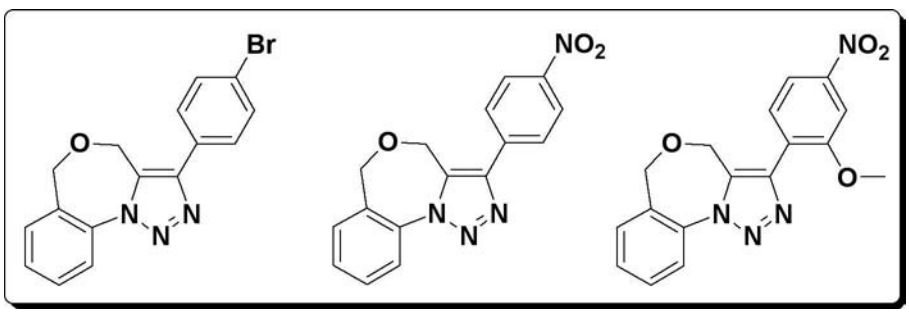


Fig. 8 : Novel triazole containing heterocycles

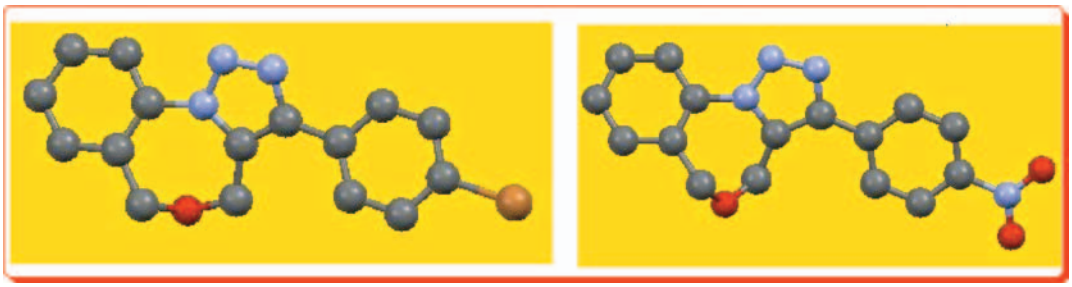


Fig. 9 : ORTEP diagram of the triazolo heterocycles

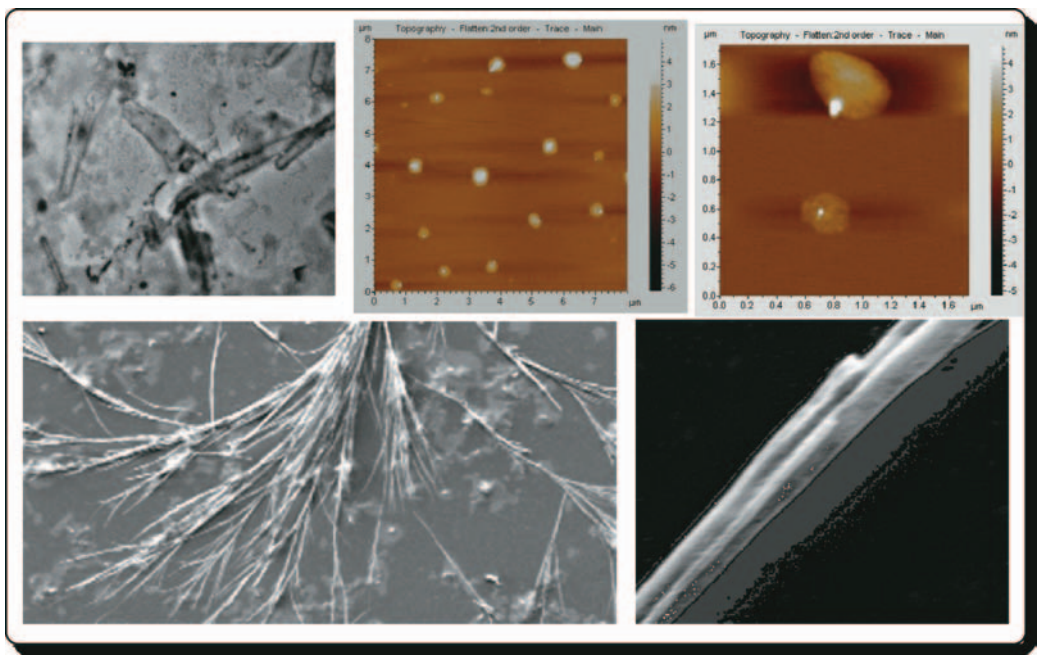


Fig. 10 : TEM, AFM & SEM images of the peptide

have synthesized iron oxide nano-particle of uniform size, about 5 nM. Currently we are pursuing the drug-delivery property of this nano-carriers (Fig. 11).

Secondary-structure elucidation of short peptides (in collaboration with Dr. N. C. Maiti). Short peptides tend to form unique secondary structures. Recently in our laboratory we have synthesized few short peptides of biological importance and studied their structural conformation by different

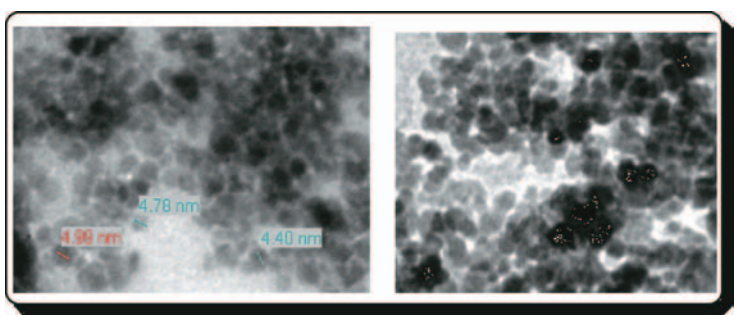


Fig. 11 : TEM images of IO nano-particles

biophysical methods. In order to ascertain its potential interactions with the specific biological targets, it is very important to understand the secondary structure and conformation of these peptides. One of these synthesized and purified short peptides was studied extensively and the preliminary result shows that it may have a mixed conformation. The Fig. 12 depicts the FTIR spectra of solid powder taken at room temperature. It shows two absorption peaks at 1617 and 1646 cm-1. These peaks are due to amide II vibration and usually assigned to protein/peptide secondary structure. From theoretical analysis and some empirical relationship, secondary structure content is assigned according to this amide II vibration mode. For non-alpha–non-beta structures the peak appears at >1660 cm-1, alpha-helix and random structure appears at 1660–1640 cm-1 and beta-sheet appears at 1640–1620 cm-1. The peptide show bands at 1646 cm-1 indicate it could be either alpha-helix or random. Again the band at 1617 cm-1 could be due to beta sheet conformation.

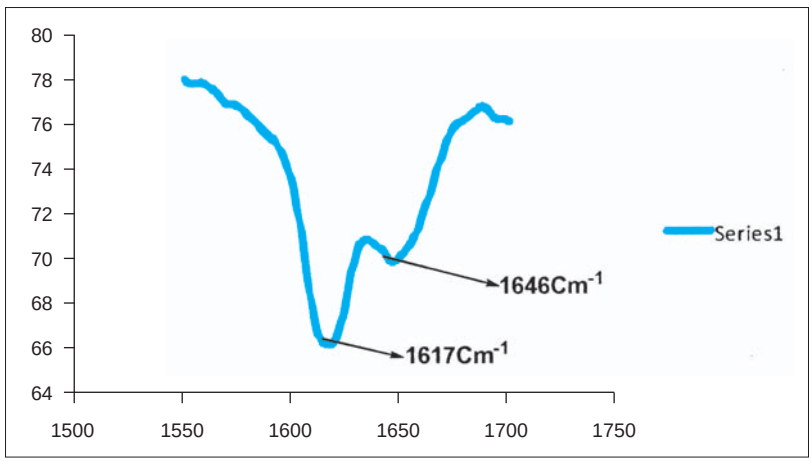


Fig. 12 : FTIR spectra of the studied peptide

Due to special geometry of the peptide and the two FTIR bands, we expect that conformation of the peptide may be extended alpha helix and the peptide remains with mixed conformation. Detailed DFT analysis and NMR investigation, currently undergoing in our laboratory could define the exact structural content of the peptide.

NATURAL PRODUCT CHEMISTRY

Dr. Sibabrata Mukhopadhyay and group

Chemical investigation of medicinal plants for bioactive substances

An interesting PDE 4 inhibitor, **ICB/11/D-8** was isolated from a medicinal plant *which* inhibits asthma *in vivo*. A number of carbazole alkaloids e.g. girinimbine, koenimbine, mahanimbine were isolated from the cold methanolic extracts of leaves and barks of the plant *Murraya koenigii* (curry patta). Interesting chemical reactions were studied on those alkaloids, viz. (1) Acid catalysed hydrolysis of girinimbine resulted in hydroxylation at the aliphatic double bond. (2) Girinimbine on treatment with BF_3 –etherate, a dimeric carbazole alkaloid was the major product. The point of attachment was established by detailed spectroscopic studies like ^{1}H-NMR and ^{13}C-NMR and 2D NMR. (3) Koenimbine was also treated with BF_3 –etherate. But in this case, a trimeric carbazole alkaloid was the major product and the point of attachment was also different due to the presence of a methoxy group at the

C-6 position. (4) Reaction of mahanimbine with BF_3 –etherate yielded a totally different cyclised product, whose structure was established spectroscopically.

Dr. Chinmay Chowdhury and group

Bioactive constituents from medicinal plants and preparation of their analogues for anti-cancer activities

During the course of studies on isolations and structural modifications of bioactive natural products, we have chosen andrographolide **31** for chemo-selective functionalization at C14 hydroxy in order to develop the pharmacophore(s) possessing better apoptotic index than andrographolide.

Initially, the hydroxyl groups at C3 and C19 of andrographolide were protected to furnish 3,19-isopropylideneandrographolide, which served as the key intermediate in the preparation of analogues library. Synthesis of the intermediate esters was smoothly achieved by the treatment of the 3,19-isopropylideneandrographolide with acid anhydrides (e.g. succinic, glutaric, maleic and phthalic anhydride) in dry dichloromethane in the presence of catalytic amount of 4-dimethylaminopyridine (DMAP) at room temperature. Finally, the removal of the isopropylidene moiety of these intermediates led to the isolation of desired analogues **32-35** (Fig. 13). In order to understand the role of the α-alkylidene part attached to the γ-butyrolactone ring of andrographolide for structure-activity relationship (SAR) studies, we prepared the corresponding saturated derivatives **36-39**.

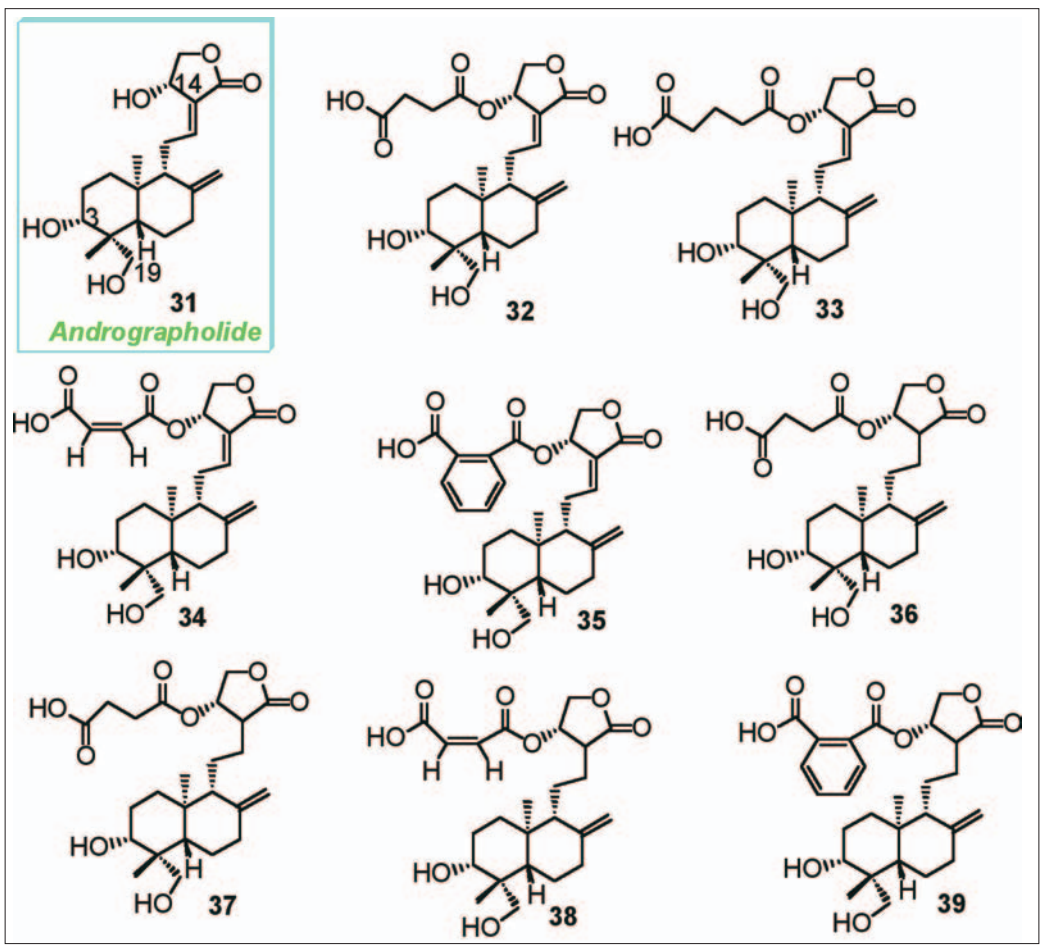


Fig. 13 : Preparation of andrographolide analogues

In vitro screening was carried out in selected human leukemic cell lines (U937, K562, THP1); parallel to this, cytotoxicities against normal cell-lines (NIH3T3, L132) were also checked. The standard MTS-PMS cell viability assay was carried out for determining the antiproliferative activities of the compounds synthesized. Interestingly, two of the synthesized analogues (**32** and **35**) inhibited the proliferation of U937 and THP1 cells by 50% or more at concentration less than 6.5 µM, while others displayed the cytotoxicity at higher concentrations. Among the analogues synthesized, the most active agent was **32**, while **35** was slightly weaker. Thus, analogue **32** emerged as the best lead candidate. In addition, evaluation of the induction of apoptosis by analogue **32** was carried out using flow cytometry (Fig. 14) and confocal microscopy (Fig. 15). Cells (U937) treated with an IC_{50} concentration (5.47 µM) of 32 for 24 h showed Annexin-V positivity that was ten fold higher than untreated cells (46.02% vs 4.6%) (Fig. 14). The confocal images of cells similarly treated with 32 and stained with Hoechst 33258, showed formation of apoptotic bodies along with membrane blabbing, whereas untreated cells had intact nuclei as shown in Fig. 15.

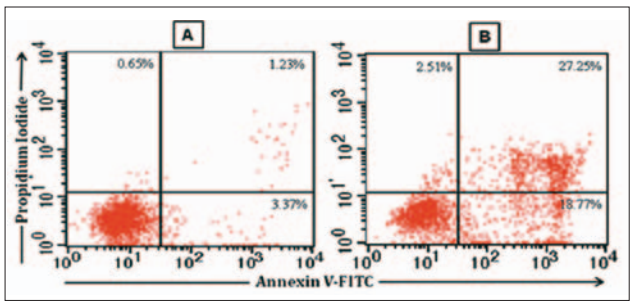


Fig. 14 : Untreated U937 cells (A) following treatment with 32 (5.47 µM) for 24 h (B).

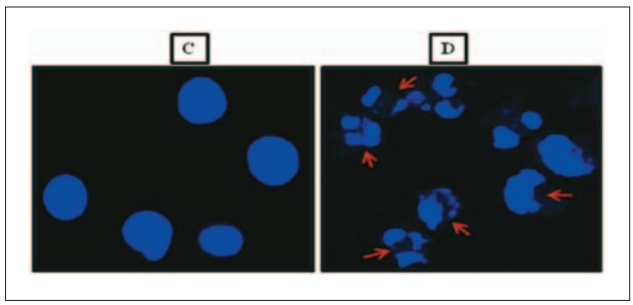


Fig. 15 : Untreated U937 cells (C) following treatment with 32 (5.47 µM) for 24 h (D).

CHEMISTRY

Dr. Sukdeb Bandyopadhyay, Dr. Nirup Bikash Mondal and group

Chemical investigation of medicinal plants for bioactive substances

The aim of the subproject is to identify useful bioactive compounds from natural sources and development of methodologies for making them readily available.

Main findings. Chromatographic separation of the methanolic extract of the leaves of *Azadirachta indica* led to the isolation of a sulfonoglycolipid characterized as a sulfonoquinovosyldiacylglyceride (SQDG) (Fig. 16) by extensive 2D NMR and mass spectral analysis. SQDG induces apoptosis against acute lymphoblastic leukemia (ALL) MOLT-4 cell lines in a dose dependent manner, with IC_{50} 8.3 µM. The compound showed significant DNA binding properties as evidenced by the enhancement of melting temperature and perturbation of the characteristic B-form of calf thymus DNA as revealed by CD evidence. The DNA binding was also characterized by isothermal calorimetry, where a predominantly enthalpy driven binding to CT DNA was noted. The findings point to its possible usefulness as an anti-cancer agent.

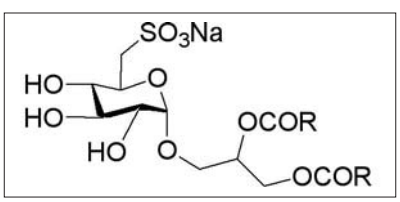


Fig. 16.

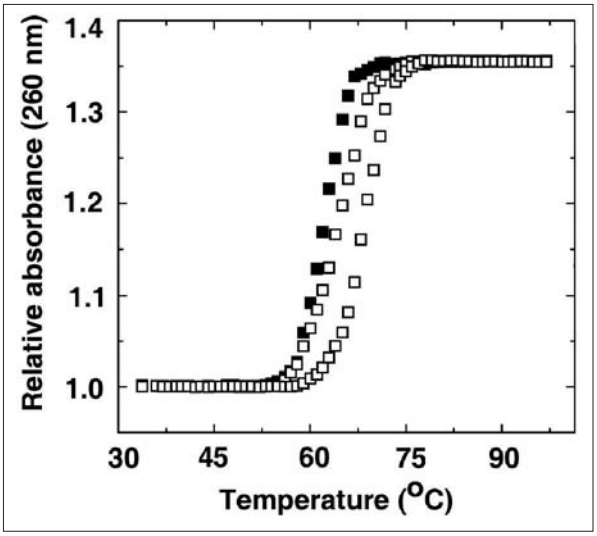


Fig. 17 : Thermal melting profiles of CT DNA (40 μM) (n) treated with SQDG at a drug/nucleotide molar ratio of 0.35 and 0.65 (□) in 10 mM CP buffer, pH 7.0.

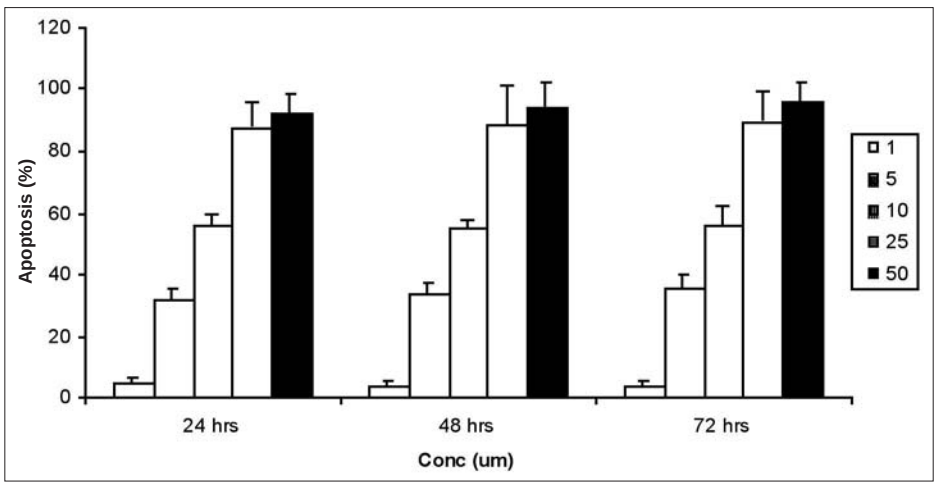


Fig. 18 : Effects of sulfonoquinovosyldiacylglyceride (SQDG) on MOLT-4 cell viability. MOLT-4 cells (1 x 10^5 cells/well) were incubated in the presence or absence of SQDG at different concentrations (0 to 50 μM) for different time periods (24 hr to 72 hr). The bars represent ± standard deviation of 6 independent experiments.

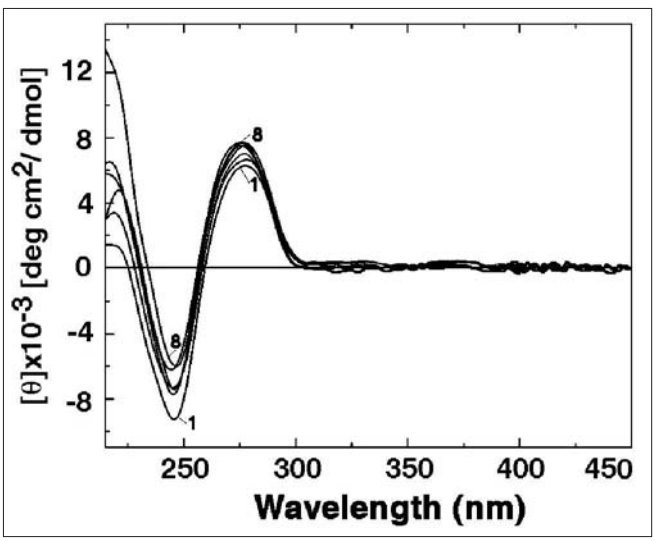


Fig. 19 : CD spectra resulting from the interaction of SQDG with CT DNA (60 μM). Curves 1-8 denote the interaction of DNA treated with 0, 3.2, 6.3, 8.5, 12.5, 18.3, 25.0 and 30.2 μM of SQDG.

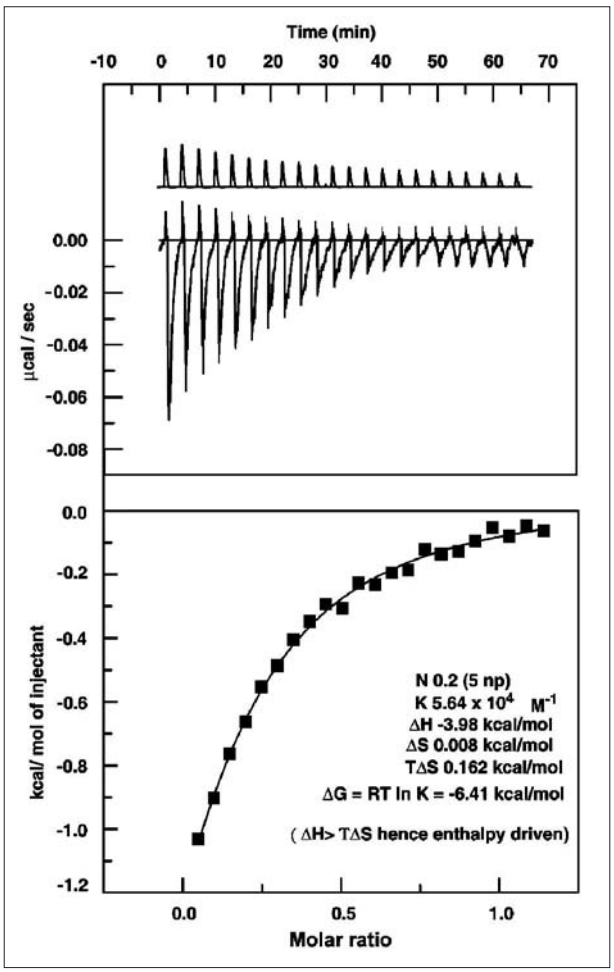


Fig. 20 : ITC profile for the titration of SQDG into a 50 µM solution of CT DNA in 10 mM CP buffer, pH 7.0 at 20°C. Each heat burst curve in the upper panel is the result of a 7 µL injection from 500 µM solution of SQDG into the DNA solution. The upper panel shows the heat burst for the injection of SQDG into the same buffer as control (curves offset for clarity). Lower panel represents the corresponding normalized heat signals versus molar ratio. The data points reflect the experimental injection heat while the solid line represents the calculated fit of the data.

Dr. Saraswati Garai

Isolation and characterization of bioactive saponins from the Indian medicinal plant Bacopa monniera

Bacopasaponins have been isolated from *Bacopa monnieri* and their corrosion inhibition studies on mild steel in 1M HCl solution have been done by gravimetric and potentiodynamic polarisation methods. The maximum observed inhibition efficiency was 95%. The results obtained from both gravimetric and potentiodynamic polarisation techniques were very similar. Bacopasaponins showed good corrosion inhibition efficiency and behaved as mixed type inhibitors. The inhibition efficiency was increased with the increase in concentrations and reached to the highest value (95%) at 200ppm.

Corrosion inhibition effect of crude methanolic extract of *Artemisia pallens* as well as active component arbutin on mild steel in 1 M HCl has been studied by weight loss, potentiodynamic polarization technique and XPS, FTIR, SEM and Raman spectroscopy, electrochemical impedence spectroscopy (EIS). Inhibition efficiency of 98% with crude extract and 93% with arbutin was achieved at 500mg/l at 303°K. Thermodynamic and kinetic parameters were obtained from weight loss of different experimental temperatures, which suggested at different experiment temperatures (303-343°K) the adsorption of the crude extract as well as arbutin on mild steel surface obeyed Langmuir absorption isotherm.

BIOPHYSICAL CHEMISTRY

Dr. G. Suresh Kumar and group

Nucleic acid polymorphic structures and their interaction with plant alkaloids

Studies on the binding of isoquinoline alkaloids to quadruplex DNA. Interaction of isoquinoline alkaloids berberine (**40a**), palmatine (**40b**), coralyne (**40c**) and sanguinarine (**40d**) with human telomeric quadruplex DNA sequence, d[$AG_3(T_2AG_3)_3$] has been investigated and compared with ethidium (**40e**). Absorption and fluorescence studies revealed non cooperative 1:1 binding. Coralyne showed highest affinity of the order of 10^6 M^{-1} and for others it was ~10^5 M^{-1}. The binding affinity varied as coralyne > sanguinarine > berberine > palmatine. Ethidium showed affinity close to sanguinarine. Comparative fluorescence quenching and polarization anisotropy of the emission spectra gave evidence for a stronger stacking interaction of coralyne, and sanguinarine compared to berberine and palmatine. Circular dichroic spectral perturbation of the quadruplex structure was similar in all the cases, but a strong induced circular dichroism for the bound molecules was observed only for coralyne and sanguinarine. The interaction of all the alkaloids was exothermic. Binding of coralyne and sanguinarine was predominantly enthalpy driven while that of berberine and palmatine was entropy driven. Heat capacity values of -169, -198 -105 and -95 cal/mol K respectively for coralyne, sanguinarine berberine, and palmatine, suggested significant differences in the hydrophobic contribution in the binding. These results suggest strong and specific binding of these molecules to the G-quadruplex and highlight the differences in their structure in the interaction.

Elucidation of the structure-activity relationship of 9-ω-amino alkyl ether analogues of berberine through binding to DNA. To understand the structure-activity relationship of isoquinoline alkaloids, absorption, fluorescence, circular dichroism, and thermodynamics were employed to study the interaction of five C-9-O-amino alkyl ether analogs (**40f**) from the plant alkaloid berberine with double-stranded calf thymus DNA. The C-9 derivatization resulted in dramatic enhancements in the fluorescence emission of these compounds. The most remarkable changes in the spectral and binding properties were in the BC4 and BC5 derivatives. Interactions of these analogues, which have an additional recognition motif with DNA, were evaluated through different spectroscopic and calorimetric titration experiments. The analogs remarkably enhanced the DNA binding affinity and the same was directly dependent on the alkyl chain length. The analog with six alkyl chains enhanced the DNA binding affinity by about thirty three times compared with parent berberine. The binding became more entropically driven with increasing chain length. These results may be of potential use in the design of berberine derivatives and understanding of the structure–activity relationship for improved therapeutic applications.

Binding of sanguinarine to double stranded RNAs: Insights into the structural and energetics aspects. Elucidation of the molecular aspects of small molecule-RNA complexation is of prime importance for rational RNA targeted drug design strategies. Towards this, the interaction of the cytotoxic plant alkaloid sanguinarine to three double stranded ribonucleic acids, poly (A).poly(U), poly(I).poly(C) and poly(C).poly(G) was studied using various biophysical and thermodynamic techniques. Absorbance and fluorescence studies showed that the alkaloid bound cooperatively to these RNAs with the binding affinities of the order 10^4 M^{-1}. Fluorescence quenching and hydrodynamic studies gave evidence for intercalation of sanguinarine to these RNA duplexes. Isothermal titration calorimetric studies revealed that the binding was characterized by negative enthalpy and positive entropy changes and the affinity constants derived were in agreement with the overall binding affinity from spectroscopic data. The

binding of sanguinarine stabilized the melting of poly(A). poly(U) and poly(I).poly(C) and the binding data evaluated from the melting data were in agreement with that obtained from other techniques. The overall binding affinity of sanguinarine to these double stranded RNAs varied in the order, poly(A).poly(U) > poly(I).poly(C) >> poly(C).poly(G). The temperature dependence of the enthalpy changes afforded negative values of heat capacity changes for the binding of sanguinarine to poly(A).poly(U) and poly(I).poly(C) suggesting substantial hydrophobic contribution in the binding process. Further, enthalpy-entropy compensation phenomena was also seen in poly(A).poly(U) and poly(I).poly(C) systems that correlated to the strong binding involving a multiplicity of weak noncovalent interactions compared to the weak binding with poly(C).poly(G). These results further advance our understanding on the binding of small molecules that are specific binders to double stranded RNA sequences.

Base pair specificity and energetics of binding of phenazinium molecules phenosafranin and safranin-O and phenothazinium molecule thionine to deoxyribonucleic acids. A comparative study: The base specificity and energetics of DNA binding of the phenazinium dyes phenosafranin (PSF)(**40g**) and safranin-O (SO) (**40h**) have been studied using various biophysical tools. The guanine-cytosine base specificity of both the compounds was established from binding affinity values and competition dialysis results and also from circular dichroism, thermal melting, and calorimetric studies. Both the dyes bind to DNA with affinity of the order of 10^5 M^{-1}, but the values are significantly higher for the guanine-cytosine rich DNAs over adenine-thymine rich ones and for phenosafranin over safranin-O. Calorimetric

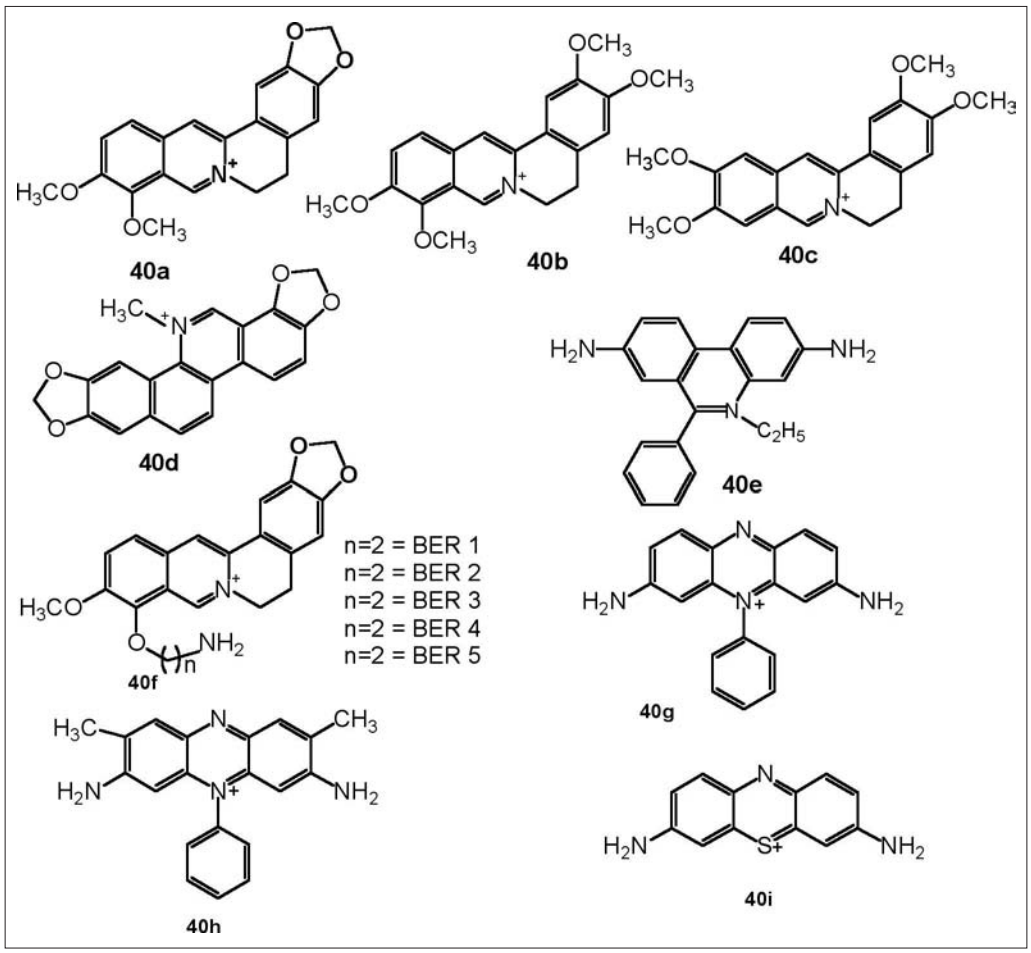


Fig. 21 : Structure of DNA and RNA binding molecules

studies revealed that the binding reactions were exothermic and favoured by negative enthalpy as well as predominantly large positive entropy contributions. The temperature dependence of enthalpy changes yielded negative heat capacity values, which were higher for PSF, compared to SO, suggesting substantial contribution from hydrophobic forces in the binding process. Enthalpy-entropy compensation behaviour was also observed for the binding of both dyes to DNAs, revealing the molecular aspects of the interaction. Taken together, the spectroscopic and calorimetric data reflect clearly guanine-cytosine base specificity of these molecules and a stronger DNA binding of PSF over SO. The results also provide some insights into the role of a bulkier substituent in the phenazinium ring in the binding process.

The sequence specificity of the intercalative DNA damage of the phenothiazine dye thionine (**40i**) was investigated using absorbance, fluorescence, circular dichroism and viscosity studies using four synthetic polynucleotides, poly(dA-dT).poly(dA-dT), poly(dA).poly(dT), poly(dG-dC).poly(dG-dC) and poly(dG).poly(dC). The binding clearly revealed the high preference of thionine to the alternating GC sequences (10^5 M^{-1}) followed by the homo GC sequences and the AT polymers. Intercalation of thionine was provided and the consequent sequence specificity of the DNA damage of thionine to deoxyribonucleic acid is advanced from this study.

Future programme of this group is to study of the various alkaloid derivatives with nucleic acids and proteins to elucidate specificity and energetics of interaction for developing synthetic alkaloids as therapeutic agents.

Dr. R.C.Yadav and group

Spectroscopic and thermodynamic studies of the binding of photoactive dye thionine with DNA

The hypochromic and bathochromic shifts, and also quenching of fluorescence indicated a strong affinity of the dye thionine to DNA. Base specificity of the complexation and energetics of the binding of thionine (**40i**) to DNA have been obtained. From the spectral analysis the binding is found to be non-cooperative while thermodynamic parameters suggest it as exothermic and that the hydrophobic contribution in the DNA binding with thionine exist.

NMR study of micro RNAs. NMR spectra of single stranded micro RNA 21- mer do not show peaks in the down field region. Work is in progress for the formation of duplex structure of micro RNA and the structure will be studied with the help of NOESY and other correlated NMR spectroscopy.

Studies on non linear chaotic system. Biological systems are very complex in nature and to know their dynamical behavior some models are constructed. Studies on the synchronization of non linear oscillators under various constrains are compared with biological systems. We have observed multiscroll dynamics for Chua oscillator, a modified Chua oscillator and the Lorenz oscillator. This is being extended to the Van der Poll and Duffing oscillators.

CARBOHYDRATE CHEMISTRY

Dr. Asish Kumar Sen and group

Structural studies on bacterial cell surface antigen

The purpose of the project is to isolate and elucidate the structures of the bacterial cell surface antigenic lipopolysaccharides (LPS) and/or O-antigenic polysaccharides (OPS), and capsular polysaccharides

(CPS) from both pathogenic strains (pre- and post-pandemic) of *Vibrio parahaemolyticus* O3:K6, that are responsible for gastrointestinal disease. Currently, the partial structure of the OPS of the pandemic strain of *Vibrio parahaemolyticus* O3:K6 has being elucidated. Structural studies of the CPS, LPS, O-antigenic polysaccharide from the different strains of *Vibrio parahaemolyticus* O3:K6 are under progress.

Synthesis of Oligosaccharides and carbohydrate based heterocycles

(1) We have completed the synthesis of a α-manno pentasaccharide (Fig. 22) which binds with a lectin isolated from *Musa paradisiaca* (banana). A new one-pot methodology had been developed involving chemo- and regio-selective glycosylations of suitable acceptors and *in situ* removal of *tert*-butyldiphenylsilyl group. The process demonstrated that a combination of TMSOTf and TfOH can be used as an effective reagent for the fast and selective *in situ* de-protection of *tert*-butyldiphenylsilyl group, and also serve as part of the promoter system for the subsequent glycosylation reaction.

(2) The synthesis of the tetra-saccharide repeating unit of O-antigenic polysaccharide of *Vibrio cholerae* O10 (Fig. 23) is in progress.

(3) Synthesis of new class a sugar fused azaheterocycles (Fig. 24) have been completed.

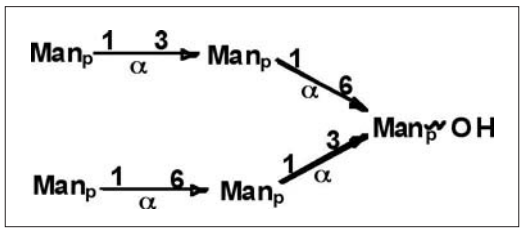


Fig. 22.

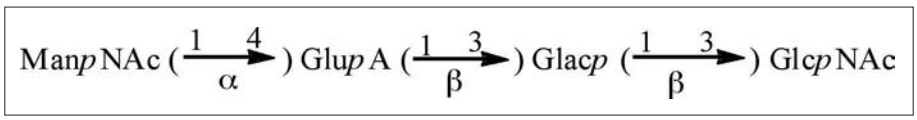


Fig. 23.

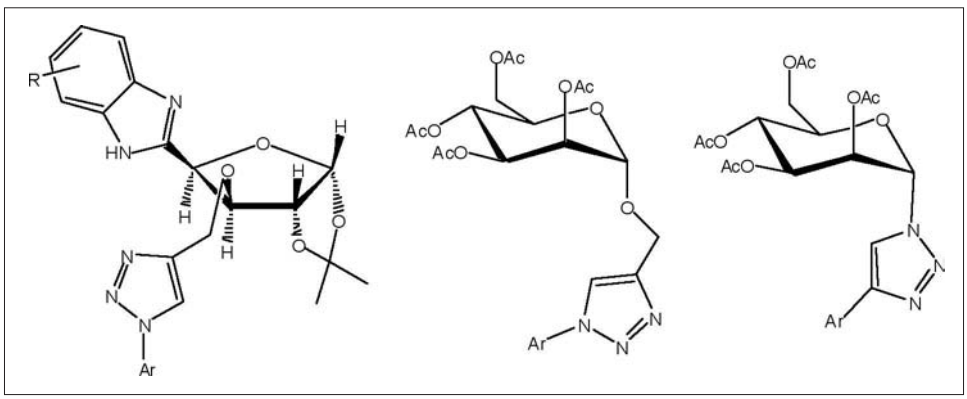


Fig. 24.

Characterization and structural modification of coir fiber for enhanced longevity

The project has been sponsored by Coir Board, Kochi from October 2006. The objective of this project is to chemically characterize the constituents of coir fibre from different varieties coir found in southern costal area of India and also to modify the coir fiber by chemical or enzyme procedure to protect them from degradation by light (UV). Grafting on coir fibre was done with the UV absorbing group to improve the surface as well as the bulk mechanical properties. The Scanning Electron Microscopy of modified fibers showed distinct change of the nature of the surface of the fibre.

OPERATION AND MAINTENANCE OF SOPHISTICATED INSTRUMENTS

Technical Staff

Asit Kumar Das, Tapas K. Sarkar, Diptendu Bhattacharya, Gautam Gupta, Sandip Chowdhury, Sekhar Ghosh, Sarit K Sarkhel, E. Padmanaban, Nimai C. Pradhan, Rajendra Mahato, Sandip Kundu, Santu Paul.

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Project Assistants

Sandip K Hota, Deboleena Bhattacharjya, Gautam Kulsi, Sumit Kr Pramanik, Biswajit Chakraborty

Project Trainees

Maitrayee Banerjee, Yogesh P Bharitkar, Mithun S., Dhaval Gajera, R Vanlaruata, Arpan Chowdhury, Akhilesh K Tiwari, Shekh yunus Shekh Faijulla, Anupam Joseph.

Administrative Staff

Mr. Sankar Prasad Dutta, Sr. Stenographer, Mr. Tarun Dutta, Assistant

Operation and maintenance of 600 MHz NMR Bruker spectrometer

Dr. Ranjan Mukhopadhyay, Dr. Partha Chattopadhyay (with operational support by Mr. E. Padmanaban)

The highly sophisticated 600 MHz Bruker NMR spectrometer has been maintained and analyses of **2460** samples were done during the year for both internal and external research workers. Apart from routine 1D experiments like PMR, PMR (HOD suppression), CMR, DEPT 135, DEPT 90, NOE

difference and 2H-NMR, various 2D and 3D experiments are being done regularly.2D experiments include COSY, DQF-COSY, NOESY, NOESY-WG, TOCSY, TOCSY-WG, ROESY, HSQC, HMQC, HMBC, ADEQUATE and HSQCNOESY-15N.The 3D experiments mostly done were NOESY-HSQC, TOCSY-HSQC, DIPSIHSQC, HNCOCA, HNCACB and HNCA.

Operation and maintenance of 300 MHz NMR Bruker spectrometer

Dr. Ranjan Mukhopadhyay, Dr. Partha Chattopadhyay (with operational support by Dr. Tapas Sarkar)

The instrument has been extensively used during the year. During the period, NMR analyses of **4222** samples (internal 3325 and external 897 samples) were carried out. These covered 1D experiments like routine ^{1}H, ^{13}C (proton decoupled), ^{13}C (proton coupled), DEPT-45, DEPT-90 and DEPT-135. Proton decoupling, 1D-NOE (Nuclear Overhauser Effect) difference experiments and high temperature NMR for many samples were also done. Apart from the 1D experiments as mentioned above, 2D NMR experiments of many samples were also done during the period. These included ^{1}H-^{1}H and ^{1}H-^{13}C COSY (Correlated Spectroscopy), NOESY (Nuclear Overhauser Effect Spectroscopy), HMBC (Heteronuclear Multiple Bond Correlation) and HSQC (Heteronuclear Single Bond Coherence).

Jasco 4200 FT/IR and Jasco 410 FT/IR Spectrophotometer

Dr. P. Jaisankar

The JASCO FT/IR 410 and 4200 Spectrophotometers have been routinely maintained and extensively used to analyze both internal and external samples. About 800 samples have been analyzed during the year. The instruments have given support to the NIPER students also.

LC-MS-MS-Q-TOF Micromass instrument

Dr. Asish K. Banerjee (with operational support by Shri. Diptendu Bhattacharya and Shri Santu Paul)

One LC-MS-MS (Q-TOF Micor) instrument was installed in the middle of 2003. Since then it has been in use for routine mass spectral analysis of both internal and external samples. Small molecules as well as macromolecules like proteins, carbohydrates etc. are being analyzed.

Perkin-Elmer 2400 CHNS/O analyzer Series II System

Dr. Asish K. Banerjee (with operational support by Shri Santu Paul)

The analyzer has been continuously used for routine C, H and N analyses of organic samples.

Jeol MS-700 mass Spectrometer

Dr. Chinmay Chowdhury (with operational support by Shri Sandip Chowdhury)

The Jeol MS-700 instrument has been utilised successfully for routine mass-spectral analysis (EI, FAB, CI etc) as well as HRMS of both internal & external samples.

VP-ITC Model Isothermal Titration Calorimeter and VP-DSC Model Differential Scanning Calorimeter

Dr. Suresh Kumar

The VP-ITC model ultra sensitive isothermal titration calorimeter and VP-DSC model differential scanning calorimeter (both from Microcal, LLC USA) for studying the energetics of biomolecular interactions is providing service to researchers from several divisions of our institute.

Jasco J 815 Spectropolarimeter

Dr. Suresh Kumar

The circular dichroism unit is providing services to both internal and external researchers. Solution conformation of peptides/proteins, nucleic acids and chiral small molecules are being routinely analyzed.

Single crystal X-ray spectrometer

Dr. Partha Chattopadhyay (with operational support by Shri Sandip Kundu)

Single crystal X-ray spectrometer, Bruker Kappa Apex-2, has been maintained and samples are analyzed to serve institute research worker. During the period 55 internal samples were analyzed and 33 structures were solved.

Gas Liquid Chromatograph

Dr. Asish K Sen (Jr.)

Two Gas Liquid Chromatography instruments (Agilent 6890 plus fitted with FID detectors) has been maintained and samples are analyzed throughout the year to cater both in-house and external research workers and industries. During the year, ~160 samples within the institute and ~40 outside samples have been analyzed.

Shimadzu GC-Mass Spectrometer (GP5050A)

Dr. Asish K Sen and Mr. Asit Kumar Das

GLC-MS (Shimadzu, Japan) facility offered to IICB scientists and research fellows, and Scientists, academicians and Industries form elsewhere. During the year, 270 DI & 109 GC-MS samples within the institute and 10 DI & 58 GC-MS outside samples have been analyzed.

DIONEX ICE 3000 Ion Chromatograph

Dr. Asish K Sen and Mr. Asit Kumar Das

This facility has been extended to IICB scientists and scientists from outside.

STRUCTURAL BIOLOGY & BIOINFORMATICS

Prof. Siddhartha Roy, Drs. M. C. Bagchi, Chitra Dutta, Debasish Bhattacharyya, Nanda Ghoshal, Soumen Datta, Subrata Adak, Krishnananda Chattopadhyay, Jayati Sengupta and Nakul Maiti

Prof. Siddhartha Roy and group

Alternative Sigma Factors in the Free State are Equilibrium Mixtures of Open and Compact Conformations

Bacterial sigma factors associate with the core RNA polymerase and turn on a set of genes. The activities of the sigma factors in turn are often regulated by regulatory circuits, the details of which are not always well-understood. Based on representative experiments, it is generally believed that the free sigma factors are incapable of binding to promoters and they acquire the ability to bind promoters with high specificity only as a part of the holoenzyme through a conformational switch. The nature of this conformational switch remains unresolved.

As has been amply demonstrated in the past, many regulatory proteins are not rigid. In fact a large number of them are probably highly flexible and perhaps partially disordered. The role of disorder in specific interactions is just beginning to be understood. We felt that a study of the dynamical properties of free sigma factors may play a crucial role in the understanding of the conformational switch. We have studied the dynamical properties of two sigma factors σ^{32} of *E.coli* and σ^{F} of *M. tuberculosis* in the free-state and its implications for the conformational switch upon holoenzyme formation.

To understand the positional relationship of C-terminal half vis-à-vis the N-terminal domain, we have attempted to measure the distance between residues 37 (end of region 1) and 262 (region 4.2). These residues were labeled with a fluorescence donor (AEDANS) and acceptor (IAF) and energy transfer was measured. Fig. 1 shows the excitation spectra of the double labeled Ec σ^{32} in comparison with the same protein in 5 M GuHCl. Previously we have shown that the protein is completely unfolded in 5 M GuHCl and thus, should not show any significant FRET. As apparent from the figure, there is significant energy transfer as the excitation spectrum in the native state has significantly higher intensity around 340-350 nm (IAEDANS absorption band) when compared to the completely unfolded protein at 5 M GuHCl.The calculated energy transfer efficiency is 39%, corresponding to a distance of about 42 Å. Upper and lower limits calculated from steady-state anisotropies by method of Lakowicz are 53.3 Å and 37.1 Å, respectively. This derived distance agrees well with a modeled closed form of the protein, suggesting no large scale open-close from equilibrium. However, other measurements show some clear evidence of close-open state equilibrium.

Mtσ^{F} has a single cysteine residue (C47) and a single tryptophan residue (W112) which is located within region 2.4. We have created 3 cysteine mutant in different region within Mt σ^{F} and all cysteine mutant was found to be reactive and can be labeled with fluorescence probes. Fluorescence energy transfer between W112 (donor) and AEDANS-C47, A6C, V19C, L256C (acceptor) was determined in the time resolved mode. The obtained distance (R) was approximately 37 Å, 36 Å, 32 Å, 43 Å respectively (Table 1). The estimated distances in few cases somewhat larger and in few cases somewhat

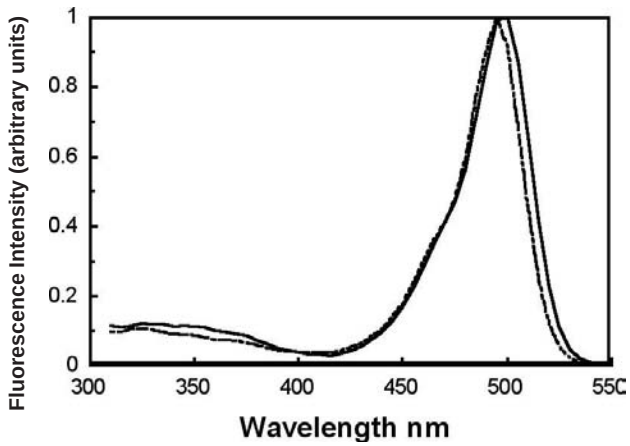

Fig. 1 : Fluorescence Resonance Energy Transfer of between residue 262C-AEDANS and 37C-AF in the double mutant LV37,262CC-Ecσ32. Comparison of excitation spectra of AF-37C, AEDANS262C-Ecσ^{32}, in presence (dotted line) and absence (solid line) of 5 M GuHCl. The protein concentration was 1 μM. Emission wavelength was 570 nm. The experiments were performed in 50 mM potassium phosphate buffer, pH 7.9 containing 300 mM KCl and 25% glycerol.

smaller than the modeled distance. However, considering uncertainty in the modeled distance and flexibility of the probe linker, this value is inconsistent with neither compact structure nor totally flexibile structure. So it may be concluded that bacterial sigma factor in free state contain open and closed state in equilibrium (Fig. 2).

Table 1 : Fluorescence Energy transfer and estimated distances between W112 and several cysteines.

Protein	Life-time (ns)[1]	E	R(Å)[2]	Rmax(Å)[3]	Rmin(Å)
Mtσ^F	3.26	0.08	38.2		30
C47-AEDANS- Mtσ^F	2.99				
V19C,C47A-Mtσ^F	3.28	0.192	32.3		
V19C,C47A -AEDANS-Mtσ^F	2.65				
A6C, C47A- Mtσ^F	3.13	0.111	36	46	35
A6C, C47A-AEDANS- Mtσ^F	2.78				
L256C, C47A- Mtσ^F	2.79	0.04	43.2	57.5	33
L256C, C47A-AEDANS- Mtσ^F	2.67				

[1]Reported lifetime is the second order average of bi-exponential fit; $\tau_{av} = (\alpha_1\tau_1^2+\alpha_2\tau_2^2)/(\alpha_1\tau_1+\alpha_2\tau_2)$

[2] The distances were calculated using an R_0 of 25.4 Å.

[3]Upper and lower limits of distances were calculated from steady-state anisotropy values by method of Lakowicz.

Fig. 2 : Cartoon figure depicting the proposed equilibrium of two conformations of the Sigma factors

Dr. M. C. Bagchi & group

Mathematical Modeling in Drug Design using Structural Descriptors

The major objective of the present project is to study some important topological and other structural parameters of known active compounds as well as many active analogs of the same using various linear statistical methods and non-linear counter propagation neural networks for developing quantitative structure activity relationships of anti-tubercular and anti-cancer compounds.

a) Computer Assisted Design of Potent EGFR Kinase Inhibitors Using Virtual Combinatorial Libraries

We have made an attempt to design 4-anilinoquinazoline compounds having promising anticancer activities against epidermal growth factor (EGFR) kinase inhibition, using virtual combinatorial library approach. Partial least squares method has been applied for the development of a quantitative structure-activity relationship (QSAR) model based on training and test set approaches. The partial least squares model showed some interesting results in terms of internal and external predictability against EGFR kinase inhibition for such type of anilinoquinazoline derivatives. In virtual screening study, out of 4860 compounds in chemical library, 158 compounds were screened and finally, 10 compounds were selected as promising EGFR kinase inhibitors based on their predicted activities from the QSAR model. These derivatives were subjected to molecular docking study to investigate the mode of binding with the EGFR kinase, and the two compounds (ID 3639 and 3399) showing similar type of docking score and binding patterns with that of the existing drug molecules like erlotinib were finally reported.

b) Activity prediction of anti cancer compounds by Genetic Algorithm based PLS models

We are involved in the formulation of three-dimensional quantitative structure-activity relationship (3D-QSAR) model for 6-(2,6-dichlorophenyl)-pyrido[2,3-d]pyrimidin-7(8H) one compounds based on computed molecular descriptors. Molecular field analysis technique has been employed to find out specific contribution of structural features such as steric, electrostatic and hydrophobic fields of these compounds showing anticancer activities by the inhibition of EGFR kinase. 3D QSAR model is developed based on the training set using genetic algorithm feature selection combined with partial least square method. The training model is then used to predict the biological activities of some similar class of compounds which were synthesized only but the activities were not tested. An accuracy of activity prediction has been cross-checked by introducing a new way of QSAR model validation approach utilizing random normalization correction procedure in the data set.

Dr. Chitra Dutta and group

Significant Di-peptide Relative Abundances - Niche-specific signatures of microbial proteomes

Microbial gene products evolve under diverse selective constraints operative at different levels of system organization - from sub-molecular to supra-kingdom. A question, therefore, arises: could there be any compositional attribute of proteins that would characterize a microbial species and hence, be regarded as its proteome signature? This endeavor addresses the issue. In order to qualify as a signature, the particular characteristic of the proteins should exhibit minor variations within a species, but significant divergences across microbes, especially those belonging to diverse lineages or distinct habitats. Studies on protein evolution reported so far have either emphasized on the species-level or

phyla-level trends, ignoring intra-species divergences among proteins of distinct functional/structural classes; or remained confined to sub-molecular, domain- or site-specific variations in amino acid selection. The present study takes into account of similarities/divergences in protein features both within and across microbes and proposes a novel set of sequence parameters, **DIPRA$_S$** - Statistically **S**ignificant **D**i-peptide **R**elative **A**bundances - that can serve as potential proteome signatures of microorganisms.

The DIPRA$_S$ profile of any protein dataset is comprised of 400 components, each of which represents the statistical bias (expressed in a ternary scale) in the usage of a specific di-peptide in the dataset. Cluster Analysis (CA) on DIPRA$_S$ profiles of members of different major functional classes of COGs from a large number of microbes of varying taxonomy, GC-content and environmental niche, revealed species-specific grouping of proteins under single nodes, irrespective of their functional classes. It is worth mentioning that CA on relative amino acid usage and dipeptide usage frequencies did not exhibit any general species-specific trend. CA of DIPRA$_S$ profiles at proteome levels yielded niche-specific clusters, differentiating thermophilic/ hyperthermophilic microbes from mesophiles, halophiles from non-halophiles and sulphur-metabolizers from methanogens, while within a specific cluster of extremophiles, organisms often segregated according to their kingdoms, phyla or classes. For instance, within a cluster of sulfur-metabolizing archaea, the euryarchaeal members segregated from their crenarchaeal counterparts, and within the crenarchaeal sub-cluster, sulfolobales, desulfurococcales and thermoproteales exhibited distinct, class-specific co-segregation, in general (Fig. 3). In an attempt to find out the sources of such inter-niche as well as inter-phylum variations in DIPRAS profiles, 2-dimensional MDS (Multidimensional Scaling) was carried out on pair-wise Euclidean distances between DIPRA$_S$ profiles of the archaea under study. Fig. 4 shows a heat-map of DIPRA values for the di-peptides having significant correlation ($p < 0.0001$) with dimension 1 of MDS (along which the sulphur-metabolizers and methanogens segregate on the 2-dimensional MDS plot).

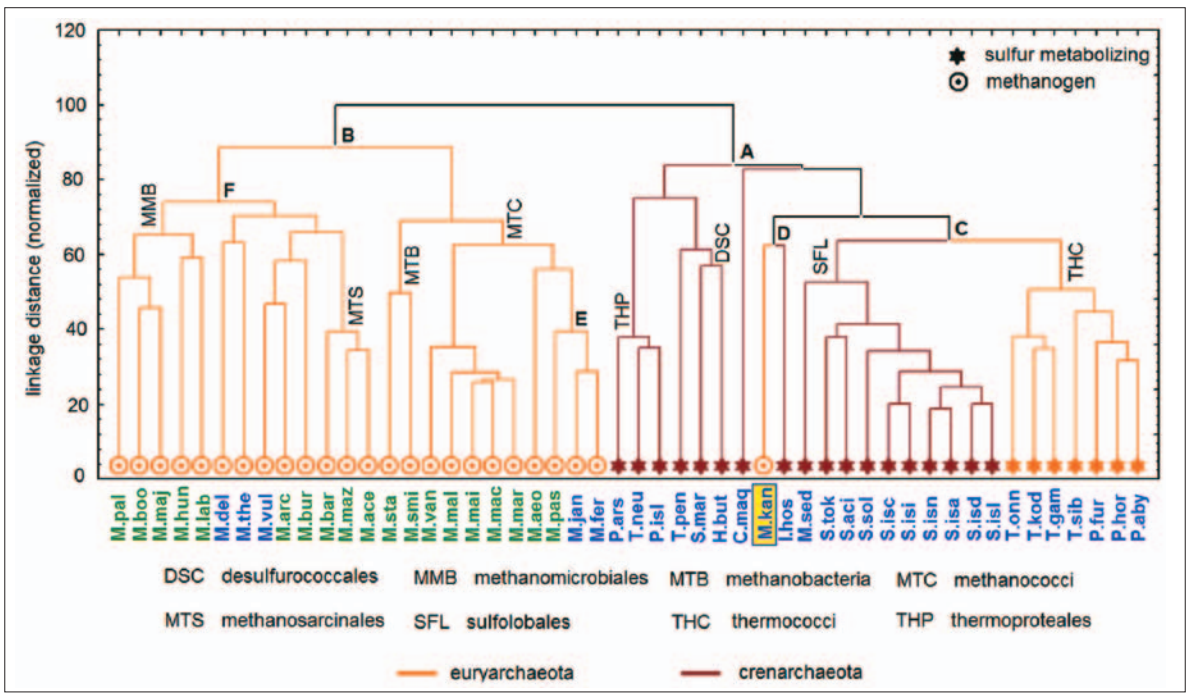

Fig. 3 : Niche-specific segregation of methanogenic and sulphur-metabolizing archaea in cluster analysis of DIPRA$_S$ profiles of the respective proteomes.

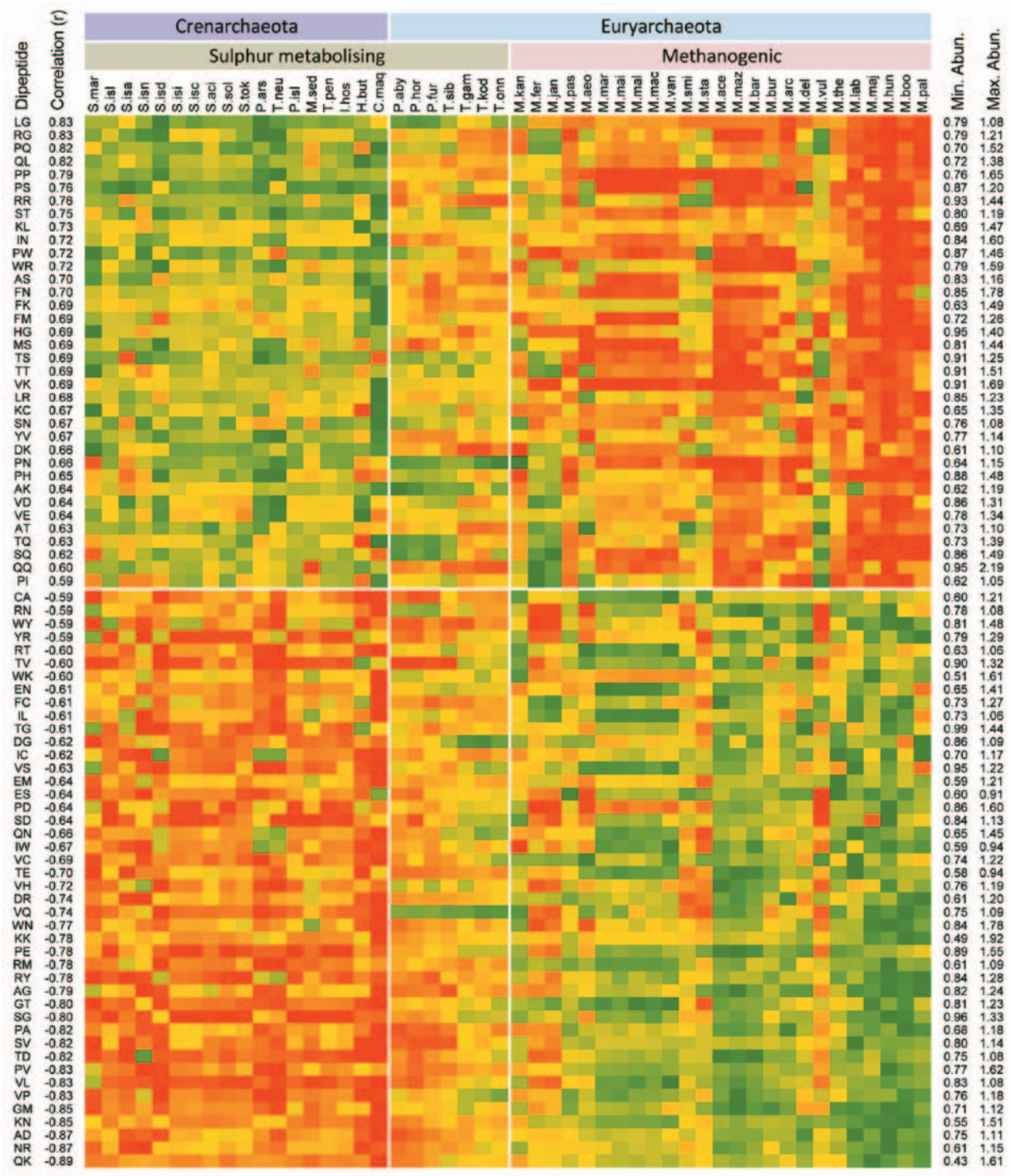

Fig. 4 : Heat-map of Dipeptide Realtive Abundance values for 80 di-peptides having significantly biased usage between methanogenic and sulphur-metabolizing microbes. The correlations values of di-peptide abundance values with dimension1 of MDS have been shown in the left side of the heat-map, while the maximum and minimum values of di-peptide abundance are shown in the right side. The systematic increase or decrease in dipeptide relative abundance values (absolute values) of different di-peptides across the organisms of distinct phyla (euryarchaeota and crenarchaeota) and diverse ecological adaptations is apparent from the gradients of red (towards minimum) to green (towards maximum) colors in the heat-map for different dipeptide relative abundance values.

All these observations suggest that the trends in amino acid usage in microbial protein sequences are context-dependent and the nature of such dependence is niche-specific and, to some extent, lineage-specific. Microbes belonging to different ecological niches might, therefore, be under distinct selection pressures in favour of, or against specific di-peptides, and such selections might have facilitated acclimatization of the respective organisms to specific environmental niches/life-styles. Such distinctive sets of DIPRAS profile of a proteome can be used as finger-prints of different groups of microbial proteomes, and may facilitate characterization of metagenomic sequences; enable better understanding of molecular evolution of extremophiles, and aid in engineering proteins to function optimally at desired physico-chemical environments.

GC-rich intra-operonic spacers in prokaryotes: Possible relation to gene order conservation

Genome-scale compositional analyses of non-coding sequences from 410 microbes of varying GC-content, lineage, environment/life-style, reveal presence of a distinct trend in GC-usage in spacers between intra-operonic and extra-operonic gene-pairs. For most of the microbes, average GC-content of the intra-operonic spacers are consistently higher than those between extra-operonic unidirectional gene-pairs. Also, unidirectional gene-pairs exhibiting higher cross-species conservation, irrespective of their operonic context, house relatively GC-rich spacers. A few prokaryotes, most of which represent known cases of genome degradation, stand out as exceptions defying this trend. GC-enrichment of intra-operonic spacers therefore appears to be an evolutionary strategy facilitating preservation of operonic gene-order.

ProHspDb: Prokaryotic Heat Shock Protein Database

Heat Shock Proteins (HSPs), ubiquitously found in all life forms, play pivotal roles in protecting cellular integrity upon heat shock and other stress conditions. Many of them also act as molecular chaperones. A huge number of HSP-encoding genes have been annotated from numerous organisms. But no public domain database is available yet that can provide comprehensive information on all bacterial/archaeal HSPs annotated so far. To address this issue, we present ProHspDb version/release 1.0 [http://www.igdd.iicb.res.in/hsp/home.aspx] - an integrated, curated and systematic repository of growing number of heat shock protein data of prokaryotes. Currently the database (ProHspDb Release 1.0) covers 7559 HSP-encoding genes from 934 bacteria and 53 archaea. It aims to provide non-redundant information on sequences along with physicochemical, structural and functional features for all annotated HSPs from prokaryotic genomes. Entries are hyperlinked to major gene-related data resources and there is a provision for BLAST search against ProHspDb entries. ProHspDb is currently designed to work best with Internet Explorer 8 (optimal Resolution 1440_900). The ProHspDb web portal, being freely available is expected to be useful to the researchers working on the heat-shock/stress-response phenomena, molecular chaperones, protein folding, protein translocation, molecular adaption and evolutionary processes in prokaryotes.

Dr. Debasish Bhattacharyya and group

Functional regulation, assembly and stability of proteins/enzymes, characterization of venom toxins, the drug 'Placentrex' and exploring the biosynthetic pathway of podophyllotoxin

a) Kinetic stability and aggregation of proteins

Kinetic stability of proteins, which is caused by a high-energy barrier between the native functional

state and the denatured state, is of considerable interest to biotechnologists because the barrier prevents a protein from being naturally inactivated. In the recent past we have demonstrated that bromelain, a cysteine protease from pineapple, possesses the characters of a kinetically stable protein like resistance to SDS binding etc. In support of this property, we quantified how much SDS remained bound to bromelain in a SDS solution and the nature of binding. Advantage was taken in specific binding of free and loosely protein bound SDS to Extracti Gel column Matrix (detergent removal gel from Pierce) whereas the extraneous fluorescence probe Rhodamine B quantified the protein bound SDS in the unabsorbed fraction when the SDS/protein solution is passed through the gel. The protocol was extended with reference proteins of both kinetically stable and unstable category. The results obtained were at par with the SDS-protein binding ratio of 1.4 (wt/wt) for the unstable proteins whereas this ratio was low for kinetically stable proteins. Thus a new protocol has been recommended for testing a protein regarding its stability character based on the binding of SDS.

b) Biochemical characterization of the drug 'Placentrex'

The drug house project on 'Placentrex', an aqueous extract of human placenta and a product of M/s Albert David Ltd., is continuing in this laboratory over a decade. Major thrust of the project is on identification of bioactive components and their mechanism of actions. It has been confirmed that the drug contains a peptide that stabilizes trypsin after reversible binding. It offers one of the regulations of proteolytic activity that is essential for efficient wound healing. In its continuation, it has been investigated whether the drug can activate matrix-metalloproteases. During control experiments, it was observed that the drug itself demonstrates proteolytic activity in zymography with suitable substrate. 2-dimensional gel electrophoresis of the drug in presence of substrate reveals existence of one spot. Molecular weight and partial amino acid sequencing using mass spectrometric analysis identified the protease. At present we attempt to purify and quantify the protease.

c) Toxicological studies of Russell's viper venom

Snake venoms offer a wide range of enzymes that are toxins, at the same time pharmacologically important because sometimes they offer a template for designing new drugs. L-amino acid oxidase from Russell's viper venom in particular was characterized earlier in terms of its kinetic and inhibitory properties. At present we are involved in developing suicidal substrate of the enzyme and establishing its mechanism of its interaction. Reversible restoration of fibrinolytic activity while complete detoxification of Russell's viper venom upon heat denaturation has been reported. In addition, efficacy of selected medicinal plants, traditionally known as 'antivenin', is also under investigation.

d) CSIR Network project (NWP-008) on Podophyllotoxin

The subunit assembly, regulation and deregulation of the homodimeric enzyme UDP-galactose 4-epimerase have been elaborately studied in this laboratory leading to a unique and complete molecular model of the enzyme. The interrelation between the subunits of the enzyme has been further extended with inhibitors to yield accurate information about the catalysis of the enzyme In the assay of epimerase, UDP-glucose dehydrogenase is used as a coupling enzyme. Partial purification of the enzyme from beef liver was an uncertain job as the quality of the raw material remained questionable. To overcome this difficulty, we replaced the raw material with goat liver that is freshly available from local market. Suitability of the goat liver enzyme in epimerase assay has been confirmed. Finally, the synthetic

biology under network program on Podophyllotoxin from the plant Podophyllum hexandram is a challenging job. We have synthesized intermediate biosynthetic products to be used as substrate for selected enzymes. Procedures are complicated. Successful results are yet to come.

Dr. Nanda Ghoshal and group

In-silico studies for rational drug design and Receptor Modelling

A. Rationalizing fragment based drug discovery using FB-QSAR, FB-QSSR, multi objective (MO-QSPR) and MIF studies: A case study using BACE1 inhibitors

To expand the boundaries of QSAR paradigm, and to rationalize FBDD using in silico approach, a fragment based QSAR methodology referred as FB-QSAR has been proposed. The FB-QSAR methodology was validated on a dataset consisting of 52 Hydroxy ethylamine (HEA) inhibitors, as potential anti-Alzheimer agents. To address the issue of target selectivity, a major confounding factor in the development of selective BACE1 inhibitors, FB-QSSR models were developed using the reported off target activity values. A heat map constructed, based on the activity and selectivity profile of the individual R-group fragments, and was in turn used to identify superior R-group fragments. Further, simultaneous optimization of multiple properties, an issue encountered in real-world drug discovery scenario, and often overlooked in QSAR approaches, was addressed using a Multi Objective (MO-QSPR) method that balances properties, based on the defined objectives. The results obtained from FB-QSAR were further substantiated using MIF (Molecular Interaction Fields) studies.

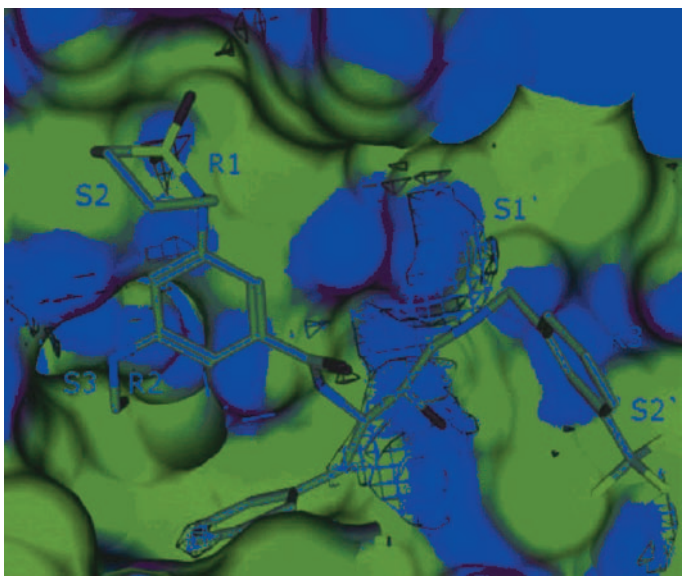

Fig. 5 : The activity contour map of bace1. The interaction potential contour shown: red color mesh represents hba (e = -2.5 kcal); blue color mesh represents hbd (e = -2.5 kcal); white color mesh represents dry (e = -3.3 kcal) (hydrophobic) probe which models hydrophobicity

B. A Review work: Pharmacophore models for $GABA_A$ modulators: implications in CNS drug discovery

$GABA_A$ ion channel is a validated drug target, implicated in the pathophysiology of various neurological and psychiatric disorders. Structural investigations on $GABA_A$ are currently precluded in the absence

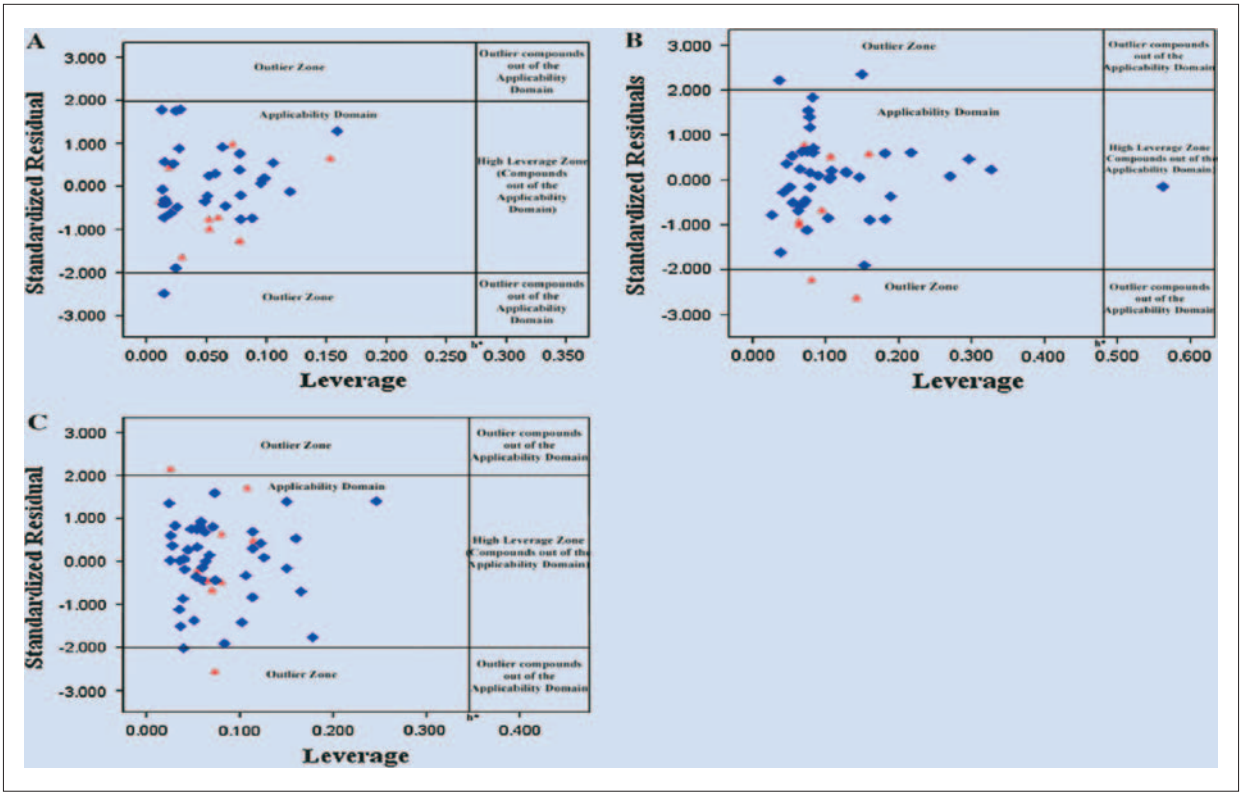

Fig. 6 : Williams plot for the obtained model BACE1 (A), BACE1-BACE2 (B), BACE1-CATD (C). Test set compounds are denoted as red triangle, Training set compounds are denoted as blue.

of experimentally resolved structure. Pharmacophore modelling circumvents such issues and proves to be a powerful and successful method in drug discovery. Recent advancements in pharmacophore modelling that can leverage CNS drug discovery programs and deliver astounding results have been reviewed. Such advancements should be used to confront activity profiling and early stage risk assessment in a high-throughput fashion. Extending such technologies has the potential not only to reduce time and cost, but also to prevent late stage attrition in drug discovery.

C. Deciphering the structure of opioid receptors with homology modeling based on single and multiple templates and subsequent docking: A comparative study

Opioid receptors, belonging to the rhodopsin family of GPCRs, are the principal targets for opioids, which have been used as analgesics for centuries. In the absence of crystal structures of opioid receptors, 3D homology models have been reported with bovine rhodopsin as a template, though the sequence homology is low. Recently, it has been reported that use of multiple templates results in better model for a target having low sequence identity with a single template. With the objective of carrying out a comparative study on the structural quality of the 3D models based on single and multiple templates, the homology models for opioid receptors (mu, delta and kappa) were generated using bovine rhodopsin as single template and the recently deposited crystal structures of squid rhodopsin, turkey β-1 and human β-2 adrenoreceptors along with bovine rhodopsin as multiple templates. Results of comparison indicate that homology models of mu and kappa with multiple templates are better than those built with single template, whereas, in many aspects, the homology model of delta opioid receptor with

single template is better with respect to the model based on multiple templates. As the crystallographic structures are not yet known, this comparison will help in choosing better homology models of opioid receptors for studying ligand receptor interactions to design new potent opioid antagonists/ agonists.

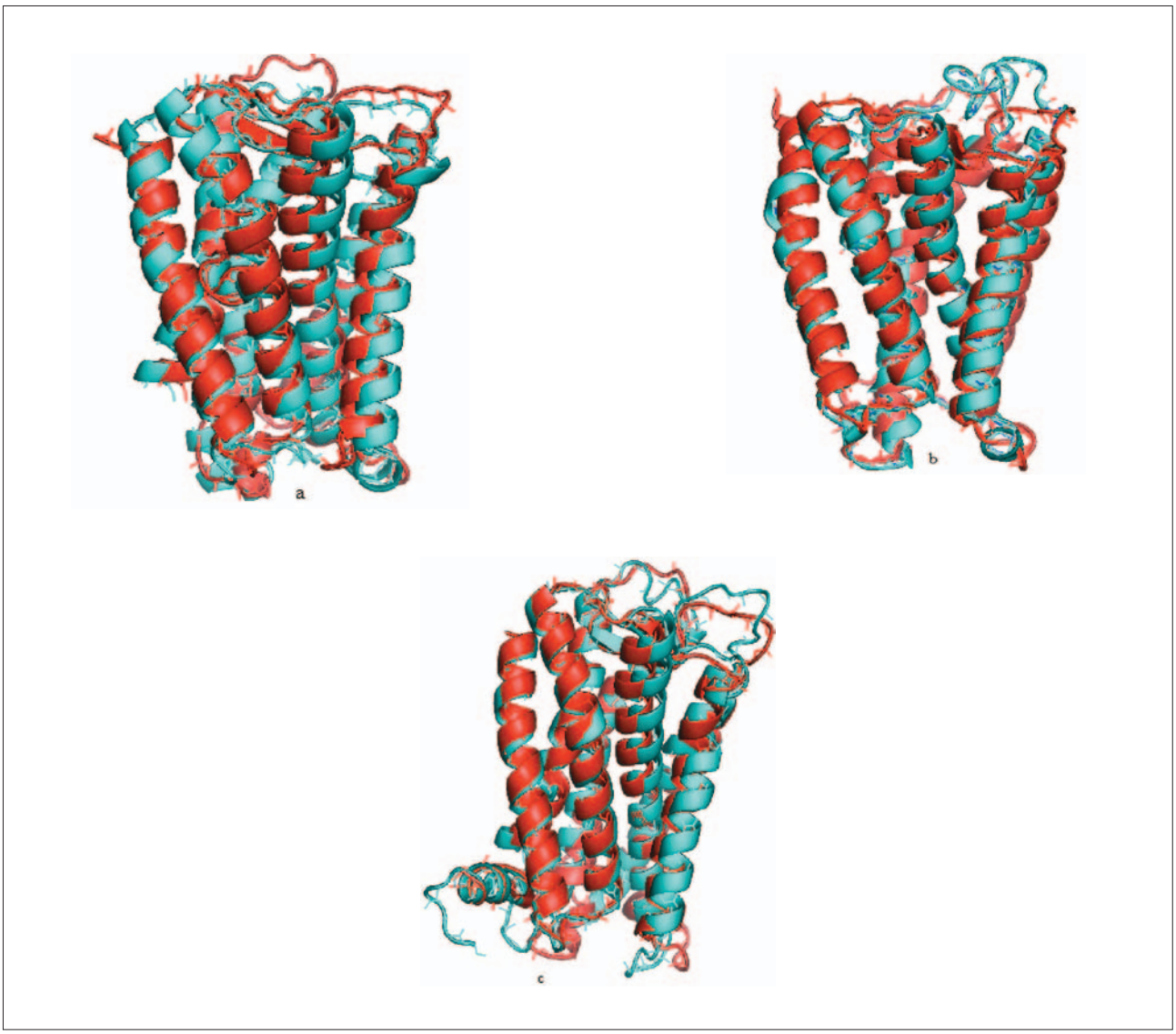

Fig. 7 : Superimposition of homology models based on single with bovine rhodopsin (red) and multiple templates (cyan) from TM1 to TM7 a) kappa b) delta c) mu.

Dr. Subrata Adak and group

Endoplasmic reticulum stress-induced apoptosis in Leishmania through Ca^{2+}-dependent and caspase-independent mechanism

Numerous reports have shown that mitochondrial dysfunctions play a major role in apoptosis of *Leishmania* parasites but the endoplasmic reticulum (ER) stress induced apoptosis in *Leishmania*

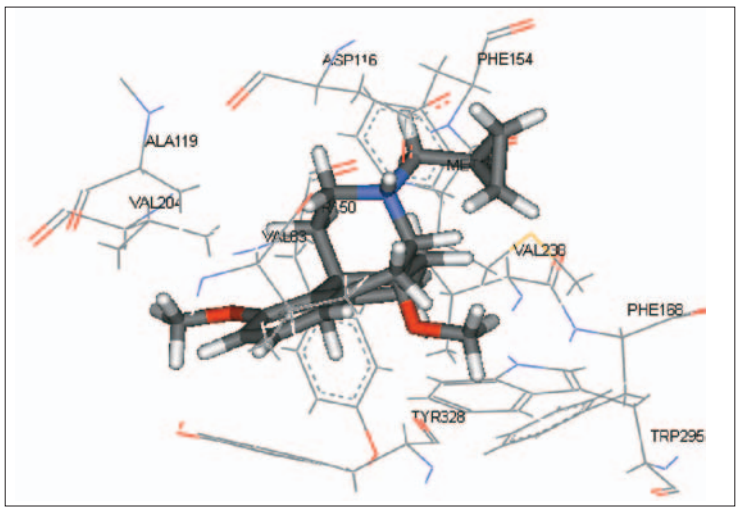

Fig. 8 : Binding of cyprodime to mu opioid receptor model with MSA (docking of only one ligand to one receptor model is shown for brevity)

remains largely unknown. In this study we investigate ER stress induced apoptotic pathway in *L. major* using tunicamycin (TM) as an ER stress inducer. ER stress activates the expression of ER-localized chaperone protein BIP/GRP78 (binding protein/identical to the 78 kDa glucose regulated protein) with concomitant generation of intracellular reactive oxygen species (ROS). Upon exposure to ER stress, the elevation of cytosolic Ca^{2+} level is observed due to release of Ca^{2+} from internal stores. Increase in cytosolic Ca^{2+} causes mitochondrial membrane potential depolarization and ATP loss as ablation of Ca^{2+} by blocking voltage-gated cation channels with verapamil preserves mitochondrial membrane potential and cellular ATP content. Furthermore ER stress induced ROS dependent release of cytochrome c (Cyt C) and endonuclease G (Endo G) from mitochondria to cytosol and subsequent translocation of Endo G to nucleus is observed. Inhibition of caspase like proteases with caspase inhibitor Z-VAD-FMK or metacaspase inhibitor antipain does not prevent nuclear DNA fragmentation and phosphatidylserine exposure. Conversely significant protection in TM induced DNA degradation and phosphatidylserine exposure was achieved by either pretreatment of antioxidants (N-acetyl-L-cysteine, GSH and L-cysteine), chemical chaperone (4-phenyl butyric acid) or addition of Ca^{2+} chelator (1,2-bis(2-aminophenoxy)ethane-N,N,N,N-tetraacetic acid-acetoxymethyl ester). Taken together these data strongly demonstrate that ER stress induced apoptosis in *L. major* is dependent on ROS and Ca^{2+} induced mitochondrial toxicity but independent of caspase like proteases.

Dr. Saumen Datta and group

Genome encoded TTSS Proteins: Yspc, SycB

This TTSS encodes Yersinia secretory apparatus (Ysa) proteins constituting injectisome, Yesinia secretory proteins (Ysp) or virulent proteins and their putative chaperone proteins like SycB. We are doing many biophysical and biochemical studies to characterize individual YspC, SycB and their complex YspC-SycB complex. For explaining some results we have generated a comparative model of SycB, which is presented here (Fig. 9).

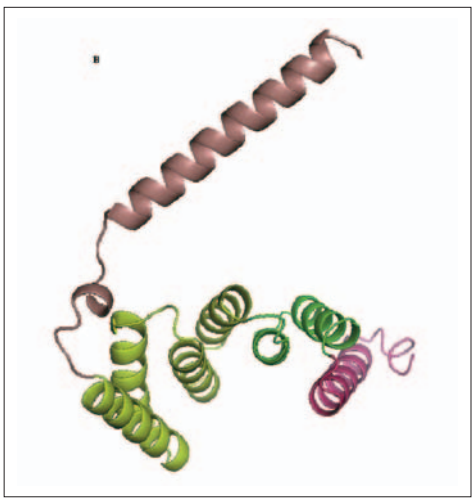

Fig. 9 : Homology model of SycB. Model shows a cartoon representation of SycB with N-terminal colored in chocolate brown. 2 TPR region shown in lemon green, 1 TPR like region shown in green and a pink C-terminal helix followed by a coiled region.

Plasmid encoded TTSS Proteins: LcrG, LcrV.

These are translocatory proteins and mainly control the secretion of virulent proteins. To facilitate crystallization we did some Dynamic Light Scattering (DLS) experiments to optimize monomeric form of the complex, which is presented here (Fig. 10).

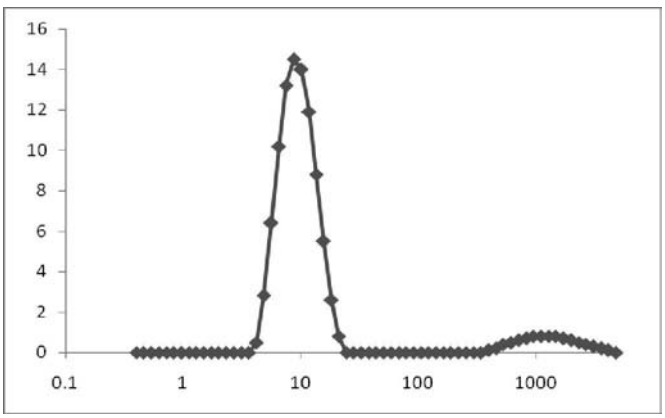

Fig. 10 : Dynamic Light Scattering (DLS) profile of LcrG-LcrV complex (15 mg/ml in pH-8.)

Dr. Krishnananda Chattopadhyay and group

Effect of arginine and other stabilizers on protein aggregation using fluorescence correlation spectroscopy and other biophysical methods

We have been studying protein conformation, dynamics and aggregation using different biophysical methods including Fluorescence correlation spectroscopy (FCS). FCS is an important technique to measure the diffusional and conformational fluctuations of fluorescently labeled molecules at single molecular resolution. These fluctuations could be analyzed by using suitable correlation functions yielding useful information regarding the shape and/or conformational dynamics of a protein. In a recent study, we have shown by a number of orthogonal techniques including analytical ultracentrifugation, dynamic light scattering and native gel electrophoresis that aggregation of bovine serum albumin can be minimized by using high concentration of arginine. Urea induced unfolding transition of cytochrome

c has been studied by FCS. Measurements of microsecond dynamics using appropriately labeled cytochrome c indicates formation of an intermediate state, which has been found to be absent in the presence of arginine. The hydrodynamic radii of the protein in its native, unfolded, and intermediate states have been determined using FCS. Fluorescence correlation spectroscopy is used to monitor self-association of negative (SDS) and positively (DTAB) charged surfactant monomers at single molecular resolution. Tetramethyl rhodamine 5 maleimide (TMR) has been chosen as a probe because rhodamine dyes have been shown to bind surfactant micelles. Correlation functions obtained by the FCS experiments have been fit using conventional discrete diffusional component analyse and maximum entropty method (MEM). The values of hydrodynamic radius increase with surfactant concentration as the monomers self-associate. Effects of several solution additives including arginine on the self-association property of the surfactants have been studied. Urea and glycerol have been found to inhibit self-association while arginine shows dual nature. Arginine favors self-association of SDS while with DTAB it inhibits micelles formation.

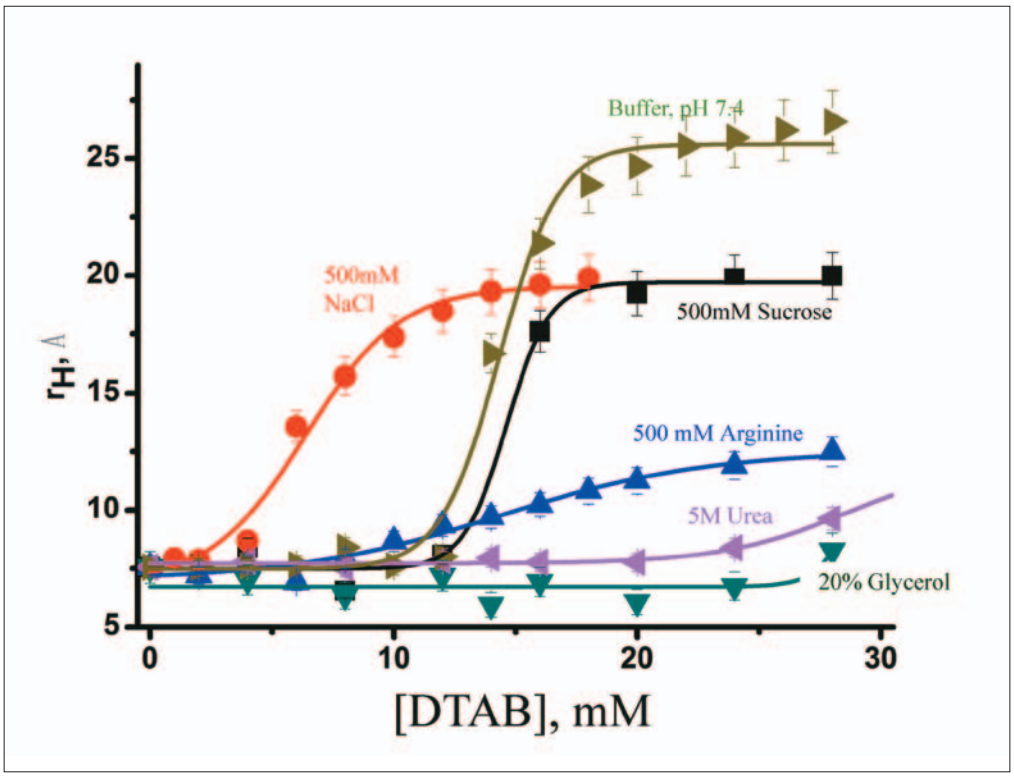

Fig. 11 : FCS experiments on the self-association of DTAB. The values of diffusion time (.D) are plotted with the concentration of DTAB in the presence of different solution additives

Dr. Jayati Sengupta and group

Cryo-EM reveals unique structural features in Mycobacterium 70S ribosome

Mycobacterium is well-known for its antibiotic resistance property. However, mycobacterial tolerance to antibiotics has been studied mostly at cellular level since this property has been traditionally attributed to its impermeable cell wall. Interestingly, many of these antibiotics target translation. Therefore, a detailed structural investigation on the mycobacterium ribosome may reveal additional insights into the drug resistance property of this organism.

We have reconstructed a 3D cryo-EM map (thanks to Dr. Zheng Liu and Xing Meng of the Wadsworth Center, Albany, NY, USA for their kind help with EM data collection) of the 70S ribosome from *Mycobacterium smegmatis*, a saprophytic cousin of the etiological agent of tuberculosis in humans, *Mycobacterium tuberculosis*.

In comparison with ribosomal structures from other bacterial species, the density map of mycobacterial 70S ribosome shows remarkable structural features. Dramatic changes in the periphery due to additional rRNA segments and extra domains of some ribosomal proteins are evident. The most prominent one is a long helical structure (which we term the 'steeple') in the large subunit near the L1-stalk related to an extra helix in the 23S rRNA secondary structure. Its upper end is located at the exit of the mRNA channel. We propose that the unusual structural components likely participate in facilitating and modulating various steps of translation that is unique to mycobacteria.

Although the *M. smegmatis* 70S ribosome possesses conserved core structure of bacterial ribosome, the new structural features, unveiled in this study, demonstrates structural diversity in bacterial ribosomes.

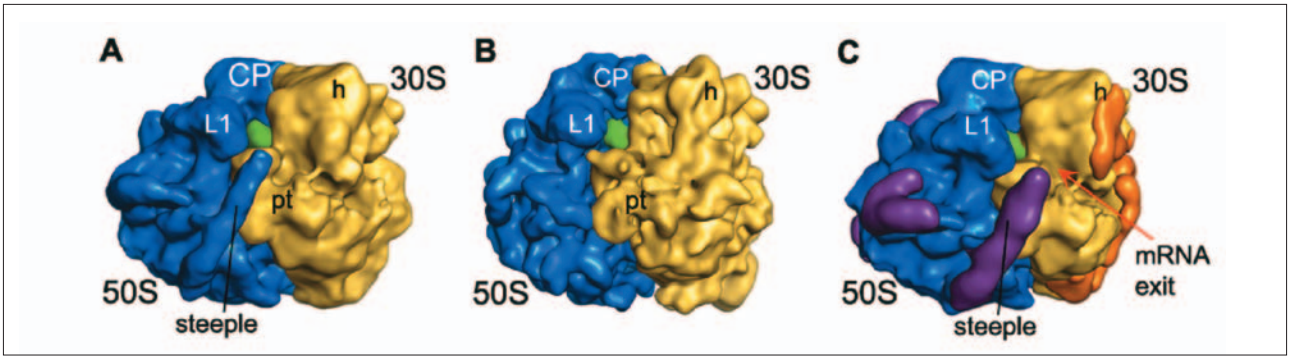

Fig. 12 : Comparison of the 70S Ribosome from *M. smegmatis* with the *E. coli* 70S ribosome. The cryo-EM map of the Msm70S (A) is shown together with the cryo-EM map of the Eco70S (B). The ribosomes are shown from the L1 side. The small subunits are shown in yellow, the large subunits in blue, and the P site-bound tRNA in green. The additional densities due to the presence of larger r-proteins and rRNA helices have been shown in orange and purple coloured surfaces on the Msm30S and Msm50S respectively (C). Landmarks for the 30S subunit: h, head; pt, platform. Landmarks for the 50S subunit: CP, central protuberance; L1, L1 protein.

Dr. Nakul C Maiti and Group

Structure of Natively Unfolded Proteins

Research in my laboratory focuses on structure and sequence aspects of natively unfolded proteins (NUPs). NUPs are class of proteins that do not adopt any well-defined three dimensional folded structures and exist as ensembles of rapidly interconverting conformations even under physiological conditions. ~ 30% of all eukaryotic proteins belong to this class. We recently utilized in-silico methods and algorithms to characterize the sequence aspects of unfolded human proteins those are linked to amyloid diseases formation and propagation.

Dr. Saikat Chakrabarti and Group

Computational Analyses of Host-Pathogen Interactions

Our current research interests are to study the structure, function, evolution and network properties of the proteins that are crucial for several kinds of pathogen mediated disorders. Our primary emphasis

is towards understanding the different modalities and specificities of host-pathogen protein-protein interactions (PPI). Computational analysis and prediction of such interactions is an important unsolved problem. Therefore, development of new computation techniques that integrate various modes experimental information for a better understanding of host-pathogen interaction mechanism is due. We aim to undertake a multi-faceted research plan integrating the available experimental information with subsequent development and application of several computational techniques for better understanding and prediction of molecular mechanisms underlying specific host-pathogen interactions.

Current projects in the lab involve analyses of structural, functional, evolutionary and network behaviors of the host-pathogen (bacteria, parasite and virus) interactome where we aim to develop an extensive framework of host-pathogen PPI network using *Plasmodium* (parasite), *Bacillus* (bacteria) or HIV (virus) interactions as model systems through utilization of the available information from previous studies and systematic incorporation of experimental findings. Identification of key regulator hub proteins, which is very crucial for understanding the mechanism of interaction, will be aided by computational techniques. Similarly, effect of perturbation of such networks (hubs) will also be studied by incorporating *in-silico* mutation and knock out models.

It is also crucial to understand the structural and functional details of the host-pathogen protein-protein complexes by examining the interaction surfaces using homology modeling, protein docking and binding affinity techniques. Analysis of coevolutionary patterns between proteins involved in host-pathogen interactions is an interesting idea and can shed some insight towards specific host selection mechanism and increased virulence for pathogens. We will undertake alignment and phylogentic tree based approaches to establish meaningful coevolutionary connection between host and parasite systems by carefully investigating covariation patterns within the host-pathogen proteins of PPI networks.

Ramalingaswami Fellow

Dr. Saikat Chakrabarti.

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23 अप्रैल,2010
भारतीय रासायनिक जीवविज्ञान संस्थान
(वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद्)
4, राजा एस.सी. मल्लिक रोड, कोलकाता-700 032
4th IICB FOUNDATION DAY CELEBRATION
OBSERVED ON 23rd APRIL,2010
INDIAN INSTITUTE OF CHEMICAL BIOLOGY
(COUNCIL OF SCIENTIFIC & INDUSTRIAL RESEARCH)
4,RAJA S.C.MULLICK ROAD, KOLKATA-700 032
PROF.KANURY V.S. RAO
PROF.INDRANIL MANNA
PROF.SIDDHARTHA ROY

CELL BIOLOGY & PHYSIOLOGY

Drs. Kochupurackal P. Mohanakumar, Sumantra Das, Syed N. Kabir, Smritinath Chakraborty, Tuli Biswas, Arun Bandyopadhyay, Tushar Chakraborty, Sandhya R. Dungdung, Sib Sankar Roy, Padma Das, Mrinal Kanti Ghosh and Subhas C. Biswas

Preamble

This divisional unit of IICB comprises of scientists with interests in neurodegenerative diseases, drug addiction, stem cell biology, utero-ovarian dysfunction cancer, diabetes, coronary diseases, and responses to pathogens in hematopoietic system. They employ cellular and animal models of various diseases to investigate focused areas of their interest so as to design diagnostics and therapeutics for the ailments. These scientists have developed strong intra- and inter-institutional cooperative collaborative programs for this purpose, with success. In addition many of the members of the division participate in postgraduate teaching at various Universities, and all of them are engaged in PhD mentoring and summer training programs. Regular biweekly journal clubs are organized, which are enthusiastically attended by both students and faculty. These seminars cover the latest developments in the field, and are given generally by the graduate students in the Division. The Division also conducts regular workshops and symposia in the area of cellular physiology. Additionally the Division has started for the first time an iternal 'Research Festival of Cell Biology & Physiology' from this year, which was organized by the graduate students. Invited external reviewers not only mentored but also assessed the presentations by the students, and awarded prizes for the first three platform and poster presentations. This has greatly helped to bring together all the students and the faculty of the Division on a single platform for a day, and to get a rare review of the work done on different areas of cell biology. The research highlights from the Division for the reporting year are presented below.

NEUROSCIENCE

Dr. K. P. Mohanakumar and group

Within the period of April 2010 to March 2011, this group has concentrated work in the field of two neurodegenerative disorders, viz., Parkinson's disease (PD) and Huntington's disease (HD).

Parkinson's Disease

Creation of cybrids for investigating mitochondrial electron transport chain functions in PD

Existence of mitochondrial dysfunction is reported in the blood and brains of parkinsonian patients. Cybrids are cytoplasmic hybrids created by the fusion of anucleate cells of the 'subjects' with a rho0 (ρ0) cell line that has been deprived of its mitochondrial DNA (Fig. 1, schematic representation of creation of cybrids). Production of normal and parkinsonian cybrids and differences observed in the mitochondrial dysfunction in relation to the expression of certain nuclear encoded mitochondrial subunits and the mitochondrial electron transport chain complex activities have been delineated during the last year. Platelets from patients and age and gender-matched controls were used to create cybrids

by fusion of these platelets with the ρ0 cells (Fig. 2). PD cybrids showed significant decline in activities of mitochondrial complex I and IV as analyzed spectrophotometrically and increased expression of one of the subunits of complex I, NDUFA2 as detected by densitometric analysis following western blot (Fig. 3). These cybrids exhibiting the disease mitochondrial gene and functional expression is a reliable cellular model of PD, and with the creation of control cybrids, these are invaluable tools for mitochondrial research on this disease, and has been achieved for the first time in this part of the world.

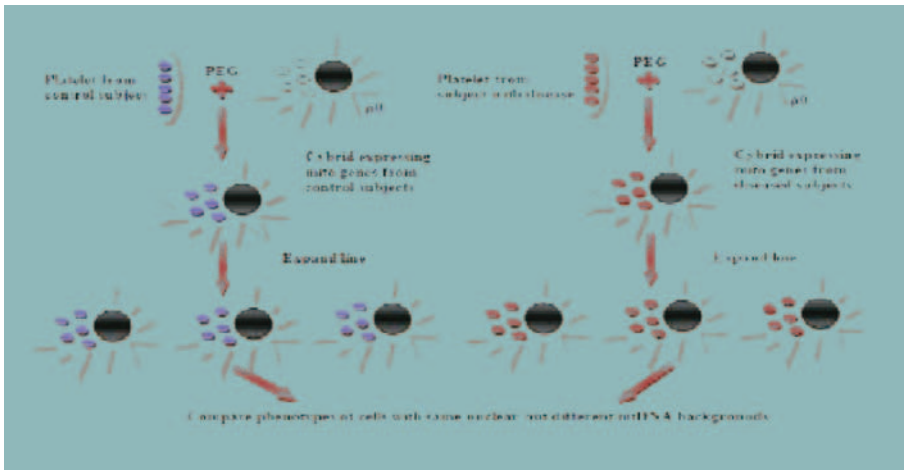


Fig. 1 : Schematic representation of cybrid preparation

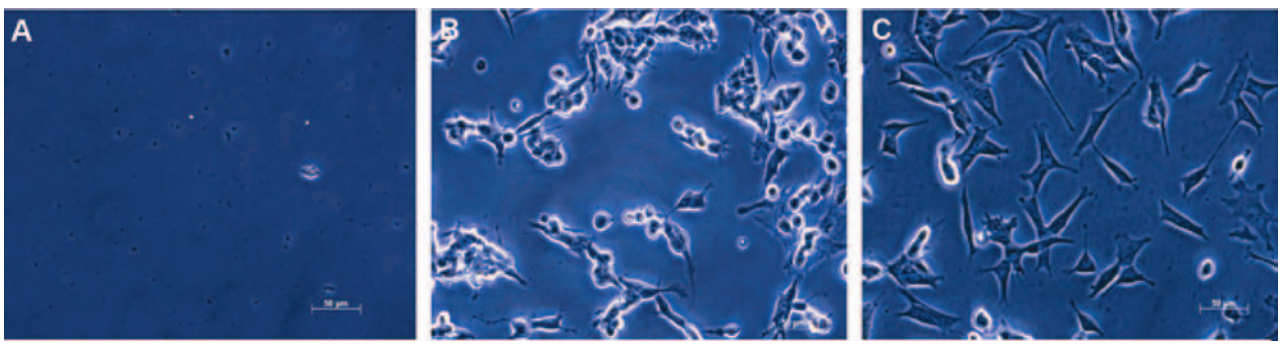


Fig. 2 : Selection procedure for cybrids: (A) Mock culture, (B) Control cybrids, and (C) PD cybrids. After the withdrawal of sodium pyruvate and uridine from the growth medium for two months, only the transformed or the fused cells (B, and C) are able to survive. The mock ρ0 cells culture in the medium without the essential nutrients for glycolysis, were unable to survive in the selection medium as shown in (A).

Ayurveda herbals and their effects on experimental PD

The extract of *Hyoscyamus niger* (HN) seeds, one of the components of *Ayurveda* medication for PD showed neuroprotection in terms of behavioral deficits and dopamine depletion in MPTP-induced parkinsonism in mice. *Hyoscyamus* species contains insignificant levels of L-DOPA, but aqueous methanol extracts of its seeds (AM-HN) significantly attenuated motor disabilities (akinesia, catalepsy and reduced swim score, Fig. 4) and striatal dopamine (DA) loss (Fig. 5) in MPTP treated mice.

Since the extract caused significant inhibition of monoamine oxidase activity and attenuated MPP^+-induced hydroxyl radical (•OH) generation in isolated mitochondria, it is suggested that the methanolic

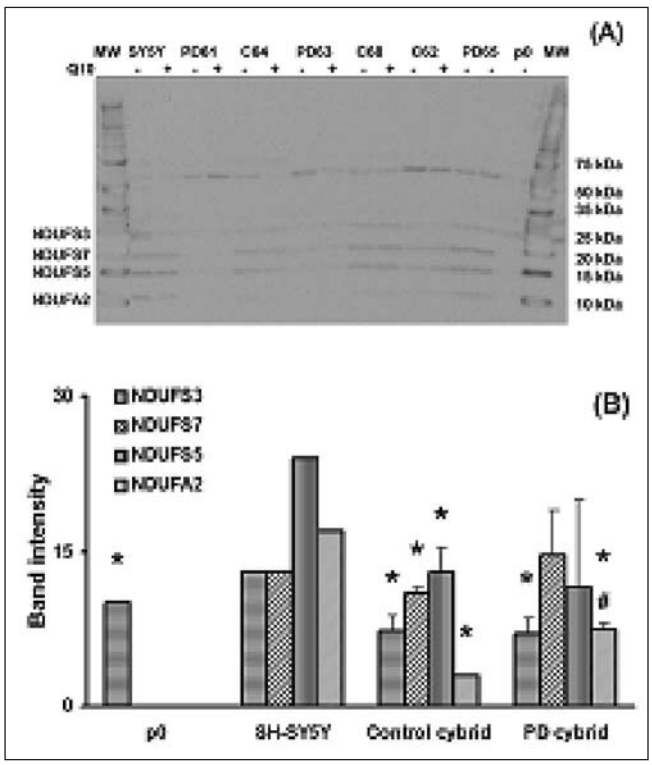


Fig. 3 : Western blot analysis for nuclear subunits of complex I: (A) Mitochondria were prepared from SH-SY5Y, ρ0 and control & PD cybrids, separated by SDS-PAGE, immune-blotted for the NDUFS3, NDUFS7, NDUFS5 and NDUFA2 subunits of complex I and visualized using chemiluminescence. Only the NDUFS3 unit was detected in ρ0. (B) Densitometric analysis of the band intensities in the immunoblot for these complex I subunits. *$p \leq 0.05$ as compared to SH-SY5Y, $^{\#}p \leq 0.05$ as compared to control cybrids by Student's 't' test.

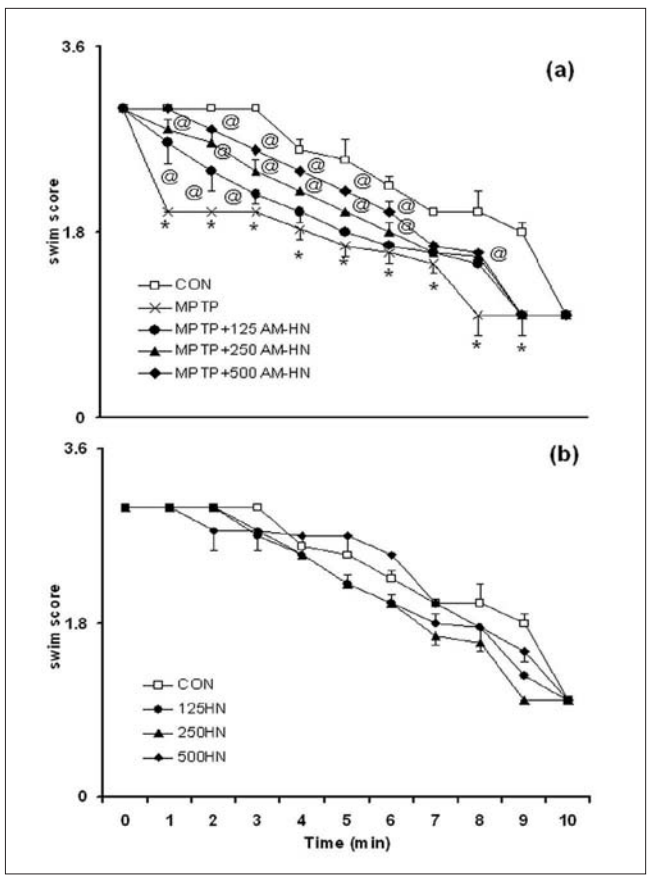


Fig. 4 : Effect of AM-HN on MPTP-induced swim-disability. Swim test was performed on the third day, an hour following the animals were subjected to akinesia and catalepsy tests. MPTP administration caused a significant diminution in swimming ability, which was dose-dependently (125–500 mg/kg) attenuated by AM-HN (a). Swimming ability of the animals treated with the extract alone was not significantly affected (b). Data represented are mean ± SEM. *$p \leq 0.05$ as compared to the control group, $^{@}p \leq 0.05$ as compared to the MPTP treated group, n = 4–6. $p \leq 0.0001$ between the groups; ANOVA followed by Friedman test. $p \leq 0.05$ Dunnett's Multiple Comparisons Test, Rank Sum Mean: [35.909; Control Rank Sum value = 70; MPTP Rank Sum value = 16). The results showed significant difference between CON vs MPTP, 125 mg/kg AM-HN vs MPTP, 250 mg/kg AM-HN vs MPTP and 500 mg/kg vs MPTP.

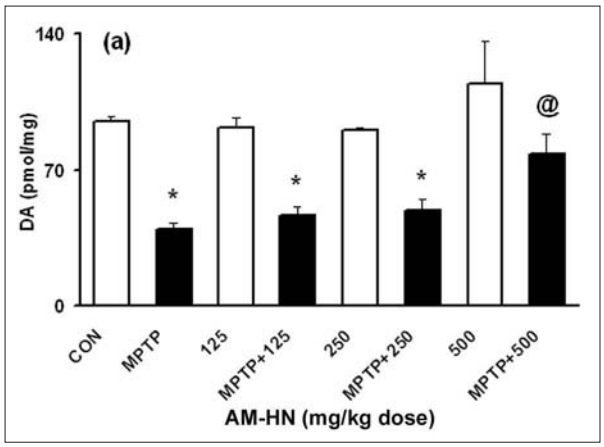


Fig. 5 : Effect of HN extracts on striatal DA levels in MPTP-induced PD animals. Striatal DA levels were analyzed using HPLC electrochemistry 16 h after the last feeding of the extract. Only the highest dose (500 mg/kg) of AM-HN demonstrated attenuation of DA loss. The data represented are mean ± SEM. *$p \leq 0.05$ as compared to the control group, $^{@}p \leq 0.05$ as compared to the MPTP treated group, n = 4–6.

extract of *H. niger* seeds protected against parkinsonism in mice by means of its ability to inhibit excess •OH generated in the mitochondria.

Pro-parkinsonian activity of molecules in Ayurvedic herbs

Behavioral and neurochemical effects of chronic administration of high doses of 2-phenylethylamine (PEA; 25-75 mg/kg, i.p. for up to 7 days), a component found in *Ayurvedic* herbals has been investigated in Balb/c mice. Depression and anxiety, as demonstrated respectively by increased floating time in forced swim test, and reduction in number of entries and the time spent in the open arms in an elevated plus maze were observed in these animals. Acute and sub-acute administration of PEA caused significant, dose-dependent depletion of striatal DA, and its metabolites levels. A significant inhibition of NADH-ubiquinone oxidoreductase activity suggests the inhibition in oxidative phosphorylation in the mitochondria resulting in •OH generation. Nissl staining and TH immnunohistochemistry in brain sections failed to show any morphological aberrations in DA-ergic neurons or nerve terminals. Long-term over-consumption of PEA containing food items could be a neurological risk factor having significant pathological relevance to disease conditions such as depression or motor dysfunction.

Chronic L-DOPA-induced 6-OHDA generation in brain is attenuated by salicylic acid

The ability of salicylic acid (SA) to attenuate long-term L-DOPA-induced 6-hydroxydopamin e (6-OHDA) formation in the striatum of mice, and to protect against the resulting dopaminergic neurotoxicity is investigated in rodents. The production of 6-OHDA from dopamine *in vitro* from

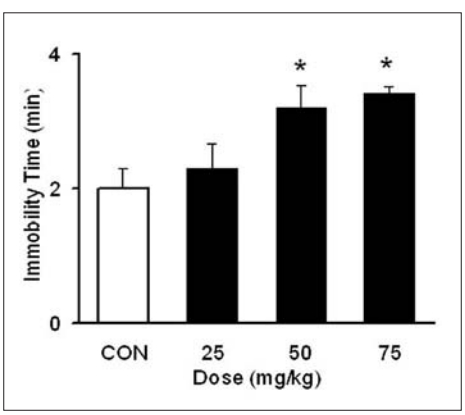


Fig. 6 : Long-term administration of PEA causes desperation-induced immobility in mice: Effect of long-term administration of PEA on immobility caused by forced swim was evaluated 24 h after the last dose of the drug. After an initial acclimatization for 2 min, the total immobility time in min was noted for a period of 6 min. Animals that received the higher doses of PEA (50 and 75 mg/kg) exhibited significantly greater immobility time. The data represented are as mean ± SEM. *$p \leq 0.05$ as compared to the control group, n = 4.

ferrous-ascorbate-dopamine (FAD) hydroxyl radical (•OH) generating system or *in vivo* in the striatum following prolonged administration of L-DOPA in mice were found to be significantly attenuated by SA. Intra-median forebrain bundle (MFB) infusion of FAD, but not equivalent dose of ferrous ion or dopamine individually, caused significant striatal dopamine depletion, which was blocked by SA administration. The dose- and time-dependent increase in the formation of 6-OHDA following L-DOPA treatment in the mouse striatum was synergistically enhanced to the systemic administration of MPTP. SA treatment significantly attenuated the L-DOPA plus MPTP-induced striatal 6-OHDA generation, and protected against striatal DA loss. The present study demonstrates a novel mode of DA-ergic neuroprotection by SA and implicates it use in the treatment of PD.

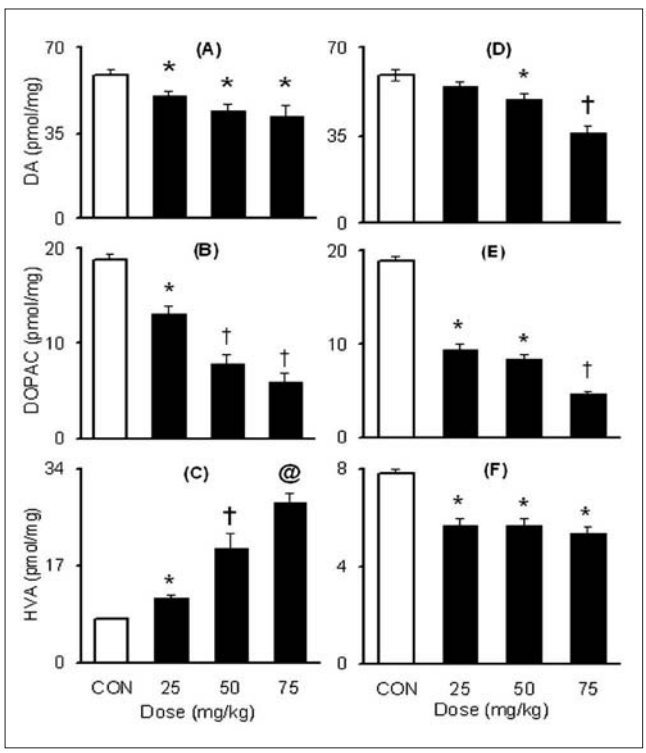


Fig. 7 : Effect of PEA on striatal DA and metabolites: Animals treated with different doses of PEA acutely (A–C), or long-term (D–F) were sacrificed respectively 30 min or 24 h following the last dose of drug. Since there appeared no significant variation in the levels of the neurochemical parameters studied between the control groups, these data were pooled (n = 8). Striata were dissected out and the supernatants resulting from homogenization in $HClO_4$/EDTA were assayed employing a sensitive HPLC-electrochemical procedure for the determination of DA and its metabolites, DOPAC and HVA. The data are represented as mean ± SEM. *$p \leq 0.05$ as compared to the control group, $^{+}p \leq 0.05$ as compared to the lower dose administered group and $^{@}p \leq 0.05$ as compared to the 50 mg/kg dose treated group, n = 6.

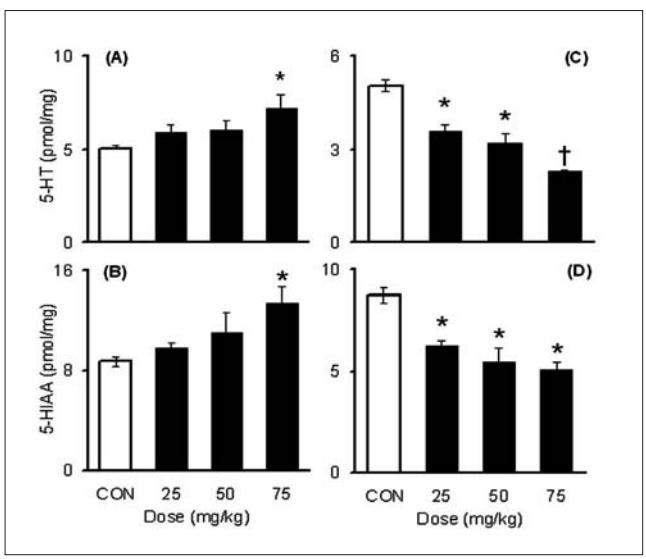


Fig. 8 : Effects of PEA on striatal serotonin and its metabolite: animals treated with different doses of PEA acutely (A, B) or long-term (C, D) were sacrificed 30 min or 24 h respectively following the administration of the last dose. Striatal serotonin (5-HT) and 5-hydroxyindole acetic acid (5- HIAA) were assayed employing a sensitive HPLC-electrochemical procedure and the data are represented as mean ± SEM. *$p \leq 0.05$ as compared to the control group, and $^{+}p \leq 0.05$ as compared to 50 mg/kg PEA administered group, n = 6–8.

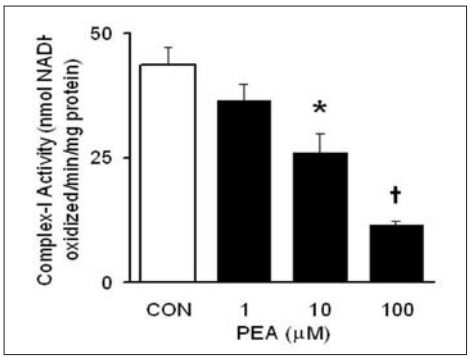


Fig. 9 : Effects of PEA on complex-I activity: Mitochondrial P_2 fraction was pre-incubated with different concentrations of PEA (1–100 mM) for 10 min at 37 °C, and the rotenone sensitive NADH-ubiquinone oxidoreductase (complex-I) activity is expressed as nmol NADH oxidized/min/mg protein (e340 = 6.23×10^{-3} M). Data provided are mean ± SEM. *$p\leq0.05$ as compared to the control; $^{+}p\leq0.05$ as compared to the 10 mM PEA treated group. n=12.

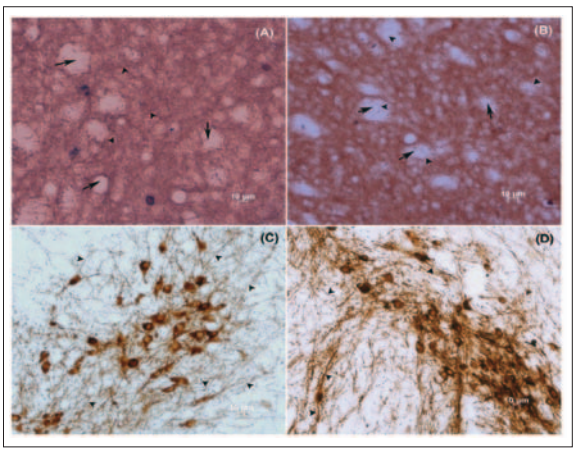


Fig. 10 : TH immunohistochemistry: Coronal sections (20 m) passing through the striatum (A, B) and substantia nigra (C, D) were cut on a cryostat and were incubated with primary antibody (anti-rabbit TH polyclonal 1:1000), followed by HRP-conjugated secondary antibody (goat anti-rabbit IgG 1:300). The sections were developed with DAB. (A) and (C) are sections from control animals; (B) and (D) are sections from treated (75 mg/kg, i.p.) animals. No microscopic changes were observed in the neurons from treated sections. Arrows indicate striosomes and the arrowheads the neuronal fibers (A–D), including axons and dendrites of the nigral dopaminergic neurons in (C) and (D).

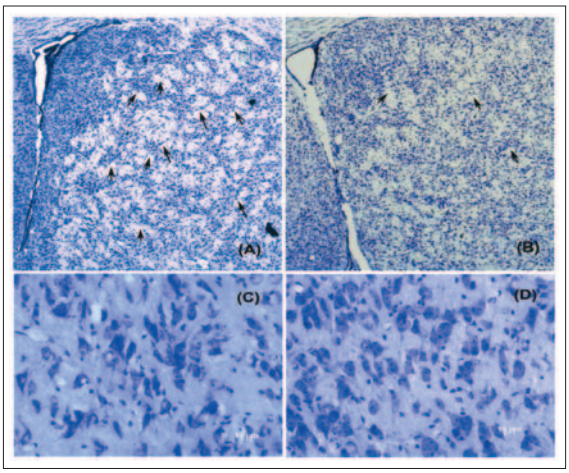


Fig. 11 : Nissl staining: Coronal sections (20 μm) passing through the striatum (A, B) and substantia nigra (C, D) were cut on a cryostat. Neurons in the striatum and substantia nigra were stained with cresyl violet following vehicle (A, C) or sub-acute PEA treatment (75 mg/kg, i.p., BD). Arrows in (A) and (B) indicate striosomes. No morphological changes were seen in any neurons from the SN region.

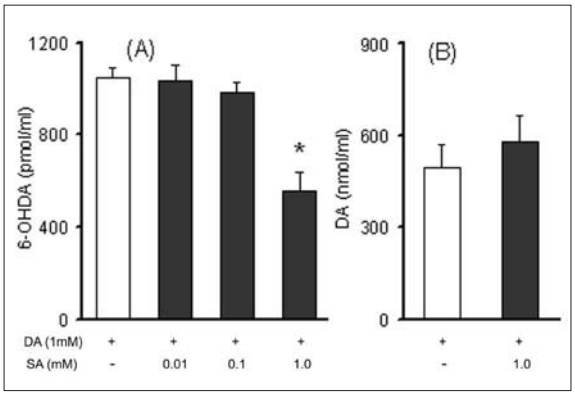


Fig. 12 : Effect of SA on the production of 6-OHDA utilizing DA *in vitro* in a FAD system. Different concentrations of SA was added to FAD system to test the effect of this molecule on the yield of 6-OHDA formed from DA (A). Results are expressed as pmol/ml of the reaction mixture and mean ± SEM. *$p \leq 0.05$ (ANOVA followed with Dunnett test, and 't'-test) as compared to 6-OHDA produced by 1 mM DA (n = 8). FAD system with 1 mM DA or SA was also assayed for the content of DA (B). Results are expressed as nmol/ml of the reaction mixture; mean ± SEM. (n = 8).

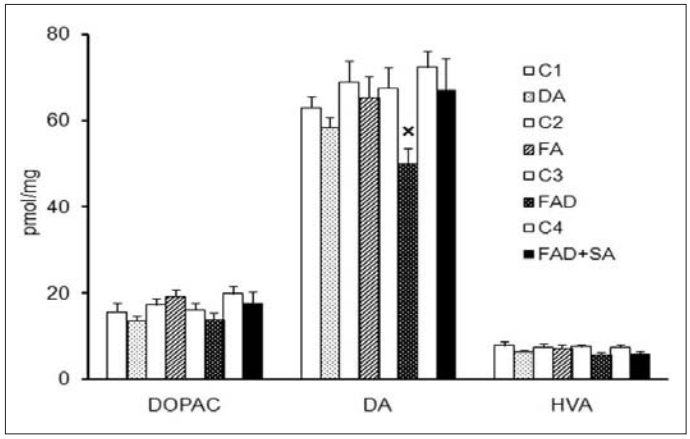


Fig. 13 : Ferrous sulfate (200 µM), ascorbic acid (1 mM), EDTA (240 µM), and DA (1 mM) in phosphate buffer at pH 7.2 (FAD) was incubated at 37 °C in the dark for 2 h. Rats were unilaterally infused into the MFB with 4 µl of the FAD, or FAD + salicylic acid (FAD+SA) or FAD without DA (FA) or DA alone (DA), similarly incubated. They were sacrificed on the 19th day, and DA and its metabolites levels in the contra- and ipsi-lateral striata were individually analyzed. Results are expressed as pmol/mg tissue and the values are given as mean ± SEM. *$p \leq 0.05$ Significantly different (ANOVA followed with Dunnett test) as compared to control (filled or shaded bars – ipsilateral striatum; empty bars - contralateral striatum which received the buffer alone; C1,C2,C3 or C4 (n = 6).

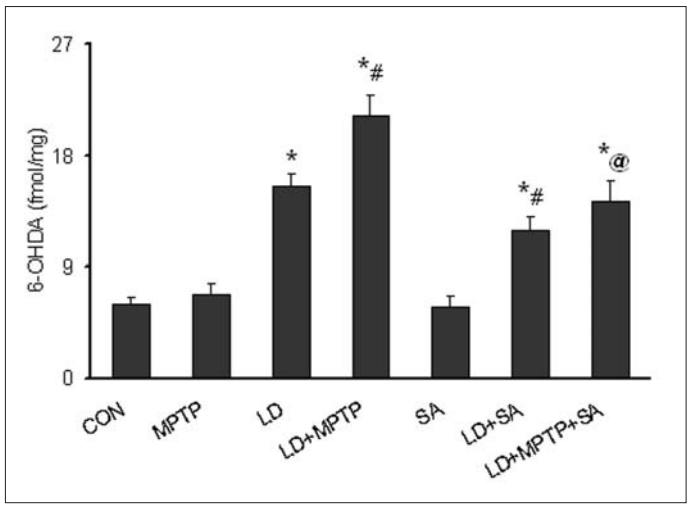


Fig. 14 : Effects of SA on L-DOPA and L-DOPA plus MPTP induced generation of 6-OHDA levels in the striatum. Mice were administered with L-DOPA (250 mg/kg, p.o.) along with carbidopa (25 mg/kg, p.o.) and SA (100 mg/kg, i.p) daily for 7 days and a single dose of MPTP (30 mg/kg, i.p.) was administered 30 min after the 7th dose of L-DOPA. SA was administered 30 min prior to L-DOPA and animals were sacrificed 2 h after the last dose of L-DOPA. Results are expressed as fmol/mg tissue and mean ± SEM. *$p \leq 0.05$ (ANOVA followed with Dunnett test), $^{\#}p \leq 0.05$ (t-test) and $^{@}p \leq 0.05$ ('t'-test) as compared to control, L-DOPA and L-DOPA plus MPTP group respectively (n = 8).

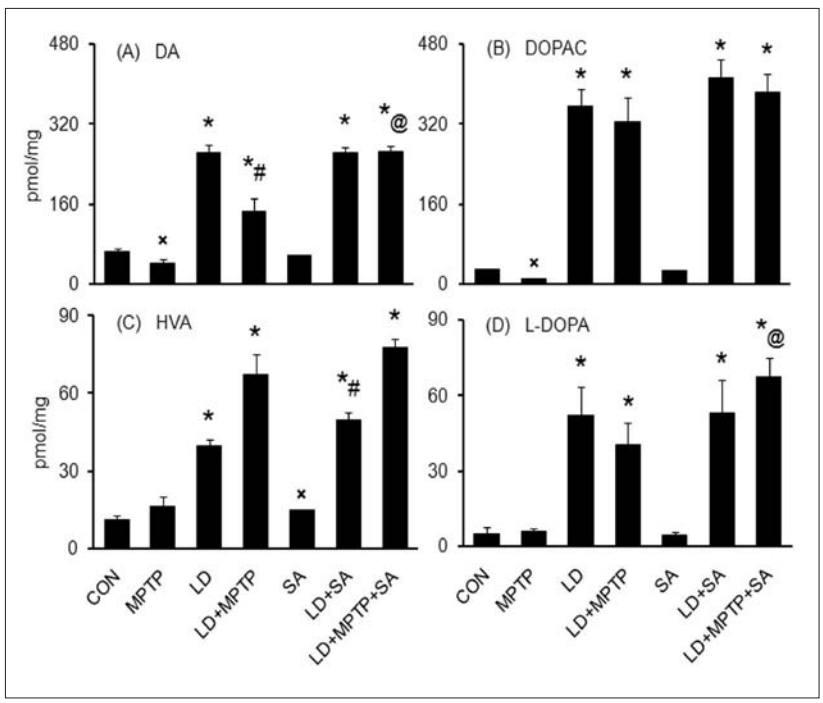


Fig. 15 : Effect of SA on L-DOPA, DA and its metabolites levels in the striatum after L-DOPA and/or MPTP administration. Mice were administered with the drugs and chemicals as in the figure legend, 12. Striata were dissected out and (A) DA, (B) DOPAC, (C) HVA (D) L-DOPA levels were measured. Results are expressed as pmol/mg tissue and mean ± SEM. *$p \leq 0.05$ (ANOVA followed with Dunnett test), $^{\#}p \leq 0.05$ (t-test), and $^{@}p \leq 0.05$ (t-test) as compared to control, L-DOPA, L-DOPA plus MPTP group respectively (n=6).

Dr. Sumantra Das and group

Treatment and understanding of addiction

Ongoing collaborative projects with a psychiatric clinic, Baulmon, Kolkata as well as Chittaranjan National Medical College, Kolkata are underway to carry out genetic epidemiological studies on opioid addiction by investigating the possible association of specific SNPs of certain candidate genes in addiction using PCR based RFLP as well as DNA sequencing analysis. Three SNPs (Fig. 16) of the CREB binding protein (CREBBP), identified in the population, were analyzed to find out the association of these SNPs with addiction. One SNP, rs3025684 in intron 21 having the contig position of 3795363, showed association with addiction (see Table).

Studies have been initiated to understand the changes in the epigenetic regulations in animals rendering them addicted to alcohol.

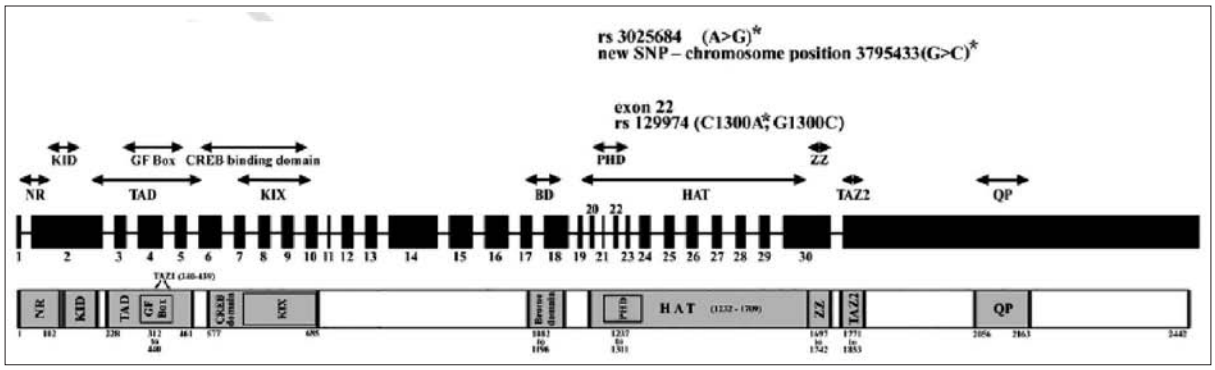


Fig. 16 : Location of SNPs of exonic region 22 of CREBBP gene found to be present in the population studied. Exons are drawn to scale and have been numbered while introns and UTRs are not drawn to scale. *indicates a novel SNP.

Table : Genotypic Distribution and Allelic Frequencies of rs3025684 SNP of CREBBP Gene in Control, Opioid and Alcoholic Groups.

Geno types	Control, n (%)	Opioid addicted n (%)	OR (95%Cl)	Alcohol addicted n (%)	OR (95% Cl)
GG	140 (93)	96 (74)	1 (referent)	86 (78)	1 (referent)
GA	8 (5)	30 (23)	5.32 (2.32-12.10)	22 (20)	4.44 (1.89 - 10.40)
AA	2 (1)	4 (3)	2.35 (0.42-13.04)	2 (2)	1.37 (0.19-9.88) P_{trend}= 0.0016
	x^2_{HW} = 14.00 (p<0.001)	x^2_{HW} = 0.74 (p<0.05)	P_{trend} <0.0001 [$x^2_{(1)}$ = 20.28, p<0.0001] [a]p <0.0001	x^2_{HW} = 0.18 (p<0.7)	[$x^2_{(1)}$ = 13.60, p=0.0011] [a]p <0.0006
G	288 (96)	222 (85)	0.24 (0.12-0.48)	194 (88)	0.31 (0.15-0.63)
A	12 (4)	38 (15) p = 0.00001**	4.11 (2.09-8.05)	26 (12) p = 0.0007**	3.22 (1.58-6.53)

[$x^2_{(1)}$, Chi-square analysis of genotype frequency.
**FDR, false discovery rate adjusted Chi-square p-values.
OR, odds ratio; Cl, 95% confidence interval; n, number of individuals/n, number of alleles; x^2_{HW}, Hardy-Weinberg-Equilibrium calculated by x^2 text.
[a]P indicates Fisher's Exact Test.

Limbal stem cell culture

A collaborative project with Regional Institute of Ophthalmology, Kolkata is looking into the regulatory mechanisms of matrix metalloproteinases in the propagation of limbal stem cells derived from cadaver eyes.

Structure, function and altered function of astroglial cells

Our earlier studies had unequivocally demonstrated a downstream role of β-adrenergic receptor (β_2-AR) system in thyroid hormone (TH) induced differentiation and maturation of astrocytes. However, radioligand binding studies using ^{125}I-pindolol (^{125}I-PIN) in absence and presence of specific β_1- and β_2-AR antagonists showed a sharp decrease in the specific binding of β_2-AR when 10-day old primary astrocytes culrures were exposed to TH for 2-12 h. The receptor concentrations came back to control values by 24 h. β_2-AR mRNA levels, measured by real-time PCR at various times starting from 2 h to 24 h, on the other hand, did not show any significant changes during TH treatment. Further studies suggested that TH promoted internalization of β_2-AR at the initial stages. Immunoprecipation studies followed by western blot analysis suggested a sharp decline in membrane β_2-AR concentrations with a concomitant increase in β_2-AR in the cytosol (Fig. 17A). The increase in cytosolic β_2-AR was not due to newly synthesized β_2-AR as evident from ^{35}S-Methionine labeling of the cells in presence or absence of the protein synthesis inhibitor, cycloheximide (Fig. 17B). Overall, our results demonstrated an unique role of TH in the sequesteration of β_2-AR probably through the induction of β-arrestin as found earlier.

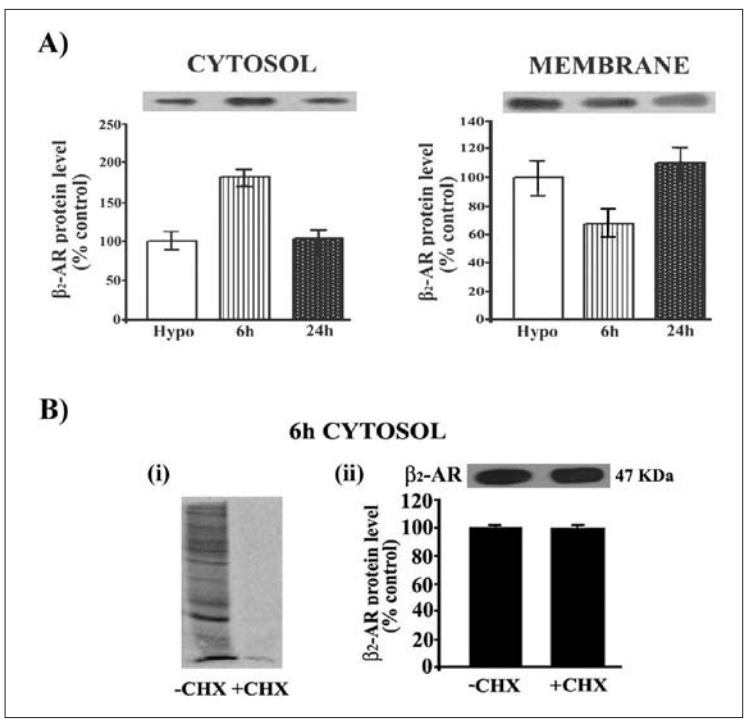


Fig. 17 : Effect of TH on the redistribution of β_2-AR in cytosol and membrane. A. Ten day old hypothyroid astrocytes were treated with TH for different time period (6 h, 24 h). Cells were extracted; membrane and cytosol were subjected to immunoprecipitation and immunoblotting. The relative intensities of the β_2-AR bands, indicated in the figure, represented as a percentage of the level of same protein in hypothyroid control. B. Another set of hypothyroid cultures were treated with cycloheximide (CHX) and [^{35}S] methionine for 2 h and then exposed to TH for 6h. (i) SDS PAGE followed by autoradiography shows inhibition of protein synthesis by CHX. (ii) cytosolic portion was subjected to immunoprecipitation and immunoblotting as in A. The relative intensities of the β_2-AR bands were calculated from densitometric scans using ImageJ. Results are mean ± SEM of at least 3 blots.

Dr. Subhas C Biswas and group

Understanding molecular basis of neurodegeneration in Alzheimer's disease

The major focus of this laboratory is to understand the molecular mechanism of neuronal apoptosis in various models of Alzheimer's disease (AD) for identification of potential targets and development of novel compounds towards these targets. Cell lines such as neuronally differentiated PC12 cells, differentiated Neura2a cells and primary cultures of rat cortical or hippocampal neurons are employed for this purpose. When these cells were treated with oligomeric β-amyloid (Aβ), they undergo death but their sensitivity towards Aβ is different (Fig. 18).

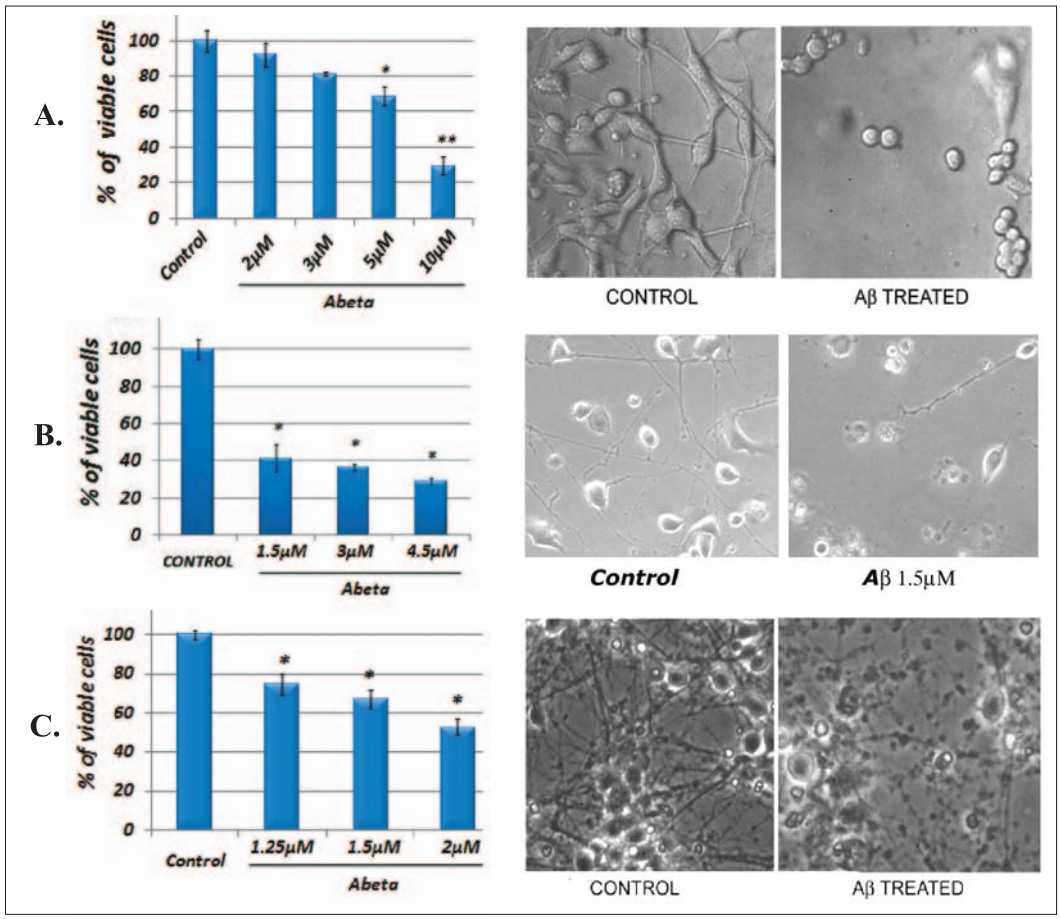


Fig. 18 : Neuronal cells undergo death following oligomeric $A\beta_{(1-42)}$ exposure. A. Differentiated PC12 cells (5DIV) were exposed to oligomeric $A\beta_{(1-42)}$ at doses 2, 3, 5 and 10 µM for 24 h. Percentage of viable cells was calculated by Trypan blue exclusion assay. Survival of differentiated PC12 cells progressively decreases with increasing dose of $A\beta_{(1-42)}$. The asterisks denote statistical significant differences from control: *p<0.05, **p<0.01. Right panel shows representative phase contrast micrographs of differentiated PC12 cells in absence and presence of $A\beta_{(1-42)}$. **B.** Differentiated Neura2a cells (5DIV) were exposed to oligomeric $A\beta_{(1-42)}$ at dose of 1.5, 3 and 4.5 µM for 24 h. Percentage of viable cells was calculated by intact nuclei counting assay. Survival of differentiated Neura2a cells progressively decreases with increasing dose of $A\beta_{(1-42)}$. The asterisks denote statistical significant differences from control: *p<0.01. Right panel shows representative phase contrast micrographs of differentiated cells in absence and presence of $A\beta_{(1-42)}$. **C.** Primary cultures of rat cortical neurons (7DIV) were treated with oligomeric $A\beta_{(1-42)}$ at dose of 1.25, 1.5 and 2 µM for 24 h. Percentage of viable neurons was calculated by Trypan blue exclusion assay. Survival of cortical neurons were progressively decreases with increasing dose of $A\beta_{(1-42)}$. The asterisks denote statistical significant differences from control: *p<0.01. Right panel shows representative phase contrast micrographs of cortical neurosn in absence and presence of $A\beta_{(1-42)}$.

Transcription factor FoxO3a is required for neuron death in AD

Transcriptional activation of pro-apoptotic genes is a pre-requisite for variety of programmed cell death. The transcription factor FoxO3a usually phosphorylated by AKT localizes in cytosol bound with 14-3-3 protein. However, upon activation in response to apoptotic stimuli it translocates to nucleus and induces its target genes. In a preliminary study, we tested the level, the phosphorylation status and the subcellular distribution of FoxO3a and whether it's required for neuron death in cellular models

of AD. We found that a slight decrease of total level, a drastic decrease of phosphorylation level and maximal translocation of FoxO3a to nucleus occurred within few hrs in neuronal cells in response to Aβ exposure. Moreover, downregulation of FoxO3a by RNAi protected neuronal cells from death and retained their overall morphology after Aβ toxicity. Thus, our findings indicate that FoxO3a is activated, translocated to nucleus and plays a necessary role in neuron death in response to Aβ toxicity.

Astrocytes are reactivated in response to Aβ

Reactivated astrocytes have been found around the Aβ plaques in human patients. The precise role of astrocytes and identity of neuroprotective/neurotoxic substances that are released by reactivated astrocytes and their role on neurodegeneration are largely unknown. In a preliminary study we found that primary cultures of actrocytes are reactivated with characteristic morphological changes in response to Aβ exposure (Fig. 19). Moreover, S100 proteins those are implicated in AD, are also upregulated in these Aβ treated cells. We plan to investigate the precise mechanism of astrocyte reactivation in response to Aβ and role of S100 proteins on neuronal death process.

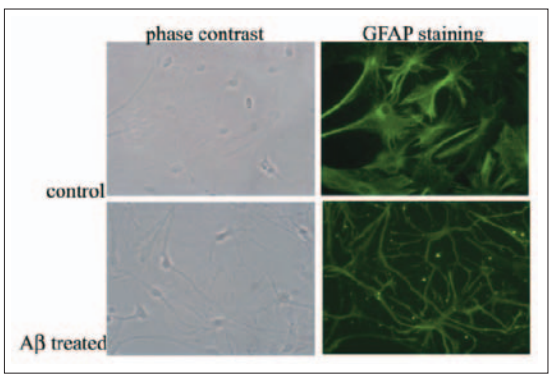


Fig. 19 : Phase contrast and fluorescent micrographs of astrocytes treated with oligomeric $A\beta_{(1-42)}$. Primary astrocyte culture (14DIV) were treated with 4 μM oligomeric $A\beta_{(1-42)}$ for 24 hrs. Then it was subjected to immunocytochemical staining with GFAP antibody. Alexa Flour 488 was used as secondary antibody. Pictures were taken under flouroscent microscope at 32x.

TOXICOLOGY

Dr. Tuli Biswas and group

N-acetyl cysteine-Atorvastatin combination provide protection against erythrocyte apoptosis during chronic arsenic exposure

Arsenic is an environmental toxicant that reduces the lifespan of circulating erythrocytes during chronic exposure. In this study, we have indicated involvement of hypercholesterolemia and reactive oxygen species (ROS) in arsenic-induced apoptotic death of erythrocytes. Results emphasized on the importance of cholesterol in promoting ROS-mediated Fas signaling in red cells. Further, we have shown an effective recovery from arsenic-induced death signaling in erythrocytes in response to treatment with atorvastatin (ATV) and N-acetyl cysteine (NAC). Combination treatment amended activation of caspase 3, capable of promoting aggregation of band 3 with subsequent binding of autologous IgG and opsonization by C3b (Fig. 20), that led to phagocytosis of the exposed cells by macrophages. This work helped us to identify intracellular membrane cholesterol enrichment and GSH depletion as the key regulatory points in arsenic-mediated erythrocyte destruction and suggested a therapeutic strategy against it.

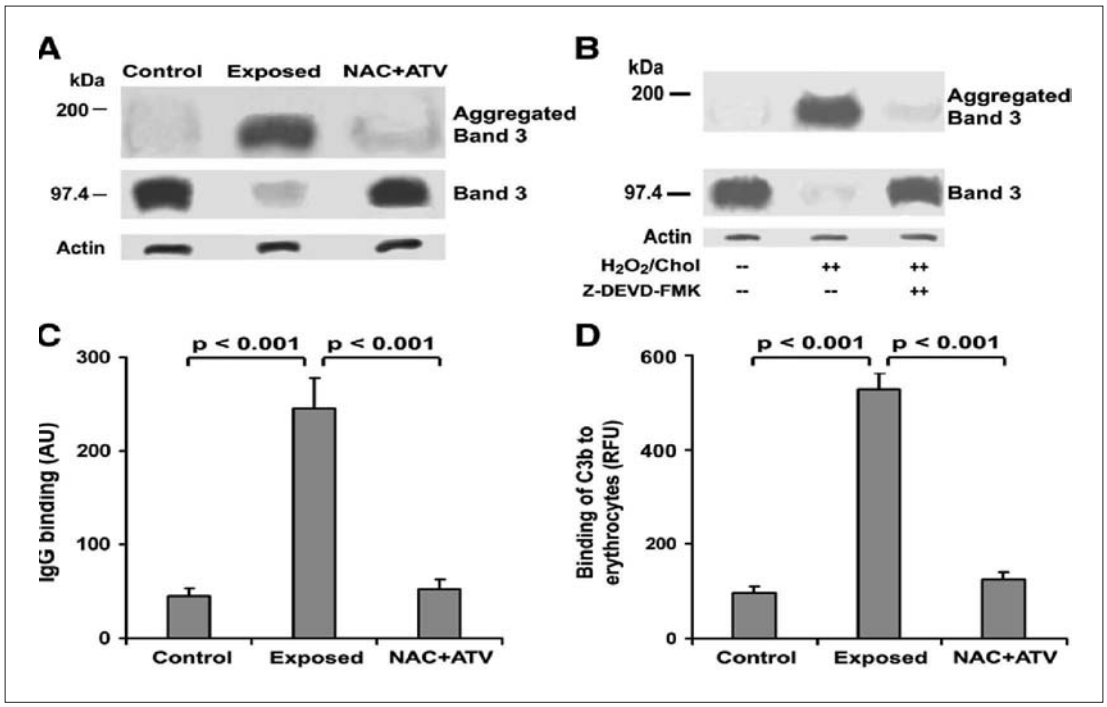


Fig. 20 : NAC–ATV treatment reduces arsenic-mediated autologous IgG and C3b binding in consequence of band 3 aggregation on red cell (A) Immunoblots indicating arsenic-mediated aggregation of band 3 before and after NAC–ATV treatment. (B) Representative Western blots assessing band 3 aggregation in erythrocytes after incubation with H2O2/ cholesterol in the presence or absence of Z-DEVD-FMK. Binding of (C) autologous IgG (AU) and (D) C3b [Relative fluorescence unit (RFU)] to erythrocyte membrane. Values were mean±S.D. Results are representative of three independent experiments with six animals in each group. Actin was used as the loading control.

CELL BIOLOGY & PHYSIOLOGY

14-Deoxyandrographolide desensitizes hepatocytes to TNF α -induced apoptosis through the release of tumour necrosis factor receptor superfamily

Andrographis paniculata (AP) has been found to display hepatoprotective effect, although the mechanism of action of the active compounds of AP in this context still remains unclear. We have evaluated the hepatoprotective efficacy of 14-deoxyandrographolide (14-DAG), a bioactive compound of AP, particularly its role in desensitization of hepatocytes to tumour necrosis factor-alpha (TNF-α)-induced signaling of apoptosis. 14-DAG down-regulated the formation of death-inducing signaling complex, resulting in desensitization of hepatocytes to TNF-α-induced apoptosis. Pretreatment of hepatocytes with 14-DAG accentuated microsomal Ca-ATPase activity through induction of NO/cGMP pathway. This resulted in enhanced calcium influx into microsomal lumen with the formation of TNFRSF1A-ARTS-1-NUCB2 complex in cellular vesicles. It was followed by the release of full-length 55 kDa TNFRSF1A and a reduction in the number of cell surface TNFRSF1A, which eventually caused diminution of TNF-a signal in hepatocytes.

Regulatory role of nitric oxide in the reduced survival of erythrocytes in visceral leishmaniasis

Nitric oxide (NO) plays a vital role in maintaining the survivability of circulating erythrocytes. Impairment of both synthesis and uptake of NO resulted in decreased bioavailability of this signaling molecule in erythrocytes in visceral leishmaniasis (VL). Combination treatment with standard anti-

leishmanial sodium stibogluconate (SAG) and NO donor isosorbide dinitrate (ISD) decreased red cell apoptosis in infected animals by deactivating caspase 3 through s-nitrosylation. Drug treatment prevented infection-mediated ATP depletion and altered calcium homeostasis in erythrocytes. Improved metabolic environment effectively amended dysregulation of aminophospholipid translocase and scramblase, which in turn reduced cell shrinkage, and exposure of phosphatidylserine on the cell surface under the diseased condition (Fig. 21). The study implicates NO to be a possible target for future drug development towards the promotion of erythrocyte survival in VL.

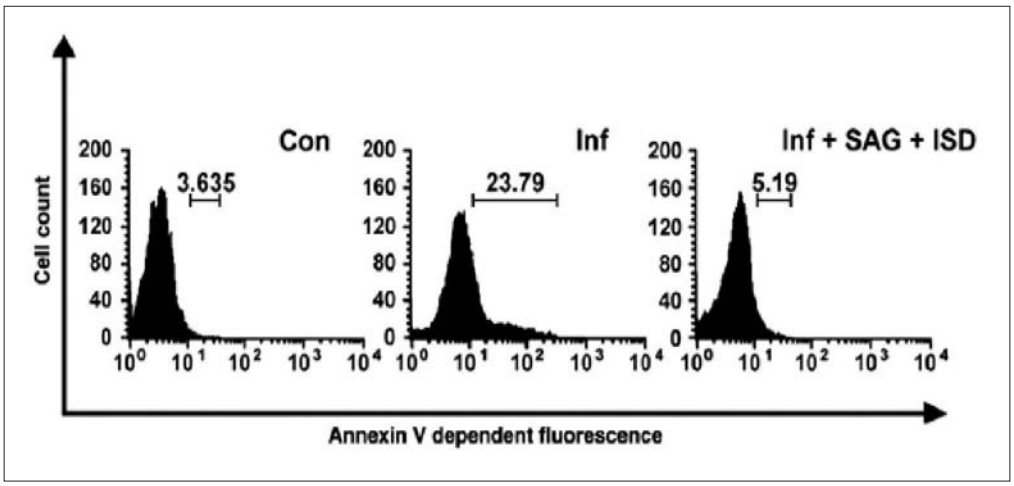


Fig. 21 : Reversal of increased PS exposure at the red cell surface of infected animals in response to ISD+SAG treatment. Externalization of PS was assessed from histograms of annexin V binding. Numbers indicated percentage of annexin V–positive cells in the respective cell populations. Results are representative of three independent observations.

MOLECULAR ENDOCRINOLOGY

Dr. Arun Bandyopadhyay and group

Mitochondrial dysfunction in heart by peroxisome proliferator activated receptor (PPAR) α signaling

The present study was undertaken to elucidate the role of metabolic remodelling in cardiac dysfunction induced by hyperthyroidism. Heart functions, cardiac remodelling, expression of the genes associated with fatty acid oxidation, mitochondrial morphology and activity and oxidative stress were examined in rats treated with 3,5,3' triiodothyronine alone (T3, 8 µg/100 g body weight, i.p) for 15 days or along with a PPARα agonist, bezafibrate (30 µg/100 g body weight, oral). Co-treatment with bezafibrate inhibited T3-induced cardiac hypertrophy, atrial and brain -natriuretic peptide expression. It also restored expression of fatty acid oxidation genes, CPT-1β and MCAD when co-treated with T3. Ultrastructure of mitochondria was damaged in T3 treated rat heart which was prevented by bezafibrate along with restoration of important mitochondrial genes prohibitin-1 and VDAC. Reduction in mitochondrial activity and myocardial oxygen consumption were also significantly checked by bezafibrate in hyperthyroid heart. Thyroid hormone-induced lipid peroxidation and depletion of total cellular antioxidants in heart were also inhibited by bezafibrate. Thyroid hormone treatment resulted into excessive increase in heart rate and contractility with marked decrease in diastolic index, stroke volume and cardiac output. Bezafibrate co-treatment prominently restored heart functions and improved

cardiac output. In summary, the results demonstrate that thyroid hormone-induced cardiac dysfunction is associated with altered energy metabolism coupled with structural as well as functional impairment of mitochondria via down regulation of PPARα signaling.

Down regulation of PPARα during thyroid hormone-induced left ventricular hypertrophy

To examine whether PPARα is directly involved with T3 induced cardiac hypertrophy, rats were treated with T3 (8 µg/100 g BW) for 15 days in the absence or presence of PPARα agonist, bezafibrate (30 µg / 100 g BW) and cardiac hypertrophy was assessed by measuring HW/BW ratio. After 15 days of T3 treatment, about 57 % increase was observed in HW/BW ratio compared to control. Co-treatment of rats with bezafibrate along with T3 prevented hypertrophy of heart by 68 % indicating that T3 induced cardiac growth was mediated via PPARα (Fig. 22A).

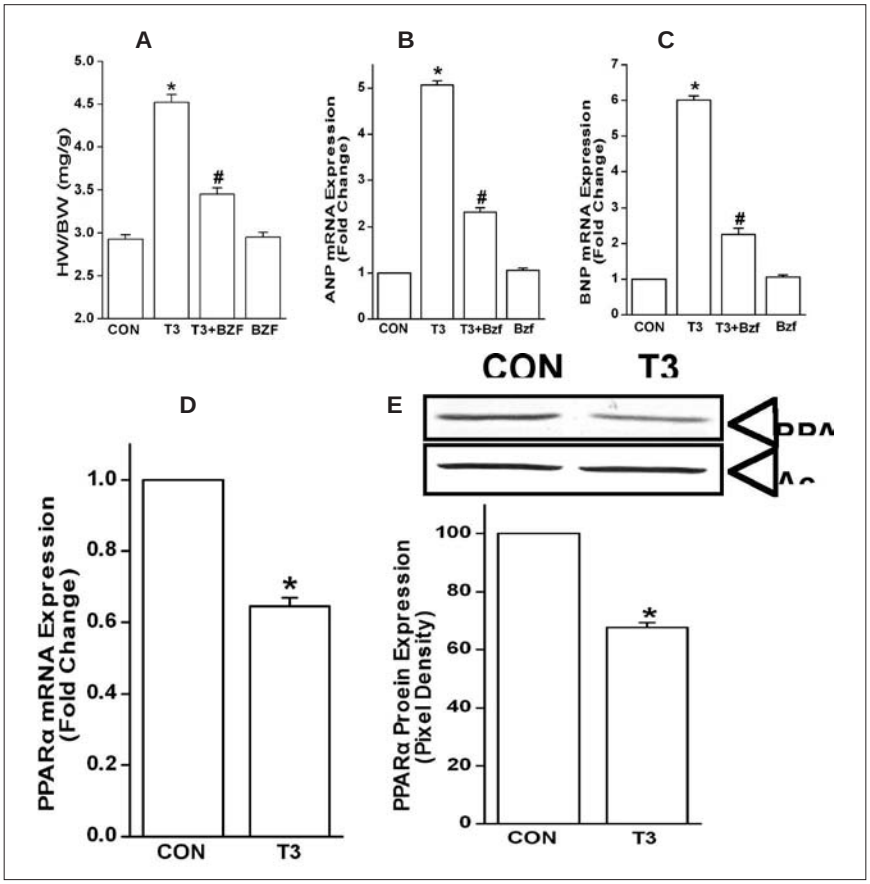


Fig. 22 : Inhibition of cardiac hypertrophy by Bezafibrate. Separate groups of rats were administered either with vehicle (CON) or T3 (T3) or T3 in combination with bezafibrate (T3+Bzf) or bezafibrate (Bzf) alone for 15 days and the degree of hypertrophy was expressed as heart weight (HW) to body weight (BW) ratio in mg/g (HW/BW). This data represents mean SEM for 20 rats in each group (A). *p<0.01 control vs. T3, $^{\#}p$<0.01 T3 vs.T3+Bzf. The mRNA expressions of ANP (B) and BNP (C) in the left ventricle were examined by real time quantitative RT PCR. *p<0.01 control vs. T3, $^{\#}p$<0.01 T3 vs.T3+Bzf, (n=6) for both (B) & (C) and the complete data set (for A, B & C) is also significant at <0.01 level, analysed by one-way ANOVA. Change in PPARα mRNA expression in left ventricle of vehicle (CON) or T3 (T3) treated rats is shown as fold change (D). The representative immunoblot (E) is showing the level of PPARα protein in the LV tissue. Lower panel shows the average pixel density of 4 immunoblots after nornalizing with Actin protein expression conducted with 4 different individual rats in each group.*p<0.01 control vs. T3, n=6 for (D) and *p<0.01 control vs. T3, n=4.

To confirm the induction of cardiac hypertrophy the expression of molecular markers of hypertrophy, ANP and BNP were also examined. The level of ANP mRNA was increased over 5-fold compared to control (Fig. 22B) whereas, the level of BNP mRNA was increased about 6-fold after 15 days of T3 treatment (Fig. 22C). Co-treatment of rats with bezafibrate prevented T3-induced expression of ANP and BNP in left ventricle (Figs. 22B, C). Both mRNA and protein levels of PPARα were significantly reduced in T3 treated rat LV compared to control (Figs. 22D, E).

Histological examination of hematoxyline-eosin stained LV cross-sections also showed the occurrence of myocyte hypertrophy by T3 that was attenuated by bezafibrate co-treatment. Taken together, the results demonstrated that hyperthyroid state resulted in the development of pathological cardiac hypertrophy by down regulation of PPARα.

Down-regulation of mitochondrial membrane proteins by PPARα in hypertrophied heart

Expression of mitochondrial inner membrane protein, prohibitin 1 was decreased significantly in T3 treated hearts compared to control (Fig. 23A). Expression of outer membrane protein VDAC was also down-regulated by T3 (Fig. 23B). Bezafibrate co-administration along with T3 significantly restored the expression of both these proteins compared to T3 alone (Fig. 23A,B).

The effect of T3 on ultrastructure of mitochondria was examined by transmission electron microscopy. The normal architecture of the mitochondria was lost, mitochondrial swelling is seen and cristae are damaged in T3 treated rat heart. Also, the ordered distribution pattern of mitochondrial in- between the myofibrils was disrupted. The overall normal architecture and distribution of mitochondria was restored when bezafibrate was co-administered along with T3.

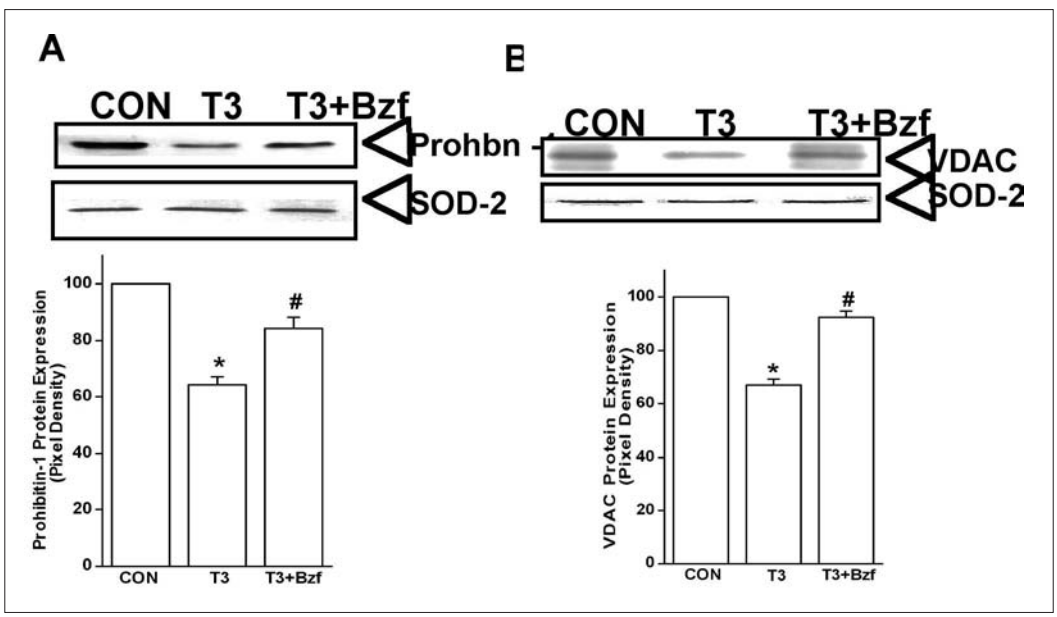


Fig. 23 : Bezafibrate inhibits structural damage of mitochondria in thyroid hormone treated rat heart. Representative immunoblots (A & B) show the level of Prohibitin-1 and VDAC protein in the mitochondrial fraction of LV tissues of vehicle (CON) or T3 (T3) or bezafibrate along with T3 (T3+Bzf) treated rats. The histograms show the average pixel density of 3 immunoblots after nornalizing with SOD2 protein expression.*p<0.01 control vs. T3 and $^{\#}p$<0.05 T3 vs.T3+Bzf (n=3) and complete data set is significant at <0.01 level (one-way ANOVA) for both (A &B).

Dr. Sib Sankar Roy and group

Pitx2 homeodomain transcription factor-mediated signaling in ovarian function

In ovarian adenocarcinoma cell line SK-OV3, PITX2-bound promoter sequences were identified by ChIP-on-Chip method. After validation, different WNT ligands were found to be up-regulated by PITX2 in this cell line. These identified WNT ligands, are the component of both canonical and non-canonical pathways. By controlling these genes, PITX2 regulates the ovarian cell growth and proliferation. A few identified target genes too are associated with cell proliferation. Their regulation of expression in normal as well as in cancer cells is being studied.

Our laboratory has shown the interaction of PITX2 isoforms with other homeodomain and non-homeodomain transcription factors in controlling their target genes in ovary. The sex-specific differential expression pattern of two specific isoforms of PITX2 has been shown during gonadal development and in adult stages (Fig. 24). Their interaction throughout the gonadal development has been studied.

Collagen metabolism and ovarian cancer

Regulation of collagen metabolism has been studied in ovary. Maintenance of normal collagen level is essential for the normal functioning of ECM. One of the most important enzymes required for the collagen biosynthesis is Procollagen Lysyl Hydroxylase (PLOD2). We have shown the regulation of

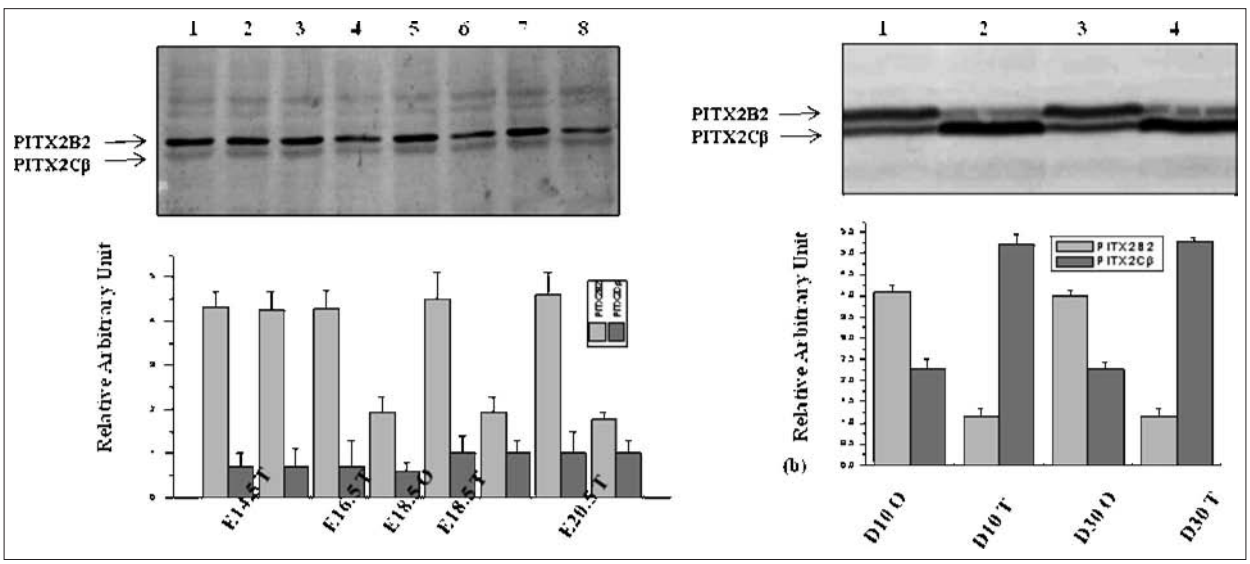


Fig. 24 : Comparative PITX2 protein expression profile in embryonic and postnatal rat gonads. Total tissue proteins from the embryonic (E14.5, -16.5, -18.5, -20.5) and postnatal gonads (D10, D30) were isolated as mentioned in methods section. The protein samples were subjected to 12% SDS-PAGE followed by subjected to western immuno-detection using Pitx2 specific antibody. Fig. 3a shows the PITX2 isoforms that expresses throughout the embryonic gestational days at E14.5, -16.5, -18.5 and -20.5 rat gonads are predominantly PITX2B2 and -Cβ along with very low level expression of PITX2B1 and Cα (Fig. 3a bands above -Cβ). The Fig. 3b shows the PITX2B2 and -Cβ are isoforms expressed at postnatal D10 and D30 gonads. The pixel density of the individual isoforms were measured using ImageJ software (NIH, USA) and shown below the specific lanes and respective isoforms are indicated with arrow. The β-actin protein expression was shown as loading control in these experiments (Fig. 3c and 3d). Below each bar diagram, the day and the tissue types are mentioned. The experiments were performed three times and the mean +SE value have been shown, *, P<0.05. 'O'-Ovary and 'T'-Testis.

Plod2 gene expression by Pitx2 homeodomain transcription factor. PITX2 binds to the bicoid elements of Plod2 promoter and that it is an upstream activator of Plod2 gene.

It is well known that few MMPs are associated with ovarian cancer. Some of these MMPs are regulated by Ets-related transcription factors including PEA3 in many tissues. We have shown the mechanism of VEGF-mediated activation of MMPs followed by invasion and scattering. In this aspect the role of Ets1 and Ets2 trans-regulators and different MAP kinase pathways have been shown. These factors influence the differential expression and nuclear translocation of Ets1 and Ets2 in this ovarian adenocarcinoma cell line, SKOV-3.

Insulin resistance and type 2 Diabetes

Mitochondrial dysfunction has been shown to be associated with insulin resistance and diabetes type 2, especially due to excess free-fatty acids, but the exact mechanism of this involvement is still unclear. The mitochondrial structural and functional defects have been shown in diabetic model system and in FFA-induced cells. The expression profile of the genes associated with mitochondrial function has been studied in palmitate-fed adipocyte and muscle cell lines and also in diabetic animal model. A few differentially expressed genes have been identified, which are very important for mitochondrial function. The exact mechanism of their altered function in free fatty acid-induced insulin resistance is being studied. The mitochondrial biogenesis and its membrane potential have been shown to be affected. Further, the regulatory factors associated with oxidative stress in insulin resistance have been identified. The mechanism of FFA-induced mitochondrial dysfunction leading to insulin resistance is being studied. As a part of the CSIR network project, three anti-diabetic molecules have been identified and their mechanism of action is being studied.

REPRODUCTIVE BIOLOGY

Dr. Syed N. Kabir and group

Physiological and pathophysiological aspects of female reproduction

Polycystic ovary syndrome (PCOS) is a heterogeneous clinical entity that encompasses broad spectra of ovarian disorders and metabolic syndrome. Recent studies document that a significant population of PCOS women do also suffer from hyperhomocysteinemia (HHcy); however, the cause and effect relationship remains elusive. We map some molecular cues to development of PCOS in an experimental rat model of HHcy induced by gavaging homocysteine through drinking water, and substantiate a causal role of HHcy in the pathogenesis of PCOS. The HHcy rats develop bilateral polycystic ovaries, hyperandrogenemia, and insulin resistance (IR). In one end HHcy induces IR and glucose intolerance by way of inhibiting glucose transport and preventing glycogen synthesis, while on the other end HHcy attenuates Wnt4 signaling cascade that triggers expression of steroidogenic acute regulatory protein and inhibition of p450 aromatase to overpower ovarian androgen synthesis. HHcy and hyperandrogenemia, individually or collectively, down-regulates follicular anti-Mullerian hormone and increases the number of recruited follicles in the growth trajectory. HHcy also down-regulates liver methylenetetrahydrofolate reductase and prohibits homocysteine transmethylation to help maintain the state of HHcy. Taken together, experimental HHcy in rats develops an array of biochemical and ovarian phenotypes that characterize the major morphologic as well as metabolic tenets of PCOS. We

conclude that HHcy may play etiologic roles in the pathogenesis of PCOS. It is also suggested that development of genetic model of HHcy by targeted gene deletion or transgenic expression of selective human genes may serve as a useful model of PCOS.

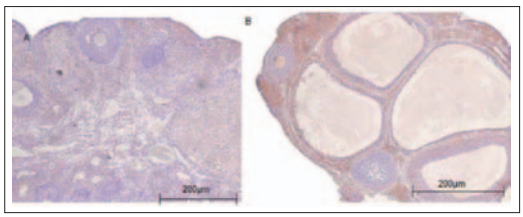


Fig. 25 : Control ovary (A) exhibits follicles at different stages of maturation, and the HHcy ovary (B) demonstrates cystic follicles.

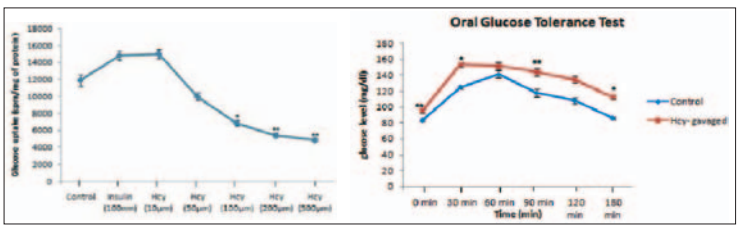


Fig. 26 : Hyperhomocysteinemia prohibits cellular uptake of glucose in vitro (A) and induces glucose intolerance (B).

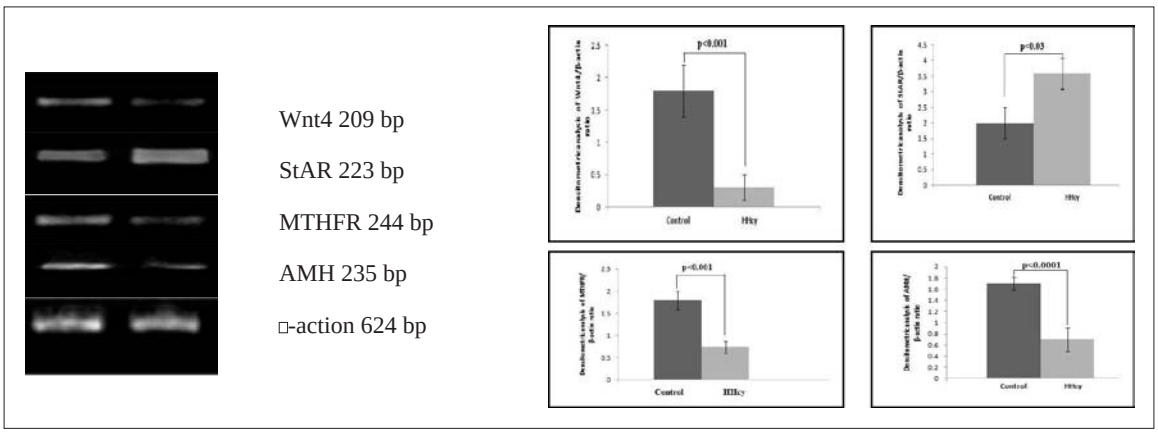


Fig. 27 : HHcy attenuates Wnt4 expression, triggers expression of steroidogenic acute regulatory protein (StAR), and down-regulates follicular anti-Mullerian hormone and liver methylenetetrahydrofolate reductase.

Animal model for premature ovarian failure

Ovary is a major target of galactose toxicity. Premature ovarian insufficiency (POI) is a frequent finding in women with galactosemia. We have earlier demonstrated that experimental galactose toxicity in rats induced by pre- and early postnatal exposure to high galactose produces sequelae of ovarian dysfunction including increased rate of follicular atresia that characterize the basic tenets of POI. galactose significantly down regulates ovarian growth differentiation factor-9 (GDF-9), an oocyte-specific factor that plays pivotal role in maintaining oocyte-granulosa-theca cell communications to promote follicular differentiation and maturation. Recent studies suggest that p53-mediated death pathways may be central in the induction of follicular atresia. There are reports that galactose up-regulates the expression of p53 that inversely correlates with GDF-9 expression. We further explored if ovarian toxic effects of galactose are mediated by p53-mediated GDF-9 down regulation pathway. The *in vitro* effects of galactose were studied in isolated whole follicles with respect to generation of reactive oxygen species (ROS) and expression of caspase 3, and in isolated granulosa cells in respects of mitochondrial membrane potential, expression of p53, and apoptosis.

Galactose exerted adverse effects on follicle survival. The galactose-exposed follicles were architecturally characterized by the presence of distorted oocytes surrounded by large number of scattered pyknotic

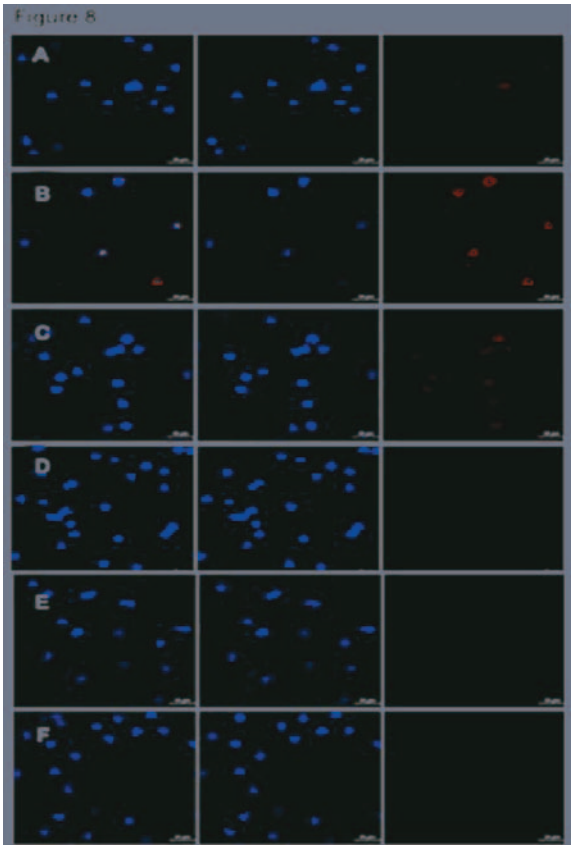


Fig. 28 : Reversal of galactose-induced granulosa cell p53 expression by co-treatment with E2 & FSH. Figure B demonstrates up-regulation of granulosa cell p53 expression over that of untreated control (A) following exposure to 50 nM galactose for 24 h. Co-treatment with 100 pg/ml E_2 (C) or 50 ng/ml FSH (E) partially reversed the galactose-induced expression of p53, while co-treatment with E_2 at 1 ng/ml concentration (D) or FSH at 200 ng/ml doses (F) reversed the p53 expression back to control level (A).

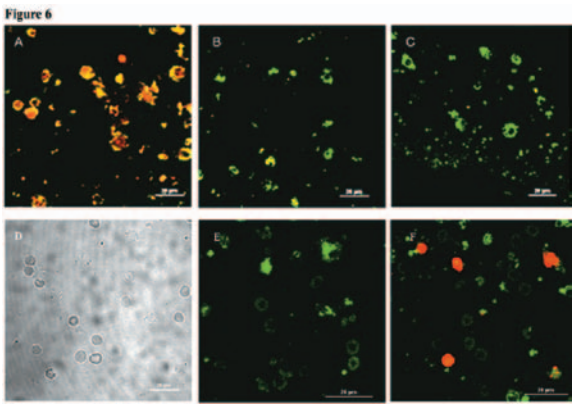


Fig. 29 : Confocal microscopic images of mitochondrial JC-1(A,B,C) and annexin V & propidium iodide (PI) fluorescence (D,E,F) in granulosa cells cultured in the absence (A,D) or presence (B&C and E&F) of galactose demonstrating galactose-induced disruption of mitochondrial membrane potential (B,C) and loss of membrane integrity (E,F) that characterize apoptotic death.

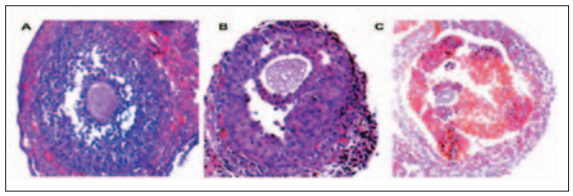


Fig. 30 : Follicles exposed to galactose at 50 nM (B) and 100 nM (C) concentrations exhibit large number of atretic cells.

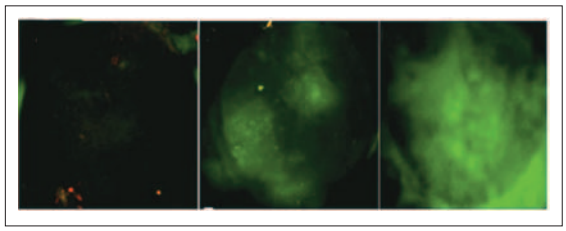


Fig. 31 : Follicles exposed to galactose at 50 nM (B) and 100 nM (C) concentrations show dose-dependent increase in intracellular ROS genaretion over that of the untreated control (A), as evaluated by fluorescence microscopy.

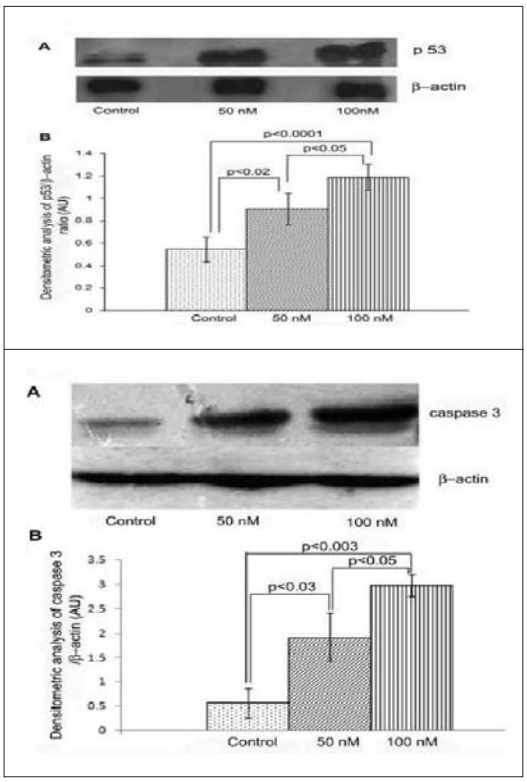


Fig. 32 : Representative immunoblots of caspase 3 protein in follicles cultured in the absence (control) and presence of galactose showing dose-dependent increase in the caspase 3 expressions.

granulosa cells arranged in asymmetric ring. In culture, galactose increased folliclular generation of ROS and expression of caspase 3. In isolated granulosa cells, galactose disrupted mitochondrial membrane potential, stimulated p53 expression, and induced apoptosis *in vitro*; however co-treatments with either FSH or estradiol significantly prevented galactose-induced granulosa cell p53 expression. Taken together with our earlier findings, the present submission interprets the observation to conclude that the ovotoxic effects of galactose involves attenuation of FSH bioactivity that renders the ovary resistant to gonadotrophins leading to increased granulosa cell expression of p53 and follicular atresia.

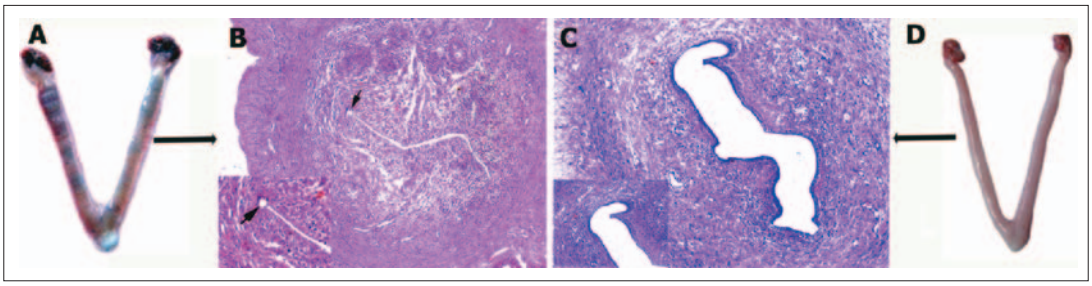


Fig. 33 : Anti-implantation activity of puerarin as evaluated by pontamine sky blue reaction (A,D), and uterine histoarchitecture (B,C) on D5.

Antifertility effects of puerarin

Postcoital contraception (PC) is one of the most widely accepted contraceptive options today. Emergency contraception is one of the most widely accepted contraceptive options today. We have earlier demonstrated that puerarin, an isoflavone glycoside isolated from *Pueraria tuberosa*, effectively prevents establishment of pregnancy in rats following administration once a day for two consecutive days after mating. This effect parallels with disruption of the downstream estrogen-signaling pathway as characterized by reversed ERα to ERβ ratio, that adversely alters the endometrial expression of leukemia inhibitory factor (LIF), cycloxygenase-2 and vascular endothelial growth factor - the three most important molecules known for their significant roles in signaling the process of implantation. Puerarin exerts neither blastotoxic, nor luteolytic effects. The pre-implantation ovarian estrogen secretory pattern also remained unaffected; however, puerarin attenuates progesterone action by down regulating uterine expression of progesterone receptor B (PRAB). The data taken together envisage puerarin as a prospective molecule that merits further exploration for the development of non-steroidal emergency/post-coital contraceptive for women.

Dr. Padma Das and group

Andrographolide analogue mediated apoptosis through Bad and Bax signaling and via mitochondrial pathways in human leukemic cells

The development of novel herbal remedies for the treatment of leukemia is important due to the side effects of existing synthetic pharmaceutical medications. We have previously shown that AG-4, an analogue of andrographolide induces apoptosis in leukemic cells. In our study we have found that growth of U937 cells was affected in the presence of Andrographolide analogue (AG-4) with an IC_{50} of 5.4 µM after 48 h treatment. AG-4 induced apoptosis was mediated by oxidative stress and showed involvement of mitochondrial pathway. Our result provided evidence that inhibition of growth is associated with increased ROS generation which leads to apoptosis induction through inhibition of

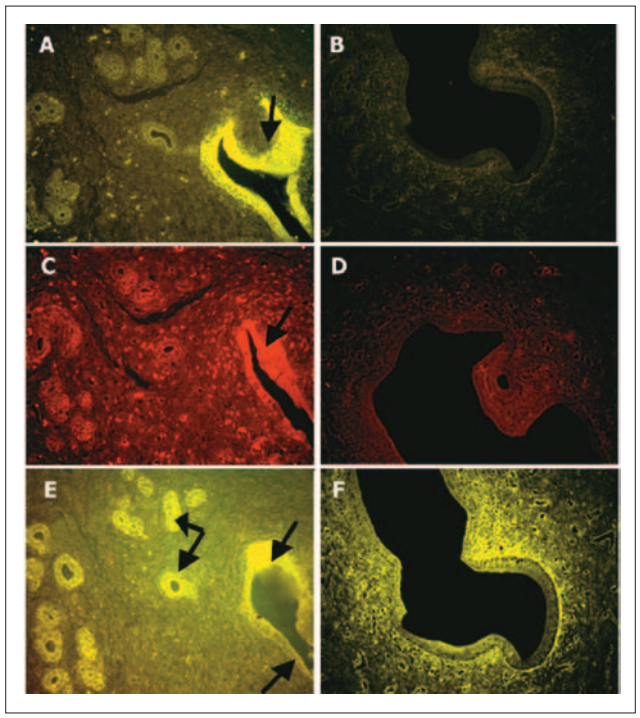


Fig. 34 : Overlaid fluorescence images of control (A, C, E) and puerarin-treated (B, D, F) day-5 rat uterus (x400) showing differential expressions of LIF (A,B), COX-2 (C,D), and VEGF (E,F). LIF is expressed in the control uterus (A) at the stromal cells surrounding the blastocyst. The treated rat uterus (B) shows absence of such signal.

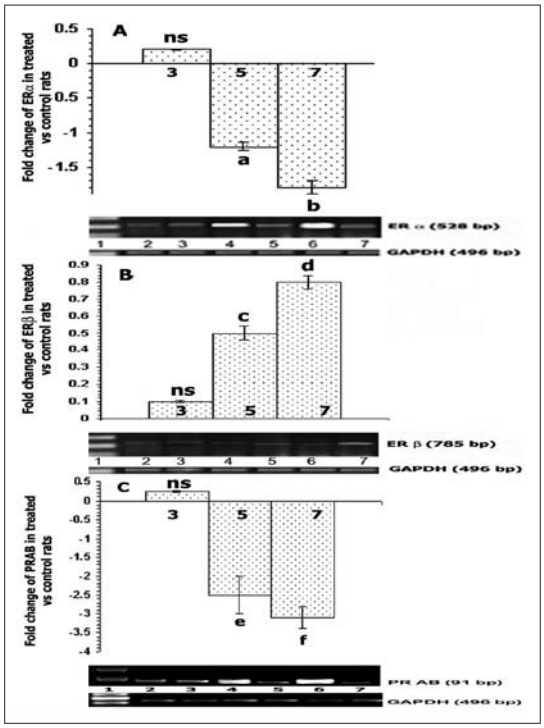


Fig. 35 : Relative expression of ERα, ERβ and PRAB mRNA in rat uterus during D3-D5 as measured by real-time RT-PCR. Puerarin treatment decreased ERα by >1.2 and >1.8 folds and increased ERβ levels by >0.5 and >0.8 folds on D4 and D5, as compared with the respective controls). PRAB mRNA levels decreased by >2.5 and >3.1 folds on D4 and D5 respectively ($P < 0.05$ vs D4 and D5 controls).

Bcl-2, Bcl-xl and concomitant stimulation of Bax, Bad protein expressions producing mitochondrial disruption, cytosolic Ca^{2+} elevation and the release of cytochrome-c. The released apoptotic proteins initiate caspase activation and PARP cleavage, trigger DNA fragmentation, cell cycle arrest and eventually cell death.

Role of the anti-proliferative activity of Sesbania Grandiflora

Sesbania grandiflora commonly known as "sesbania" and "agathi" is widely used in Indian traditional medicine for the treatment of a broad spectrum of diseases including inflammation, leprosy, gout, and rheumatism. The present study provides evidence for the antiproliferative effect of extract of *S. grandiflora* flowers in leukemic cell lines.The antiproliferative effect of *S. grandiflora* flower extract was evaluated by MTT assay. IC_{50} value of the extract in U937, THP1, HL60, Raji was found to be 18.5, 20.9, 24.6, 28.1 µg/ml. The subsequent studies were carried out in U937 cells. ROS generation was observed as early as 30 minutes after treatment. The apoptotic effect of *S. grandiflora* flower extract in U937 cells was ascertained by Annexin V assay. After 12 h, 24 h and 48 h of treatment, Annexin V positive cells increased to 18.2%, 41.0 and 57.7% respectively. After 24 h and 48 h of treatment, caspase 3 activity increased 1.5 and 4.2 times compared to control. Apoptotic U937 cells were identified based on alterations in their nuclear morphology detected by staining with Hoechst

33258. Taken together, our results suggest that *S. grandiflora* flower extract, induces apoptosis in human myeloid leukemic cells.

Regioselective one pot synthesis of 3,3'-diindolylethylene derivatives and study of their cytotoxic activity

2,2'-Diphenyl-3,3'-diindolylethylene (DPDIE) derivatives 3a-g were regioselectively prepared in one pot from indoles 1a-g in the presence of Lewis acids and were subsequently evaluated for cytotoxic activity against human leukemic cell lines, U937 and K562. The most potent compound 3g exhibited IC_{50} of 13.0-17.0 µM.

Studies of anticarcinogenic functions of compounds isolated from the edible mushroom

The main objective of the project is to study the anti proliferative effect of edible mushroom in different cancer cell line. We have just started this project and results are yet to be obtained.

Dr. Sandhya R. Dungdung and group

Biochemical and physical Characterization of Sperm Motility Inhibiting Factor from Caprine Epididymal Plasma

Epididymis plays a crucial role in the biochemical regulation of sperm motility. During transit through the epididymis the immature mammalian spermatozoa acquire forward progression, which is essential for their fertility potential. Recently from our laboratory a 160 kDa motility inhibiting factor (MIF) has been purified. The factor is a dimeric protein, made up of two subunits each having a molecular mass of 80 kDa as shown by SDS-PAGE (Fig. 36). The isoelectric point of MIF is 5.1 as determined by chromatofocusing and isoelectric focusing. It is a heat labile protein and maximal active at the pH 6.9 to 7.5. The sperm motility inhibiting protein factor at 2 µg/ml (12.5 nM) level showed maximal motility-inhibiting activity. The observation that the epididymal plasma factor lowered the intracellular

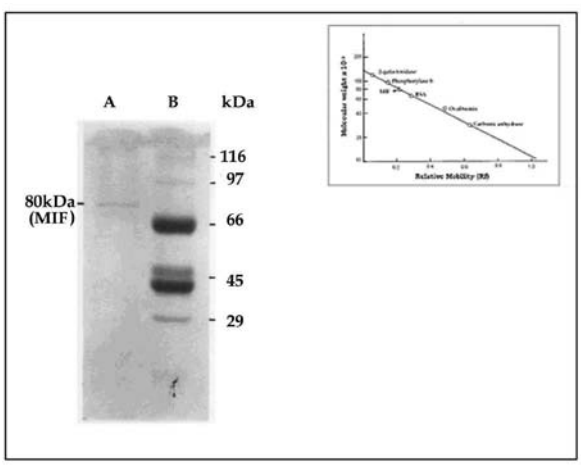


Fig. 36 : SDS-PAGE of MIF using 10% polyacrylamide gel.

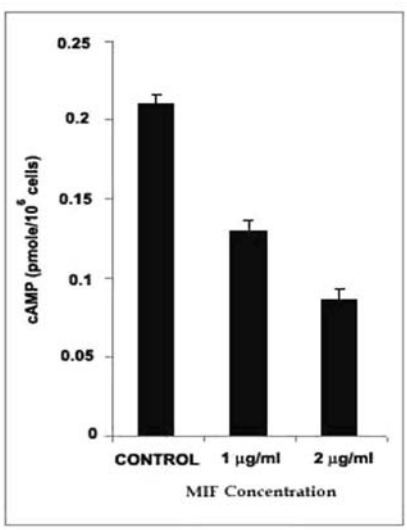


Fig. 37 : Effect of MIF on intracellular level of cAMP.

cAMP level of spermatozoa in a concentration-dependent manner suggests that it may block the motility of caprine cauda spermatozoa by interfering the cAMP dependent motility function (Fig. 37). The results revealed that the purified protein factor has the potential of sperm motility inhibition and may serve as a vaginal contraceptive.

Identification of cell surface molecules from caprine spermatozoa

Occurrence of a lectin like molecule and its receptor has been demonstrated on the maturing spermatozoa of goat epididymis. Purification and functional characterization of these molecules are under progress. The cell-surface lectin specifically interacts with receptor of the neighboring cells to cause autoagglutination demonstrated in the mid-phase of the maturing epididymal spermatozoa *in vitro*. Synchronous modulation of homologous cell surface lectin and their receptor as noted during sperm maturation constitutes a novel mechanism for cellular regulation by manipulating lectin-sugar interaction.

Further studies on upgrading the recently developed computerized spectrophotometric sperm motility analyzer (SPERMA)

Conventional methods measure sperm horizontal movement/velocity, which are not well correlated with male gamete's fertility potential. We have developed for the first time a novel computerized spectrophotometric sperm motility analyzer that specifically measures sperm vertical motility. Undertaking upward movement against gravity is much tougher as compared to horizontal movement. Consequently spermatozoa having high order of vertical velocity are likely to be better candidates for fertilizing ova. Calibration and Standardization of the SPERMA has been done with sperm cells of different species, like, goat, bull, rat, hamster and human. Biological correlation such as fertility potential of the vertical velocity of spermatozoa has been under progress. The development of multi-cuvette (multi-sample) and multi-height exposure system of the sample has been done with the collaboration with Indian Association for the Cultivation of Science (IACS), Kolkata and ELICO Ltd. Hyderabad as industrial partner (Fig. 38 A,B).

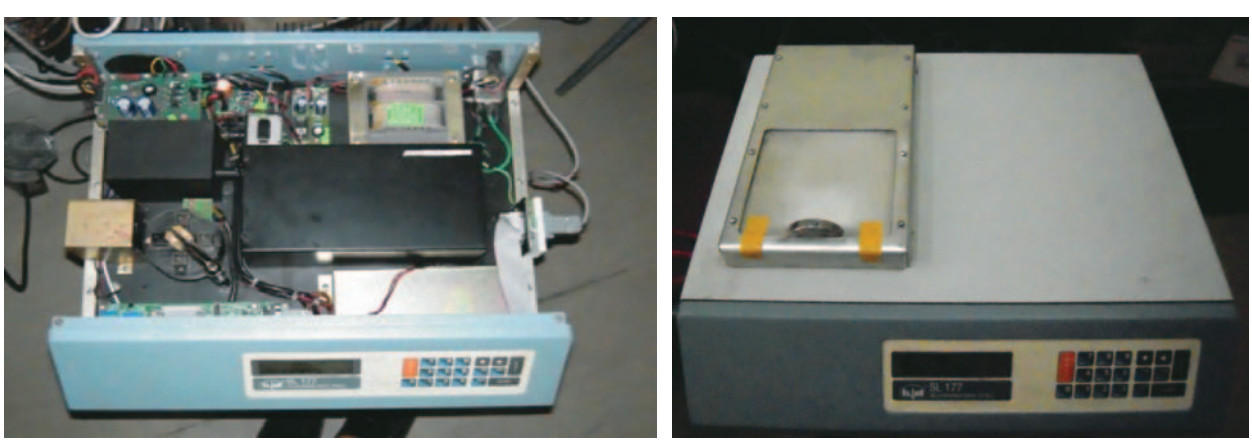


Fig. 38A & 38B : Modified SPERMA

GENE REGULATION & METAGENOMICS

Dr. Tushar Chakraborty and group

Metal Microbiome and Metagenomics

Interest in the action of microorganisms in metal bioleaching and metal bioremediation is increasing in parallel to exploitation of leaching and remediation techniques. As most of these operations are carried out in open or semi-open conditions, in large heaps or tanks, efficiency of these operations are subject to various local physical and ecological parameters. Our previous studies indicate, that dynamic flux of microbial population is involved, which adds further level of complexities.

The microbial community soil copper and uranium mines are being analyzed to identify and characterize iron and metal reducing bacteria which can concentrate, sediment out, or fix toxic heavy metals. We collected samples for isolation of native bacteria from Maanjkhand mine, tailing ponds, and trial bioleaching heaps. Characterisation, and culture of bacterial, fungal isolates are being carried out. We are doing metal tolerance study against copper, cadmium, mercury and uranium. We are doing both static and dynamic study of microbial population shift in flask as well as column, through time series analysis. The metrics are being established based on acid production and acid utilization potential. The efficiency of the process are also temperature dependent in the range of 25- 55 °C.

Batch culture of the mixed population gives very different result from column culture. The cells and products both are released at different rate. The optimal pH for Cu removal was found to be around pH 5.4 in column leaching mode, and pH 6.0 for U. Biogenic extraction of copper and uranium also involves different, but partially overlapping sets of microorganisms.

Development of Biodegradable & Green Oganozeolites

In Collaboration with Dr Arindam Bandyopadhyay (IACS): Nanomatrials are often found to be highly refractory towards biodegradation. We have developed a novel strategy to biodegrade organozeolite nanomaterials - which forms stable nanostructures even in solution state. These unusual peptide-based organozeolites were previously shown to be refractory towards Proteinase K digestion. When we tested their impact on selected laboratory strains of *E Coli* and *Psedomonus species*, we found these materials to be detrimental to their growth. However, usng a novel selection strategy we have been able to select a group of soil microorganisms which can biodegrade and use these peptide based nanomaterials as carbon and nitrogen source. Characterization of these groups of organisms is now underway.

The Human Polyoma Virus Genomic Typing

In collaboration with Dr Saumen Bhattacharjee (NBU): Human polyoma virus is endemic among Indian population. The viral reactivation and shedding has been extensively studied in our laboratory, and we have reported several genotypes of BKV from Indian subjects. Our previous genotyping was mostly based on the heterogeneous promoter- enhancer region, which is the conventional method for genotyping and classification of this type of polyomavirus. Now we have focused on the non-conventional large T-antigen and VP3 genes. The association of neoplasia and mutation are being interrogated in this new window. Two potential hot spots have surfaced out. The sample size is being

increased to confirm these novel findings. The polyomavirus JCV evolution and interrelationship between indigenous populations of north Bengal region are also being investigated.

Technology, Risk, and Perception Analysis : GMO in Indian Context

The introduction of new scientific and technology in society often creates confusion and resistance. For democratic society, like India, this poses a major challenge. The science, society, technology interface is a difficult terrain. My aim in this project is to gain direct knowledge of this landscape both as an analyst and as a participant. Using GM food and agriculture as a case study, I am analyzing various agencies and actors operating in this field, and comparing and contrasting this with the National and International scenario. My analysis and praxis shows, that the perception of science and technology by common man is undergoing a profound change, and their stand or opinion is increasingly being moderated (if not determined) by economic status.

SIGNAL TRANSDUCTION IN CANCER & STEM CELLS

Dr. Mrinal K. Ghosh and group

Signal Transduction in Cancer & Stem Cells

Cancer is one of the major health issues in all developed countries and the molecular mechanisms that directly control the initiation and progression of cancer remains uncharacterized. Our research group is involved in studying the functional role of important molecular factors like Stat3, MAPK, Akt, and β-catenin. We are trying to elucidate the molecular signaling pathways responsible for initiation and progression of cancers. We have tried to establish a relation between STAT3 activation pathway and Wnt/β-catenin signaling in glioblastoma and prostate cancer. The crosstalk of these pathways on the cell cycle profile is under investigation.

We are also investigating the role of p68 in cancer. p68 (Ddx5), a member of the DEAD box family RNA helicases, has been implicated in growth regulation and has been shown to be involved in both pre-mRNA and pre-rRNA processing. We found that upon exogenous expression of WT-TCF4 there was an increase in p68 mRNA levels, indicating regulation of p68 by Wnt signaling. It was also observed that p68 knockdown decreases the TCF4 expression. Indications suggest p68 may be involved in regulating the expression of TCF4 and β-catenin and also TCF4 dependent gene expression through TCF4 expression.

The threshold level of several molecules, tumor suppressors and oncoproteins, involved in these complex signaling mechanisms are maintained by the equilibrium between synthesis and degradation (Fig. 39), regulating the turnover of these molecules in the cell. Here comes into play the ubiquitin-proteasome system (UPS). We are looking at both aspects of ubiquitination and deubiquitination of some of the key players important in cancer. Some of the recent findings in our laboratory reveal that the UPS plays an indispensable role in regulating c-Myc. Over-expression of c-Myc is a hallmark of human cancers. Genetic amplifications (colon cancer), insertions (cervical cancer) and translocations (Burkitt's lymphoma) of c-myc gene were identified as the causal mechanism for aberrant over-expression of c-Myc protein. Several reports have now established that in many cancers c-Myc is accumulated due to its prolonged half-life contributing to an uncontrolled proliferation of cancer cells.

Till date, six different E3 ligases have been implicated in regulating c-Myc protein stability through

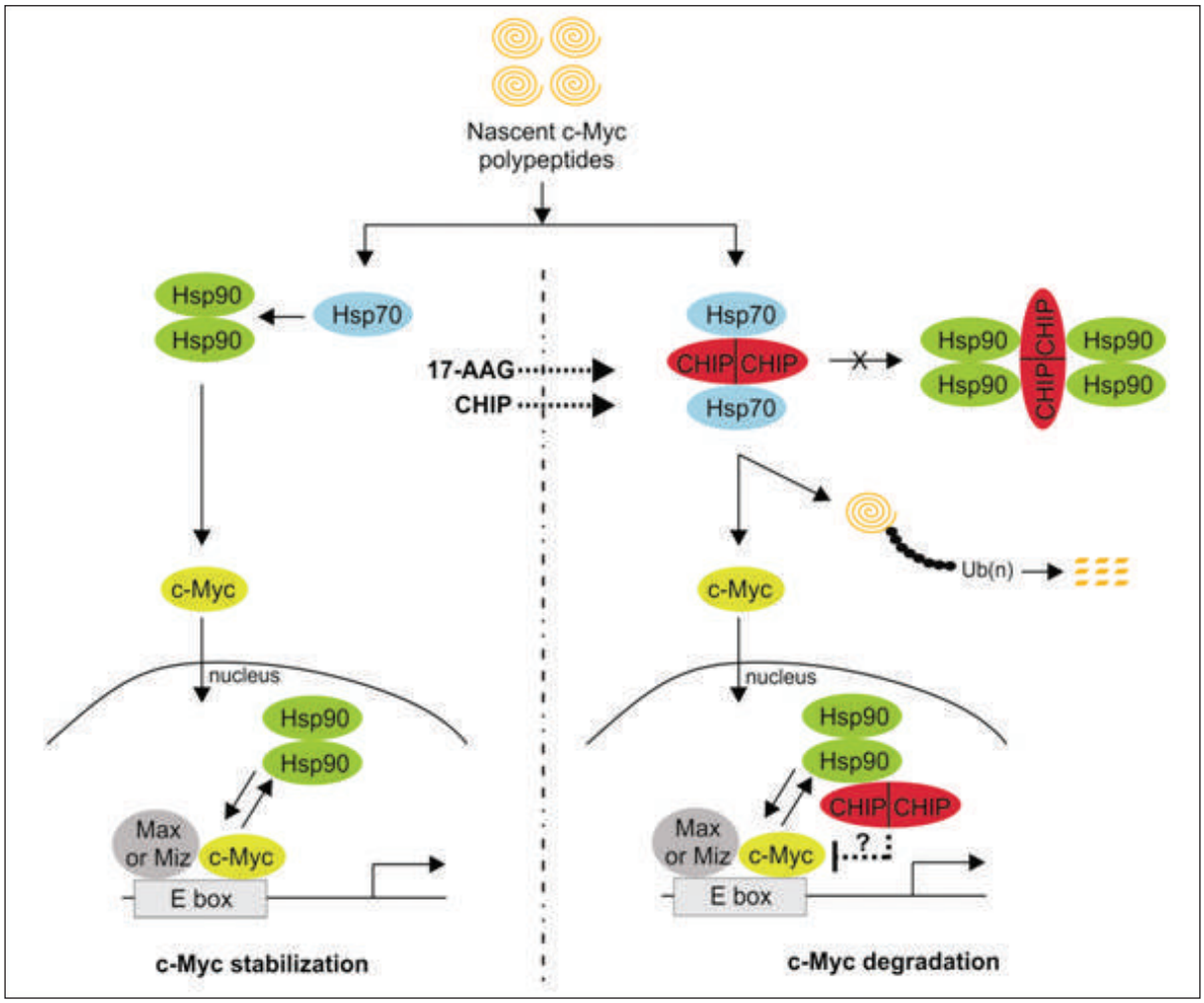


Fig. 39.

the UPS. We have identified CHIP as a novel E3 ligase of c-Myc which degrades c-Myc and reduces its transcriptional activity. Unlike all the previously reported E3 ligases implicated in c-Myc regulation, CHIP is the only U-box containing and chaperone associated protein. We show that CHIP and c-Myc can co-exist in the same complex and that c-Myc is a substrate for CHIP. Our data demonstrates that CHIP mediated degradation of c-Myc antagonizes c-Myc transcriptional activity.

In summary, our work provides compelling evidence for a significant role of CHIP in regulating c-Myc protein abundance in the cell and its transactivation potential. Our observations raise many important physiologically relevant questions such as what proportion of c-Myc is regulated by the multiplicity of mechanisms under various contexts. The ability to channel a polypeptide towards degradation pathway provides a means for the cell to dispose-off damaged, slowly folding or over-expressed proteins. Therefore, this study undermines the importance of the chaperone system in regulating protein stability and provides alternative avenues for curbing c-Myc function in cancer.

Technical Staff

Dr. Herambananda Ray, Mr. Swapan Mandal, Ms. Banasree Das, Mr. P. C. Deuri and Mr. Prabir Kumar Dey.

RAs, Pool Officers, SRFs and JRFs

Mr. Vivek Chander, Mr. Priyam Banerjee, Mr. Somaditya Mukherjee, Ms. Subhagata Roychowdhury, Dr. Kaushik Das, Dr. Sudipta Saha, Mr. Sujoy Das, Miss Arpita Bhoumik, Mr. Kaustav Dutta Chowdhury, Mr. Dijendra Nath Roy, Mr. Samir Mandal, Mr.Tathagata Sengupta, Ms. Ambili Appukuttan, Ms. Debasmita Tripathy, Mr. Joy Chakraborty, Mr. Amit Naskar, Mr. Raghavendra Singh, Mr. Debashis Dutta, Ms. Nilufar Ali, Dr. Emili Banerjee, Dr. Kusumika Gharami, Mr. Deepak Kumar, Ms. Ayantika Paul, Ms. Anindita Chakraborty, Mr. Tuhin Subhra Banerjee, Ms. Maitreyi Das, Dr. Sonali Ghosh, Ms. Debanjali Mitra, Mr. Shyam Sundar Nandi, Ms. Moitri Basu, Mr. Sudarshan Bhattacharya, Ms. Nabanita Das, Ms. Tapashi Mandal, Mr. G. Kiran Kr. Naidu, Mr. Indranil Paul, Ms. Seemana Bhattacharya, Mr. Anirban Chatterjee, Ms. Nilanjana Das, Ms. Moumita Sarkar, Mr. Syed Feroj Ahmed, Mrs. Nandini Chatterjee, Mrs. Rumana Akhter, Mr. Priyankar Sanphui, Ms. Pampa Saha, Ms. Suraiya Saleem, Ms. Poornima Chandran, Ms. Piyali Das, Ms. Sayani Banerjee, Mrs. Prarthana Chatterjee, Woman Scientist, Ms. Ghoongroo Saraswat, Mr. Deepak Kumar, Ms. Rajneeta Roy and Mr. Abhinaba Sinha.

Project Assistant/Project Associate and Trainees

Mr. Dipak Kar, Ms. Tanima Banerjee, Mr. Prasanta Ghosh, Dr. Gargi Sen, Mr. Avik Sarkar, Shreya Roy Chowdhury, Mr. Arijit Bhowmik, Ms. Satamita Deb and Dr. Neela Dey.

Network Project

ELEVENTH FIVE YEAR PLAN (2007-12) PROJECTS

In **11th Five Year Plan**, IICB is involved in 20 projects consisting of 4 Nodal Network Projects and 16 Partner Network Projects. In Partner Network Projects there are two extension Projects of Tenth Plan. One of the projects of Xth plan COR-023 is continuing in XIth Plan period as NWP-037. All the projects are mainly from Biology & Biotechnology sector except one nodal network project (NWP-033) which is from Pharmaceuticals, Healthcare & Drugs sector. During this reporting year (2010-11) R&D works of two new Interagency projects have been started, one is entitled, "Metabolic Engineering of Vinca Alkaloid Pathway" and the other entitled, "Multi-agent Therapy of Cancer: a System Biology approach".

No.	Project Title & Short Name	Project Code	Type of Project	Nodal Lab.	Nodal Scientist of IICB
1.	Evaluation and correction of mitochondrial dysfunction in disease **(Mitochondria)**	**SIP-007**	Supra-institutional	IICB	Dr. Samit Adhya
2.	Engineering peptides and proteins for new generation therapies **(Protein Engineering)**	**NWP-005**	Nodal Network	IICB	Dr. Anil K. Ghosh
3.	Development of diagnostics and target-based molecular medicines against allergy, bronchial asthma and chronic obstructive pulmonary disease **(Asthma)**	**NWP-033**	Nodal Network	IICB	Dr. Arun Bandyopadhyay
4.	New insights in cancer biology: Identification of novel targets and development of target based molecular medicine **(Cancer)**	**IAP-001**	Nodal Inter-agency	IICB	Dr. Susanta Roychoudhury
5.	Plasma Proteomics in health, environment and disease (**Plasma Proteomics**)	**NWP-004**	Partner – Network	CCMB	Dr. Rukhsana Chowdhury
6.	Nanomateials and nano-devices for application in health and disease **(Nanomaterials)**	**NWP-035**	Partner – Network	CCMB	Dr. Arindam Banerjee
7.	Pathway engineering and system biology approach towards homologous and heterologous expression of high-value phytoceuticals **(Pathway Engineering)**	**NWP-008**	Partner – Network	CIMAP	Dr. Debasish Bhattacharya
8.	Biological and chemical transformation of plant compounds for production of value added products of therapeutic/aroma value **(Aroma Value)**	**NWP-009**	Partner – Network	CIMAP	Dr. Sibabrata Mukhopadhyay
9.	Identification and validation of drug targets for selected pathogens of national importance (**Drug Target**)	**NWP-038**	Partner – Network	CDRI	Dr. Pijush K. Das
10.	*Diabetes mellitus* – New drug discovery R&D, molecular mechanisms and genetic and epidemiological factors **(Diabetes)**	**NWP-032**	Partner – Network	CDRI	Dr. Sibsankar Roy

No.	Project Title & Short Name	Project Code	Type of Project	Nodal Lab.	Nodal Scientist of IICB
11.	Zero Emmision Research Initiative **(Zero Emission)**	**NWP-044**	Partner – Network	CLRI	Dr. Suman Khowala
12.	Exploitation of India's rich microbial diversity **(Metagenomics)**	**NWP-006**	Partner – Network	IMT	Dr. Tushar Chakraborty
13.	Comparative genomics and biology of non-coding RNA in human genome **(Micro-RNA)**	**NWP-036**	Partner – Network	IGIB	Dr. G. Suresh Kumar
14.	Drug Target Development using In-silico Biology (**In-silico Biology**)	**CMM-017**	Partner – Network	IGIB	Dr. Chitra Dutta
15.	Discovery, Development and Commercialization of New Bioactives and Traditional Preparations **(Bioactive)**	**NWP-037**	Partner – Network	CSIR-HQ	Dr. Pratap K. Das/Dr. HK Majumder
16.	Integrated Analysis for Impact, Mitigation and Sustainability (IAIMS): Regional Climate Modelling at Decadal Scale **(Climate Change)**	**NWP-052**	Partner – Network	CMMACS, Bangalore	Dr. A.K. Giri
17.	Designing potential lead molecules for inhibition of siderophore biosynthesis in *M. tuberculosis*	**HCP-001**	Partner – Network	CSIR-HQ	Dr. N. Ghoshal & Dr. P. Jaisankar
18.	Synthetic Biology and metabolic engineering of Azadirachtin biosynthesis pathway	**HCP-002**	Partner – Network	CSIR-HQ	Dr. R. Bhadra
19.	Metabolic Engineering of Vinca Alkaloid Pathway	**HCP-003**	Partner – Network	CSIR-HQ	Dr. R. Bhadra
20.	Multi-agent Therapy of Cancer: a System Biology approach	**HCP-004**	Partner – Network	CSIR-HQ	Dr. Susanta Roychoudhury

NODAL PROJECTS

1. Title: Evaluation and Correction of Mitochondrial Dysfunction in Disease

Project: Supra-institutional [SIP-007]

Objectives:

[i] To investigate alterations in mitochondrial genes and proteins in primary open angle glaucoma (POAG), using POAG DNA samples and ocular cell models.

[ii] To investigate mutations in the mitochondrial genome and abnormalities of mitochondrial function in relation to the diverse phenotypes among patients with Wilson's disease.

[iii] To investigate mitochondrial gene expression and oxidative stress in hypertrophic heart induced by hyperthyroidism excess of anti-inflammatory drugs.

[iv] To test whether neurodegeneration and mitochondrial decline are correlated in human patients and in animal models of Parkinson's disease

[v] To investigate mitochondrial dysfunction in diabetes type 2 with special emphasis on the role of PGC1α and uncoupling proteins.

[vi] To investigate mitochondria of eukaryotic pathogens as possible targets for correctional measures.

[vii] To study the role of mitochondrial Reactive Oxygen Species in cancer cell apoptosis and drug resistance.

[viii] To examine mitochondrial functions in ischemic brain (rat model of neurodegenerative diseases) and delivery of correctional complexes and nanoparticles to such brains.

[ix] To develop strategies to correct the effects of disease-causing mitochondrial tRNA mutations (e.g., the tRNALys mutation in Myclonic Epilepsy with Ragged Red Fibers) using a tRNA import complex in patient-derived cybrid models, to develop methods for RNA delivery to mitochondria, and to study the pathways of the intracellular uptake and targeting of such complexes to mitochondria.

[x] To study the role of *Plasmodium falciparum* mitochondria for the parasite growth and liver mitochondrial dysfunction and associated apoptosis during host-parasite (malaria) interaction.

[xi] To study mitochondrial disorder on the development of *Helicobacter pylori* mediated and non-mediated gastropathy.

Significant achievements made during the fourth year (2010-2011):

Significant achievements: Development of new method for mitochondrial RNA therapy

Scientific Excellence

(A) Basic Research Outputs

- A cybrid containing a 1.9-kb mtDNA deletion from a patient with Kearns Sayre Syndrome is respiration-defective and grows glycolytically. When treated with a ribonucleoprotein (RNP) complex of polycistronic RNA 1 (pcRNA1) and a multi-subunit carrier complex, full-length pcRNA1 was co-transported with R8 to mitochondria, to correct the respiration defect.
- We have generated a cell line, EB delta1, with multiple mtDNA deletions, that is respiration-defective and generates high levels of superoxide, a reactive oxygen species. Treatment of EB delta1 with tagged polycistronic (pc) RNAs, encoding parts of the mitochondrial proteome, bound to a multi-subunit carrier complex, resulted in cellular uptake and transfer of the RNA to mitochondria, restoration of respiration, and suppression of superoxide levels by individual or combinations of pcRNAs.
- The mechanism of action of heme oxygenase-1 (HO-1) in mitochondrial oxidative stress (MOS)-mediated apoptotic tissue injury has been investigated *in vivo*. HO-1 is not only induced but also translocated to mitochondria during gastric mucosal injury to favor repair mechanism. Furthermore, mitochondrial translocation of HO-1 results in the prevention of MOS and mitochondrial pathology as evident from the restoration of complex-I driven mitochondrial respiratory control ratio (RCR) and transmembrane potential ($\Delta\Psi m$).
- Free fatty acid, especially palmitic acid causes increased oxidative stress and high rate of superoxide

production in muscle cells. Several important genes associated with oxidative stress are also down regulated.

- *Leishmania* parasites impair the generation of reactive oxygen species (ROS), which is a major host defense mechanism against any invading pathogen. *Leishmania donovani* infection is associated with strong up-regulation of uncoupling protein 2 (UCP2), a negative regulator of mitochondrial ROS generation located at inner membrane of mitochondria. *in vitro* knockdown of macrophage UCP2 was achieved by siRNA-mediated silencing resulting in increased mitochondrial ROS generation, lower parasite survival and induction of marked pro inflammatory cytokine response.
- Peroxisome proliferator activated receptor alpha (PPAR α) signaling is critically involved in thyroid hormone induced mitochondrial dysfunction and overt heart disease.
- Analysis of variants in Progressive Open Angle Glaucoma (POAG) patients and controls elucidated statistically higher difference in frequency of variants among patients and controls, with higher number non-synonymous changes accumulating in Complex I in the patients. Analysis of individual genes shows a significantly higher proportion of variants in ND5 and 12S rRNA genes in patients.
- A total of 12 control (CyC) and 16 Parkinson's Disease (PD) cybrids (CyPD) are created and are maintained in the lab during this period of study.

(B) Technologies developed

Development of a new method for mitochondrial gene therapy: Mitochondrial dysfunction has been documented in a broad spectrum of human diseases but currently there is no effective way to deliver therapeutic nucleic acids to mitochondria. A Leishmania-derived RNA Import Complex isolated previously at IICB was shown for the first time internationally to be capable of efficiently delivering functional RNA to mitochondria. A new protocol for preparation and use of the RNA and carrier complex has been submitted for international patent protection.

R&D Outputs up to the fourth year (2007-11):

Patents: 1 (one)
Total Number of Publications: 31 (thirty-one)
Doctorates from the Project: 15 (fifteen)

2. Title: Engineering Peptides & Proteins for New Generation Therapies.

Project: Nodal Net Work [NWP-005]

Nodal Laboratory: Indian Institute of Chemical Biology (IICB), Kolkata

Participating CSIR Institutes:

Institute of Microbial Technology (IMT), Chandigarh

Institute of Genomics and Integrative Biology (IGIB), Delhi

Centre for Cellular and Molecular Biology (CCMB), Hyderabad

Central Drug Research Institute (CDRI), Lucknow

Objectives:

[a] To engineer defensins of lesser complexity and enhanced anti-microbial properties.

[b] Designing and development of some novel small anti-microbial peptides with reduced toxicity.

[c] Development of peptidomimetics to block protein-protein interaction at the same time membrane penetration capability and increasing bioavailability.

[d] To study protein mis-folding and aggregation through engineering protein that does not mis-fold and aggregate.

[e] To engineer small peptides, which are equivalent to larger transcription factor-with Protein Transduction Domains for cell entry.

[f] Designing and development of recombinant proteins with much more stability and reduced toxicity, which can be used to cure certain life threatening diseases.

[g] New engineering techniques will be developed to produce proteins with new activities: implication in vaccine developments.

[h] To develop process for production of engineering protein.

[i] To engineer streptokinase having weaker immune response towards increasing their utility.

Progress so far and Outcomes achieved in terms of contribution to science, Technology development & commercialization :

1. Design and development of Proteins/ Peptides with increased bioactivity.
2. Branched peptide against melanoma - Provisional patent filed.
3. Branch peptide of IKK-β with anticancer activity.
4. Peptide immunogens for development of malaria vaccine.
5. Antimicrobial peptides with modulated toxicity.
6. Glutathione-S-transferase (GST) from Alternaria, human interferon beta in E.coli, serine protease from *Curvularia lunata.*
7. Fourth generation thrombolytic molecule in which anti-thrombin domains are strategically fused between the domains of streptokinase. Plasminogen activation and Protein C activation have been shown to be successful in the construct, leading to a strong candidate for advantageous thrombolysis.
8. Novel analogues of cathelicidin derived bovine antimicrobial peptides BMAP-27 and BMAP-28 and bee venom antimicrobial peptide, melittin, which showed significantly reduced toxicity but comparable bactericidal activities to their parent molecules against the tested bacteria.
9. Novel catalyst for the biofuels area consisting of the catalytic domains of an endoglucanase from *Rhodothermus marinus* (224 aa), an exoglucanase from *Cellulomonas fimi* (643 aa) and a beta-glucosidase from *Streptomyces* sp. QM-B814 (479 aa), along with a cellulose-binding domain (CDB) of one of the cellulases of *C. fimi* and expressed in the form of a fusion protein.
10. Variants of defensins with improved antimicrobial activity

11. Understanding of designing of new therapeutics:

11.1. Deamidation mediated inactivation and role of Protein Isoaspartyl Methyl Transferase in reactivation of enzymes: Deamidation mediated inactivation was studied in three enzymes Alcohol Dehydrogenase, Acid Trehalase from *S. cerevisiae* and Endo-xylanase from *Termitomyces clypeatus*. Stress induced and spontaneous deamidation was investigated with Electrophoretic mobility, MALDI TOF analysis, Isoaspartate formation and ammonia released. Significant levels of ammonia loss and Isoaspartate formation was achieved by extrinsic factors like pH and temperature whereas spontaneous deamidation resulted in accumulation of negative charges on the protein surface which showed difference in electrophoretic mobility. Deamidation affected the enzyme substrate reaction cycle decreasing the catalytic efficiency of the enzymes. Heat inactivated enzymes were able to regain their partial activity with the aid of repair conducted by Protein Iso aspartyl methyl transferase. This enzyme selectively methylates the Isoaspartyl residues and converts them into normal L aspartyl residues in proteins.

11.2. Role of Arginine and mechanism of its action in inhibiting protein aggregation: The addition of arginine has been found to inhibit aggregation of a number of model proteins at pH 7.5. The mechanism of its effect on the conformation and microsecond dynamics of cytochrome c and other model proteins has been investigated by fluorescence correlation spectroscopy at single molecule resolution. The results show the formation of an intermediate state in the unfolding pathway, which is inhibited by the addition of arginine. Arginine and other solution additives interact with the unfolded states leading to a large decrease in the surface accessibility of the unfolded chain. In addition, the results indicate that arginine may have affinity towards the native state or native like states. A number of arginine derivatives are being synthesized to study the effects of structural variation of arginine to protein aggregation.

11.3. Dominance of an epitope in the context of another protein: implication in vaccine development: In a peptide vaccine it is important that the immunodominant epitope is presented in the right context. Our studies showed that dominance of a known in the context of an unrelated protein is not always intrinsic. Such defects in the immunodominance may have serious implication in the peptide vaccine development.

R & D Outputs during the tenure (2007-11):

Publication in SCI Journals: 78 (18 publications, year 2010 - 11)

Patents (India & Foreign): 3 Indian and 1 US patent (1 patent, 2010-11)

Technologies transferred to industry: Will be done in future

Other Important Achievements: 2 Ph.Ds awarded, 6 Ph.Ds ongoing, 10 Post-M.Sc Training

3. Title: Development of diagnostics and target-based molecular medicines against allergy, bronchial asthma and chronic obstructive pulmonary disease

Project: Nodal Net Work [NWP-033]

Nodal Laboratory: Indian Institute of Chemical Biology (IICB), Kolkata

Participating CSIR Institutes:

Institute of Genomics and Integrative Biology (IGIB), Delhi

Indian Institute of Chemical Technology (IICT), Hyderabad

Industrial Toxicology Research Centre (ITRC), Lucknow

Indian Institute of Integrative Medicine (IIIM), Jammu

Objectives:

[a] Development of animal model for asthma for evaluation of lead molecules in vivo.

[b] Testing 2-3 lead molecules for anti-asthma activity.

[c] To synthesize NCEs for the biological evaluation as PDE-4 inhibitors.

[d] Toxicological and safety evaluation of lead molecules with anti-asthmatic activity; and evaluation of drug efficacy by plethysmography.

[e] Basic research on the role of Stat3 and Socs3 in asthma pathogenesis.

[f] Determination of Pharmacokinetics, Absorption/ Transport, Biotransformation, and Distribution studies.

Progress so far and outcomes achieved in terms of contribution to science, technology development:

(i) Three molecules ICB/11/D-8, ICB/14/C-6 and ICT-TA67 have been identified as potential anti-asthmatic molecules.

(ii) The synthetic route of ICB/11/D-8 is established and this molecule is being synthesized for further studies.

(iii) Synthetic ICB/11/D-8 has strong PDE 4 inhibitory activity in the range of nM.

(iv) Toxicity, pharmacokinetics and in vivo efficacy test of ICB/11/D-8 and ICT-TA67 have been completed.

(v) Mouse model of asthma has been developed in IICB.

(vi) In vivo efficacy of ICB/14/C-6 with IICT/TA-67 in combination show antiasthmatic activity.

Identification of New lead from herbal source:

(i) New plant sources have been identified for finding out potential leads: ICB-25/A001, ICB 26/A001 showed significant inhibition of PDE 4 activity.

(ii) ICB/38 and ICB/38/K are identified as pure compounds with strong PDE4 inhibitory activity.

(iii) ICB/38 shows anti-inflammatory molecule in vitro.

R & D Outputs during the tenure (2007-2010):

Total published paper during the tenure: 31 (Thirty-one)

Patent Submitted : 1 (one)

Technologies transferred to industry: Will be done in future

4. Title: New Insights in Cancer Biology: Identification of Novel Targets and Development of Target Based Molecular Medicine

Project: Inter Agency [IAP-001]

Nodal Laboratory: Indian Institute of Chemical Biology (IICB), Kolkata

Participating CSIR Institutes:

Indian Institute of Chemical Technology (IICT), Hyderabad

Centre for Cellular and Molecular Biology (CCMB), Hyderabad

Central Drug Research Institute (CDRI), Lucknow

Institute of Genomics and Integrative Biology (IGIB), Delhi

Central Glass & Ceramic Research Institute (CGCRI), Kolkata

National Inst. for Interdisciplinary Science & Tech. (NIST), Thiruvananthapuram

Participating Non-CSIR Institute:

National Center for Cell Sciences (NCCS), Pune

Objectives:

1. Identification of new lead molecules from herbal and synthetic sources against specific cellular targets using high throughput approaches.
2. Identification of novel anticancer targets based on the knowledge gained from molecular analysis of tumorigenic processes.
3. Generation of library of small molecules by diversity-oriented chemistry.
4. Deciphering the regulation of expression of target genes in normal and cancer cells.
5. Understanding the molecular interactions between target proteins and their partners.
6. Nano-structered calcium phosphate-based ceramics as drug carrier for the treatment of hepatocellular carcinoma in animal model.
7. Multi-agent-based simulations of collective cell behaviors with application to cancer.

Significant achievements made during the third year (2009-11):

Objectives 1 & 3:

- Sixteen pure compounds were tested for anti-cell proliferation activity in six different cancer cell lines. One of them showed good anti-proliferative activity (IC_{50}<10ug/ml) against several of these cell lines while two were active against only few selective cell lines. (IICB).
- Twenty numbers of derivatives of two previously active scaffolds were synthesized. Six of them were tested. One derivative showed higher activity than the parental one and other did not show activity. Additionally, few more derivatives of different nature of that compound have been synthesized. They are now being investigated (IICT).

- Eight hundred fifty-five synthetic compounds of CDRI have so far been screened for anti-cancer activity *in vitro*. Initially, solubility of compounds (in aqueous medium) was determined by laser nephalometry. The soluble ones were evaluated, using sulphorhodamine-B (SRB) based assay for cell viability, against 5 cell lines: MCF7 (breast cancer), C33A (cervical cancer), KB (oral cancer), AB549 (lung cancer) and NIH3T3 (mouse fibroblast/non-cancer control). Cell lines corresponding to certain other cancer types were also included in the screening program as and when required. The cytotoxicity profiles of standard anti-cancer drugs- 5-FU, Paclitaxel, Nocodazole, Staurosporine, Doxorubicin, Camptothecin and Centchoman were also obtained for comparative evaluation of results. Molecules showing ≥ 80% cell growth inhibition at ≤ 20 µg/ml concentration were screened subsequently, using serial dilutions, to determine IC_{50} value. Compounds with IC_{50} values at ≤ 10 µg/ml were considered as 'hits' and categorized according to their selective cytotoxicity (cancer cells vs NIH3T3). By these criteria, 48 compounds were selected as 'hits'. The best two hits, CDRI-S009-131 (active against cervical and colon cancers) and CDRI-S010-1104 (active against cervical and prostate cancers) have been selected for in-depth study. After confirmation of activity at IICB, a 1.5 g batch of CDRI-131 showing >98% purity was synthesized for in vivo screening using athymic nude mice. This screening is underway at ACTREC, Mumbai. Synthesis of a large batch of compound 1104 is currently in progress.

Objectives 2, 4 & 5:

- **Mechanism of action of anti-proliferative compounds ICB 17K1 and CM-5:** The heat shock proteins, especially Hsp90, play a significant role as molecular chaperons maintaining the conformation and stabilization of several oncogenic client proteins, such as Raf, Akt, Cdk4, Stat-3, Bcr-abl, mutant p53, VEGFR etc. Since Hsp90-dependent proteins are essential for regulating cell growth, angiogenesis, metastasis etc, Hsp90 represents a promising therapeutic target for cancer treatment.

  Plants are a rich source of unique compounds that induce growth inhibition or apoptosis in malignant human cells. ICB17K1 is a 14-carbon, macrocyclic group of compound isolated from an Indian herb. Our results indicated that anti-proliferative effect of ICB17K1 is related to deregulatory function of Hsp90 and thus by proteasome-dependent degradation of client proteins.

  In another investigation, we studied the efficacy of a herbal carbazole alkaloid compound, CM-5 in Hsp90 inhibition in pancreatic cancer. CM-5 showed anti-proliferative activity in an array of pancreatic cancer cells leading to the apoptosis. Taken together, these results provide evidence that ICB17K1 and CM-5 both are potent Hsp90 inhibitor in chronic myeloid and pancreatic adenocarcinoma.

- **Novel transcriptional regulatory function of spindle assembly checkpoint protein Cdc20:** Chromosomal instability (CIN) has been found to be a prominent cause for aneuploidy and consequently, the onset of cancer. The spindle assembly checkpoint (SAC) ensures accurate segregation of chromosomes by monitoring kinetochore attachment of spindles during mitosis. Two SAC proteins Cdc20 and UbcH10 were found to be overexpressed in many cancer types and associated with defective SAC function leading to chromosomal instability. The mechanism of correlated overexpression of these two proteins remains elusive. We show that Cdc20 transcriptionally upregulates UbcH10 expression. Physical interaction between Cdc20 and APC/C-CBP/ p300

complex and its subsequent recruitment to the *UBCH10* promoter is involved in this transactivation process. This transcription regulatory function of Cdc20 was observed to be cell cycle specific. It has been hypothesized that this co-regulated overexpression of both proteins contributes to chromosomal instability.

None of the member of the above ternary complex has DNA binding property. Thus, it would be necessary to find out which protein confers DNA binding function to this complex. Further, it would be necessary to determine the cellular effect of this coordinated deregulation of expression. Future experiments will be performed to investigate these questions.

- **Regulation of SAC by tumor suppressor protein p53:** There have been limited reports on the mechanism of SAC's response to genotoxic stress. It has been shown that ectopically expressed p53 or DNA damage induced endogenous p53 can downregulate *Cdc20* transcriptionally. A consensus p53 binding site on the *Cdc20* promoter has been identified and has shown that it is being used by p53 to bind the promoter and bring about chromatin remodeling thereby repressing *Cdc20*. Additionally, study revealed that p53 also dowregulates *Cdc20* promoter through *CDE/CHR* element but in a p21 independent manner. This CDE/CHR element mediated downregulation occurs only under p53 overexpressed condition but not in the context of DNA damage.

- **Mechanism of NME-2 mediated suppression of metastasis:** Based on genome-wide promoter localization NME2 was shown to be a repressor of the focal adhesion factor vinculin. Cell-based experiments suggested that NME2-mediated suppression of metastases was through its regulation of vinculin. Earlier experiments were in lung cancer A549 cells. In order to check the generality of the effect we sought to check breast cancer cells. Our experiments were based on the hypothesis that NME2 being a metastases suppressor would impact epithelial to mesenchymal transition in breast cancer cells. Therefore we have started initial experiments to generate stable lines with increased levels of NME2 and preliminary results indicate that according to our expectation, increased levels of NME2 does lead to decreased invasiveness of aggressive breast cancer cells.

  In future, the above experiments will be further confirmed using few other stable clones and fully characterized before further experiments are done to understand the mechanism by which NME2 mediates suppression of metastases.

- **Study of induction of apoptosis by anticancer molecules:** Staurosporine is a protein kinase-C inhibitor from Streptomyces sp. It has potential anti-neoplastic activity. Ability of starurosporine to induce apoptosis is well studied in tumor cell lines, neurons and primary cell lines, but there is no report on its effect on mitochondrial membrane potential and cell cytoskeleton. We have analyzed the effect of staurosporine on KB cells in terms of nuclear fragmentation, caspase-3 activity, mitochondrial membrane potential and cell cycle analysis. Availability of these methods will help us decipher the mechanism of action of new chemical entities.

- **Identification of targets for breast cancer:** C/EBP family of proteins is reported to be down-regulated in breast cancer patients. We have shown that overexpression of human C/EBPs, in particular hC/EBPα, induces apoptosis in breast cancer cells via extrinsic pathway. Expression plasmids for C/EBP alpha, beta and delta were transiently overexpressed in MCF7 cells using lipofectamine. 24 and 48 h post-transfection, cells were analysed by flow cytometry for apoptotic activity via Annexin V-PI dual staining. A significant increase in population of apoptotic cells was seen within the C/EBP transfected cells. Apoptotic population was further assessed by Hoechst

staining and DNA fragmentation. Quantitative PCR against genes of apoptotic pathway was analysed to show that C/EBP induced apoptosis is Caspase dependent, and mitochondrial pathway may not play any significant role. Further, by crystal violet staining of C/EBP transfected cells, we found that these proteins also induce growth inhibition. Based on our data, we hypothesize that during breast tumor development C/EBP proteins are down-regulated in order to evade apoptosis. Hence their over expression in these cells is sufficient to induce apoptosis and inhibit proliferation.

- **Potential ovarian cancer biomarker:** Ovarian cancer is one of the major health problems for women of above 40 yr age and the exact causes of cancer remain unknown. Survival rate for ovarian cancer depend on the stage of the disease, the age and health of the woman. There are no routine screening tests for ovarian cancer. Biopsy of the ovary is the way to detect and diagnose the staging of ovarian cancer. In addition, determination of CA 125 in blood includes one of the major diagnostic tools for ovarian cancer. Endometriosis, a disease frequently associated to infertility is considered as risk for having ovarian cancer. Endometriosis is defined as implantation of endometrium-like tissues outside the uterus. The strong association between ovarian cancer and endometriosis (that could be viewed as a neoplastic process without metastasis) has been evidenced by histopathology and epidemiology. Both endometriosis and ovarian cancer share common antecedent mechanisms including genetic predisposition, immune dysregulation, toxin exposure and environmental factors. Recently, we have reported the strong association of matrix metalloproteinase (MMP)-9 expression with the severity of endometriosis both in humans and in mice. Future studies are going on with proper statistics to detect biochemical marker for stages of ovarian cancer.

- **Proteome Analysis of Glioma and Diagnostic/Prognostic Correlations**

A. Glioblastoma Cell secretome study

Three GBM cell lines HNGC2, U87MG and LN229 were chosen for the study. Proteins and peptides released by these cell lines were investigated using LC MS based profiling of proteins from the conditioned media collected from these cells.

B. Identification of differentially expressed membrane and nuclear proteins in glioma patients using iTRAQ method.

Membrane and nuclear proteins are involved in major cellular functions such as signaling and cell cycle regulation. The expression levels of many of these proteins are altered in cancer cells. Tissue subcellular fractionation was carried out to extract membrane and nuclear proteins from pooled control (epilepsy patients) samples and tumor samples of different grades (grade II, III and IV). After iTRAQ labeling and SCX fractionation, protein samples were analysed by LC-MS/MS approach (Orbitrap velos).

C. Clinical tissue sections and Antibody tissue micro arrays

Approach: Twenty glioma or other cancer specific antibodies have been selected from literature and the analysis is being performed on archival tissue samples, while another 20 antibodies have beeen selected from the existing data for validation on prospective tumour samples.

Results: Immunohistochemistry using 20 antibodies has been performed on TMA from nearly

150 retrospective (archival) and prospective tissue sections. Images are currently being studied at NIMS Hyderabad and Mumbai site of HPR, Sweden (a collaborative activity).

Objective 6

- Curcumin loaded PGLA nanoparticles were found to be effective in DEN induced rat hepatoma model.
- These curcumin nanoparticles induced apoptosis in these tumor bearing rats.

Objective 7

- A new hypothesis on the effect of heterozygous APC mutation on colon cancer initiation proposed and tested computationally using the agent based model

R & D Outputs during the third year (2010-2011):

Total Number of Publications: 25 (twenty five)

No. of Project Assistants engaged: 17 (seventeen)

Patent Submitted: 1 (one)

PARTNER NETWORK PROJECTS OF IICB

Partner Network Projects	Objectives
Discovery, development and commercialization of new bioactives and traditional preparations **(COR-023)**	, To revisit Indian biodiversity and Indian Systems of Medicine in the light of current day knowledge in search of therapeutic principle(s) under four disease areas of national importance, namely, Leishmaniasis, Gastric ulcer, Immunomodulation, and Parkinson's disease.
Drug target development using in-silico biology **(CMM-017)**	, *In silico* analysis of genome/proteome architectures of various pathogenic bacteria, parasites and fungi for identification of virulence determinants. , Studies on mouse and human genome characteristics in an attempt to detect the host factors regulating or regulated by the pathogen invasion.Clustering of some host-parasite interaction pathways with a view to identify some of the networks crucial for the host-parasite interplay. , Development of novel software/algorithms relevant to the study.

Partner Network Projects	Objectives
Comparative genomics and biology of non-coding RNA in human genome **(NWP-036)**	, To investigate posttranslational control mechanisms involving such RNAs, , To identify co-regulated gene networks using siRNA, , To develop new RNA-based methods for influencing gene expression in subcellular compartments such as mitochondria, and to investigate the structural basis of the interactions between non-coding RNAs and their protein targets.
Exploitation of India's rich microbial diversity **(NWP-006)**	, To develop state-of-the-art molecular genetics approach to address the relationship between metal microenvironment and microbial communities.
Zero emission research initiative **(NWP-044)**	, To identify & scale up of technology and their extension for minimizing environmental risks from leather sector to near zero values.
Diabetes mellitus – New drug discovery R&D, molecular **(NWP-032)**	, To understand the basic mechanism of insulin resistance and defect in signaling of type 2 Diabetes. , To identify possible drug targets. , To develop drug against those targets.
Identification and validation of drug targets for selected pathogens of national importance **(NWP-038)**	, Identification of pathogen-specific, differentially-expressed proteins of *Leishmania donovani.* , Validation of identified protein as drug targets. , Development of target-specific assays and screening of available synthetic/natural libraries.
Biological and chemical transformation of plant compounds for production of value added products of therapeutic / aroma value **(NWP-0009)**	, Up-scaled isolation of parent anti-cancer molecules targeted for chemical and biological transformation. , Chemical transformation of selected phyto-molecules for value addition.
Pathway engineering and system biology approach towards homologous and heterologous expression of high-value phytoceuticals **(NWP-008)**	, Elucidation of the naturally occurring pathways of podophyllotoxin biosynthesis. , Metabolic engineering of podophyllotoxin pathway in a suitable host. , Metabolic engineering of isoflavone biosynthesis pathway,

Partner Network Projects	Objectives
	, Reprogramming of these metabolic pathways in the selected host perhaps using synthetic transcription factors. , Creation of novel genetic switches for use in synthetic biology. , Standardization of purification of the compound from metabolically engineered organism.
Nanomaterials and nano-devices for application in health and disease **(NWP-035)**	, To synthesize, purify, characterize and study suitable linear and denditric peptides for producing and stabilizing metal nanoparticles and cadmium sulfide (CdS) nanoparticles (semiconductor quantum dots). , To examine the cell entry of peptide capped cadmium sulfide (CdS) quantum dots using selective cell lines like normal cell lines (ordinary T-lymphocyte) and diseased cell line (fibroblast T-lymphocyte) and to check the locations of the quantum dots inside the cell, if the nanoconjugate (i.e. peptide capped CdS quantum dots).To explore self-assembling synthetic peptide based new nanoporous materials and to vary the pore size by varying the peptide based molecular building blocks for achieving the selective gas adsorption properties from a mixture of gases of different molecular dimensions. , To check the biodegradability of these peptide based nanoporous materials. , To fabricate pseudopeptide based nanofibers by peptide capped gold and silver nanoparticles and to study the important electrical and other material properties of these nano materials. To study the self-assembling synthetic peptide based various nanostructures like nanofibrils, nanorods and nanotubes and to use these peptide nano-structures as templates for the production of gold/silver nanowires and nanocrystals.
Plasma proteomics in health, environment and disease **(NWP-004)**	, To identify disease specific biomarkers in easily accessible body fluids, which would constitute safe, effective and non-invasive methods for development of new diagnostic and prognostic approaches. , Plasma proteome profiling in the areas of Arsenicosis, Leishmaniasis, Cardiac diseases and ALL will be undertaken.

Partner Network Projects	Objectives
Integrated Analysis for Impact, Mitigation and Sustainability (IAIMS): Regional Climate Modeling at Decadal Scale **(NWP-052)**	, To study the change in arsenic concentration in soil and groundwater trend affected by change of climate - flood or drought and/or land-management practices. , To determine the different rice varieties dependence on bioaccumulation of arsenic under different cultivation methods to combat the crisis of arsenic contamination of rice under severe environmental conditions like flood or drought. , The effect of environmental parameters associated with climate change on the relative activities of the arsenic transforming microbes will be investigated. Specifically, (a) Isolation and identification of bacteria from aquifers (b) Identification of genes associated with arsenic oxidation/ reduction/ detoxification and other processes. (c) Regulation of expression of relevant genes by environmental parameters.
Designing Potential Lead Molecules for Inhibition of Siderophore Biosynthesis in Mtb **(HCP 001)**	, Development of new safer drugs to treat tuberculosis.
Synthetic Biology & Metabolic Engineering of Azadirachtin Biosynthesis Pathway **(HCP 002)**	, Construction of random BAC library from genomic DNA of *A. indica.* , Genome and transcriptome sequencing and computational analysis for assembly of the EST sequences. , Development of assays to measure the toxicity of azadirachtin. , Isolation of secondary metabolites from leaves and seed and synthesis of the intermediates. , Cloning of the genes of coding for azadirachtin biosynthesis pathway enzymes in heterologous hosts and developing expression system in *E. coli*/yeast for functional evaluation, like enzyme assays, of targeted genes. , Reconstruction of biosynthetic pathway of azadirachtin by using information obtained through genetic and biochemical approaches. , Designing and development of related synthetic biotools like engineering of efflux pumps for transport of metabolites

Partner Network Projects	Objectives
	and utilization of these biotools in optimization of the pathways in heterologous hosts. , Establishing a computational framework (programs and software/hardware) for simulation of biochemical reaction network dynamics. Building up of computational capabilities and web servers for whole genome annotation. , Use of deterministic models to understand the effect of changes in regulatory and metabolic pathways.
Metabolic Engineering of Vinca Alkaloid Pathway **(HCP 003)**	, Assembly of pathway of vinblastine from tabersonine. , Identifications of the N-methyl transferase and hydratase enzymes. , Secologanin synthesis from geraniol. , Development of tools and novel model systems for synthetic biology.
Multi-agent Therapy of Cancer: a System Biology approach **(HCP 004)**	, Genetic and functional characterization of lung adenocarcinoma and glioma cell lines for pathway analysis. , Mechanistic evaluation of naturally occurring anti-cancer molecules through pathway analysis of these well characterized cell lines.

PUBLICATION & INFORMATION AND PLANNING, MONITORING & EVALUATION

Dr. Pijush K. Das, Dr. K. P. Mohanakumar, Dr. Uday S. Chowdhury, Dr. Tanmoy Mukherjee, Dr. Aparesh Bhattacharya, Dr. Moonmoon Bhaumik, Dr. Prasanta Chakraborty, Dr. Siddhartha Majumder, Mr. Arupesh Majumdar, Mr. Sekhar Mukherjee, Mr. Swadesh K. Sahoo, Mr. Binayak Pal, Mr. Nikhil K. Das, Md. Ayub Shah, Miss Lily Das, Mr. Sukhendu Biswas, Mr. Pallab Mukherjee, Mr. Nishikanta Naskar, Mr. Bideshi Nayak, Mr. Soumalya Sinha, Mr. Samir Thami

The scientific management of the different R&D activities of the institute is the primary focus of this division. The diverse activities of this division have been carried out successfully by seven major sections, e.g. [a] Publication & Information; [b] Planning, Monitoring & Evaluation; [c] Art & Photography; [d] ISTAD-IICB; [e] Intellectual Property Management Cell; [f] Business Development Group; and [g] Human Resource Group. The details of the scientific management activities of the individual sections are given below separately for the reporting year.

PUBLICATION & INFORMATION SECTION

Dr. Tanmoy Mukherjee and group

This section is basically catering to the diverse informational activities, publication and monitoring of reports. The major contribution of this section lies in assisting scientists in day to day maintenance of the institute activities and innovations, project profiles, publication records and research utilization data. The section is involved in the following wide spectrum of programmes during the report year.

- Preparation of Annual Plan (2011-12) and Budget.
- Preparation of IICB Annual Report (2009-10) and half-yearly reports.
- Preparation of documents released during events.
- Dissemination of information to scientific milieu on relevant subjects.
- Documents on IICB inputs for "CSIR Annual Report 2010-11" and "CSIR Research Output 2010".
- Assistance to scientists, fellows and staff members for participation in seminars, symposia and conferences.
- Maintenance of data for using analytical instruments by other institutes / Universities.
- Total management of all technical queries.
- Public relations, advertisement and news and views forum.
- Organizing display of exhibition and science news dissemination.
- Advice and comments for management of parliament queries and other related crucial matters of institute.

- Organizing of 'OPEN HOUSE' and active help for 'CPYLS-2010' programmes.
- Assistance in management of Eleventh Five Year Plan (2007 - 2012).
- Monthly Report of IICB for PPD, CSIR.
- Matters for CSIR News & IICB News Letters.

Management of Exhibition

Like preceding years, P&I Section has participated in several exhibitions during 2010 -11 in and around Kolkata and also outside Kolkata organized by various organizations. IICB has a mandate to carry out basic and applied research in health problems of the country. The main objective of this section is to present recent scientific developments of the institute to the common people. Mr. Sekhar Mukherjee, a senior member of this section, looks after the exhibition cell. He also arranged two exhibitions at IICB premises on the occasion of CPYLS-2010 & OPEN HOUSE programme. List of exhibitions is given below.

EXHIBITIONS ARRANGED & PARTICIPATED 2010 - 2011

Sl.No.	Date	Theme	Organised By
1.	03 - 07 September, 2010	"STRIVING TOWARDS A GLORIOUS INDIA" National Science Exhibition 2010	Central Calcutta Science & Culture Organisation for Youth , held at Sodepur, Kolkata - 700 110
2.	14-28 November, 2010	CSIR Techno fest 2010	International Trade Fair, held at Pragati maidan, New Delhi.
3.	22 -31 December, 2010	Science Exhibition - 2010	Taldi Bahurupee Sangha, Taldi, 24-Parganas.
4.	03-07, January, 2011	98th Indian Science Congress "Science Exhibition"	SRM University, Chennai
5.	23 - 28 February, 2011	Chemtech / Pharma World Expo - 2011	Chemtech Foundation held at Bombay Exhibition Centre, Goregaon, Mumbai
6.	28 Feb - 01 March, 2011	West Bengal State Science & Technology Exhibition.	18th West Bengal State Science & Technology Congress held at Rama Krishna Mission, Narendrapur, Kolkata

Management of Laboratory Visit for Students

On the occasion of CSIR Foundation Day (2010) celebration, the members of this section have actively helped for the arrangement of 'OPEN HOUSE' programme where students from various schools/colleges/universities within and around Kolkata visited IICB. A large number of students from different schools and colleges with their teachers visited various laboratories and interacted with the scientists expressing great interest and enthusiasm. Members of this section also arranged the laboratory visit for students of outside Kolkata colleges and universities. A total of six (06) numbers

of visits were organized throughout the year (2010-11) as listed below.

Sl.No.	Date	No. of students & Name of the Institution
1.	06.06.2010	(25 Students), Presidency College, Kolkata - 700 073
2.	23.11.2010	(12 Students), JBNSTS, Kolkata
3.	19.11.2010	(20 Students), Department of Botany, Institute of Science, Mumbai
4.	16.12.2010	(20 Students), Birla High School, Kolkata
5.	05.01.2011	(24 Students), North Eastern Hill University, Guwahati
6.	24.01.2011	(45 Students), Mirza Galib College, Magadh University

Scientist Visit & Events

The P&I Section is also responsible for the announcement and arrangement of seminars for the national and international scientists who often visit the institute and like to share their research activities with IICB faculties. A list of '**Scientist Visitors**' is given in a separate page.

The Institute also organized several significant events with the assistance of this section and '**List of Events**' is also shown separately for the reporting year.

Sectional Members

Dr. Uday S. Chowdhury, Mr. Arupesh Majumdar, Mr. Sekhar Mukherjee, Mr. Nikhil K. Das, Mr. Pallab Mukherjee.

PROJECT MONITORING & EVALUATION SECTION

Dr. K. P. Mohanakumar & group

(A) PME Cell is set up in the Institute on August 5, 2009 headed by Dr. K P Mohanakumar with two existing staff. Additionally, two newly recruited staff joined PME cell to tide over the work load and to aid in the effective management of the Institute's intramural, network, grant-in-aid as well as collaborative R&D projects.

The new PME cell in IICB provided all possible help in training the newly recruited staff. PME faced a huge uphill task due to the fact that any project information available with the earlier staff under P&I.PME was very sketchy and incomplete.

1. As a first step, PME took up networking planned programs of IICB and started new files for the 11th FYP. PME also built up data on 10th Five Year Plan projects. This task is completed very successfully by 2011.
2. In addition, the PME streamlined (i) IAP (ii) NWP (iii) SIP, and (iv) HCP. The current records on 11th FYP projects are complete and up to date.

3. Database is kept on allocated funds, receipt of funds and utilization of funds in respect to NWP, IAP, SIP and HCP.

(B) Regards to all other projects (GAP, SSP and CLP) the following activities are taken up:

1. Database are developed for completed (last three years), ongoing and freshly submitted projects.
2. Contacted each scientist and requested for documents such as; (i) the copies of the sanctioned projects, (ii) copies sanction letters received from granting agencies, (iii) copies of letters that are related with funds (evidence of funds received), (iv) project reports sent, (v) Project funds utilization certificate, (vi) Utilization certificates of symposia and final project report as applicable.

   All the scientists cooperated, but many could not provide complete information, making it difficult to update the files, in cases of completed projects only.
3. Periodical information is being sent to concerned scientists regarding (i) due date for Annual Report submission, (ii) Final Report Submission, (iii) Statement of Expenditure and Utilization Certificate to be submitted.
4. All cheques / demand drafts are received and recorded in the PME data system so that project fund availability for utilization in a given project is readily accessible.
5. Information is being sent to eligible scientists whenever new LoIs/RFAs are advertised by various funding agencies in India & abroad.

(C) Currently every research project is being processed through PME, from the very initial phase of submission to a funding agency. PME scrutinizes the applications in terms of projects which are from IICB and those which are in collaboration with other institution, in which case IICB-BD cell is requested to make relevant MoUs with the collaborating institute. In these cases, PME oversees the eligibility criteria and the financial budget requested for IICB. In addition, information is monitored for the PIs who are close to superannuation, in which case an additional co-investigator is associated with the project.

Since its initiation the Division is functioning as a liaison agency between Principal Investigators in the Institute - Finance Section - Purchase Section, and the Grant Giving Agency. PME actively monitors the expenditure of all the projects carried out in IICB.

PME from 2011 onwards is geared to monitor expenditure of the Institute's all extramural and intramural research projects. All project related expenditure will be processed by PME, and we plan to help to issue Statement of Expenditure Certificate and Utilization Certificate of the externally funded projects in the near future.

A list of Extramural projects being implemented in IICB is given in a separate page as '**External Funding**'.

Sectional Members

Dr. Prasanta Chakraborty, Mr. Sukhendu Biswas, Mr. Soumalya Sinha and Mr. Samir Thami.

ART & PHOTOGRAPHY SECTION

Dr. Tanmoy Mukherjee and group

Art Section under the supervision of Mr. S.K. Sahoo has rendered full support to all the staff members during scientific seminars/symposia and all national events by preparing displays, illustrations, posters, exhibits, and slides. Diagrams, charts, graphs for publication in national and international journals are prepared in this section. They are working in collaboration with the photography Section for making each exhibition a great success to highlight the institute achievement. The section also participated in preparing artwork and cover design for Hindi Day and Hindi Report. This section also carried out work for decoration of floor & institute during various scientific and official programmes. Art Section provided following art works to the Institute during this year.

Photography Section under the able guidance of Mr. Binayak Pal has been successful in procuring a digital camera for coverage of most of the events taking place in the institute. The section is continuously supplying all the photos for publications, Annual Reports, Journals and other related documents. Besides, they are also assisting the scientists of the institute. Apart from that they also handled photographs of scientific activities and experiments slides for publication in different international journals.

Sectional Members

Mr. Swadesh K. Sahoo, Mr. Binayak Pal, Mr. Nishikanta Naskar.

ISTAD SECTION

Diverse activities of this section were personally supervised by the Head of the Division, Dr. Pijush K. Das with the active help of Dr. Samir K Dutta.

INTELLECTUAL PROPERTY MANAGEMENT CELL

Dr. Tanmoy Mukherjee and group

CSIR-IICB is continuously developing its knowledgebase through high science and the inventions with potential of commercialization are protected as patents and copyrights by its Intellectual Property Management (IPM) cell. The IPM cell in CSIR-IICB, in co-ordination with Intellectual Property Unit (IPU) of CSIR, is engaged in protecting the technologies developed with an objective to put forward these technologies towards the benefit of common people in our country and abroad. With the help of a new Comprehensive Patent Database prepared by this cell, now information about a patent filed by CSIR-IICB, since 1990 is just a click away.

This cell has continuously maintained liaison with Scientists of CSIR-IICB and IPU, CSIR to protect Intellectual Properties of CSIR-IICB/CSIR. The IPM Cell, CSIR-IICB provided all information, clarifications, explanations and reports to IPU, CSIR regarding new patent applications, granted patents

and renewal or lapsing of existing patents in consultation with concerned inventors within corresponding time-limit. During the reporting period, a large number of correspondences were made with IPU, CSIR, a significant number of responses were conveyed to IPU, CSIR for patent applications in India and abroad and a considerable number of communications were made with CSIR-IICB scientists regarding patent queries to provide necessary information to IPU, CSIR to obtain productive results. The IPM Cell always extended co-operation to the scientists, CSIR-IICB in writing and filing patent applications. This cell has prepared, maintained and disseminated all information regarding patent application, status of the application, renewal etc. as and when it was required. IPM cell, CSIR-IICB has provided all necessary information to Business Development Group of IICB for licensed out patents; sent information on patent and technology transfer to IPU, CSIR regarding Audit and Parliamentary Question; prepared necessary documents on patents licensed out by CSIR-IICB; prepared year wise documents on total Patents of CSIR-IICB filed and granted; prepared Commercial Working Report of CSIR-IICB Patents for IPU, CSIR; approved number of Declaration forms for non patentability of publication and sent Renewal / Lapse recommendations of CSIR-IICB patents for 2011-12 to IPU, CSIR.

Apart from these, some of the significant jobs done are as follows:

1. Maintenance of CSIR-IICB Patent Database to keep it up-to-date
2. Commercial Working Report for 16 Indian Patents of CSIR-IICB prepared and sent to IPU, CSIR.
3. Renewal / Lapse recommendations of CSIR-IICB patents prepared for IPU, CSIR. Reports Prepared for 61 Foreign Patents and 11 Indian Patents.
4. Year wise documents prepared on total Patents of CSIR-IICB filed and granted.
5. Response to IPU, CSIR regarding IPER, IPRP, OA, Designated Countries and other queries relating to patent application and filing.
6. Information on patent and technology transfer to IPU, CSIR regarding Audit and Parliamentary Questions.
7. Approval of Declaration forms for non patentability of publications.

During reporting period, the performance at a glance of IPM Cell is as follows:

Patents Filed :

National Patents Filed	...	6 (Complete Filing 1 + Provisional 5) Filing 1)
International Patents Filed	...	5
Total No. of Patents Filed	**...**	**11**

Patents Granted :

National Patents Granted	..	1
International Patents Granted	...	3
Total No. of Patents Granted	**...**	**4**

FILED IN INDIA

S. No.	Title	Inventors	Filing date
1.	Synthetic phosphodiesterase 4 (PDE-4) inhibitor with antiasthmatic activity	Vasanta Madhava Sharma Gangavaram, Jhillu Singh Yadav, Radha Krishna Palakodety, Arun Bandyopadhyay, Siddhartha Roy, Santu Bandyopadhyay, Rakesh Kamal Johri, Subhash Chander Sharma, Balaram Ghosh, Mabalirajan Ulaganathan, Sakshi Balwani, Bholanath Paul, Ashok Kumar Saxena	17.01.2011
2.	Tryptamine derivatives, their preparation and their use in gastropathy	Uday Bandyopadhyay, Chinmay Pal, Samik Bindu, Susanta Sekhar Adhikari	14.09.2010
3.	Biomarker for valvular heart disease	Arun Bandyopadhyay, Tanima Banerjee, Somaditya Mukherjee, Santanu Dutta	13.10.2010
4.	A synthetic peptide formulation against melanoma and other cancers over-expressing S100B	Amlanjyoti Dhar, Shampa Mallick, Israr Ahmed, Aditya Konar, Santu Bandyopadhyay, Siddhartha Roy	31.01.2011
5.	A molecule from herbal origin for the treatment of bronchial asthma	Sibabrata Mukhopadhyay, Mumu Chakraborty, Tulika Mukherjee, Arun Bandyopadhyay, Dipak Kar, Tanima Banerjee, Aditya Konar, Debaprasad Jana, Siddhartha Roy, Santu Bandyopadhyay, Balaram Ghosh, Mabalirajan Ulaganathan, Rakesh Kamal Johri, Subhash Chander Sharma, Gurdarshan Singh, Bholanath Paul, Vasanta Madhava Sharma Gangavaram, Jhillu Singh Yadav, Radha Krishna Palakodety	04.02.2011
6.	Two main component molecules: Mahanine and Mahanimbine (dehydroxy mahanine) from Murraya koenigii for the treatment in glioblastoma and cervical carcinoma and Mahanimbine exhibits broad spectrum of anti cancer activity	Chitra Mandal, Bikas Chandra Pal, Kaushik Bhattacharya, Suman Kumar Samanta, Sayantani Sarkar, Ranjita Das	11.03.2011

FILED ABROAD

S. No.	Title	Inventors	Country	Complete filing date
1.	Methanolic extract of piper betel leaves for the treatment of human malignancies by inducing oxidative stress	Santu Bandyopadhyay, Bikas Chandra Pal, Jayashree Bagchi Chakraborty, Srabanti Rakshit, Labanya Mandal, Kausik Paul, Nabendu Biswas, Anirban Manna	USA	17/06/2010
2.	Methanolic extract of piper betel leaves for the treatment of human malignancies by inducing oxidative stress	Santu Bandyopadhyay, Bikas Chandra Pal, Jayashree Bagchi Chakraborty, Srabanti Rakshit, Labanya Mandal, Kausik Paul, Nabendu Biswas, Anirban Manna	Europe	24/06/2010
3.	Methanolic extract of piper betel leaves for the treatment of human malignancies by inducing oxidative stress	Santu Bandyopadhyay, Bikas Chandra Pal, Jayashree Bagchi Chakraborty, Srabanti Rakshit, Labanya Mandal, Kausik Paul, Nabendu Biswas, Anirban Manna	China	16/07/2010
4.	ELISA and dipstick based immunoassay for field diagnosis of visceral leishmaniasis (kala-azar) and PKDL	Ali Nahad, Saha Samiran	Brazil	29/10/2010
5.	Triazine-aryl-bis-indoles and process for preparation thereof	Vasanta Madhava Sharma Gangavaram, Jhillu Singh Yadav, Radha Krishna Palakodety, Arun Bandyopadhyay, Siddhartha Roy, Santu Bandyopadhyay, Rakesh Kamal Johri, Subhash Chander Sharma, Balaram Ghosh, Mabalirajan Ulaganathan, Sakshi Balwani, Bholanath Paul, Ashok Kumar Saxena	World	31/12/2010

GRANTED IN INDIA

S. No.	Title	Inventors	Grant date	Patent No.
1.	A hybrid cell vaccine against leishmaniasis (Kala-azar)	Suniti Bhaumik, Rajatava Basu, Kshudiram Naskar, Syamal Roy	22/02/2011	246235

GRANTED ABROAD

S. No.	Title	Country	Inventors	Grant date	Patent No.
1.	A herbal extract and herein a molecule, from Murraya koenigii for treatment of prostate cancer	Great Britain	Swati Sinha, Bikas Chandra Pal, Samir Bhattacharya	21/04/2010	GB2443588
2.	Antimonocytic activity of betel leaf extract	Germany	Santu Bandyopathyay, Bikash Pal, Samir Bhattacharya, Mitali Ray, Keshab Chandra Roy	29/04/2010	10085492
3.	Acaciaside-B: A prophylactic contraceptive for human immunodeficiency virus infection/acquired immune deficiency syndrome	South Africa	Kabir Syed Nazrul, Ray Heramba Nanda, Pal Bikash C, Mitra Debashis	28/07/2010	2009/08410

Sectional Members

Mr. Arupesh Majumdar, Mr. Nikhil K. Das.

BUSINESS DEVELOPMENT GROUP

Dr. Asish K. Sen (Jr.) and group

MAJOR ACTIVITIES OF THE GROUP:

1. Liaison with private Industries/ R&D Institutes/ Academic Institutions/ other potential clients.
2. Negotiating Business Plans with Industries and drawing agreements and MoUs.
3. Matters related to Service Tax (registration and filing returns).
4. Conducting meetings (Industry-Institute meet; Introduction of new schemes, Arrangement of visitors and their interactions with scientists, etc.).
5. Parliamentary related matters - Responses to Parliamentary questions, etc.
6. Distribution of money earned under royalties.
7. Periodic preparation of lists of knowledgebase/products available, dissemination of information on technologies, etc.

HUMAN RESOURCE GROUP (HRG)

Dr. Siddhartha Majumdar and group

Human Resource Group (HRG) of CSIR-IICB was set up in April 2005 to promote professional Human Resources Management in this institute by evolving and implementing HR development plan. To advance the academic mission of the institute, HRG provides leadership for continuous improvement in academic program, student affairs activities.

The services include: oversight, guidance and support of required educational services and is responsible for different academic and developmental training programs.

Activities, Guidance and Initiatives:

- Coordinates the in-house IICB PhD Course Work programme for the IICB Research Fellows as a part of the Academic Affairs of the Institute.
- Defining, assessing and developing institute's specific training needs.
- Coordinates some selected academic & science-admin affairs concerning Research Fellows/ Associates and linkages with other organization/ Agencies/Institutes.
- Collects and disseminates comprehensive data and information assisting in strategic planning for IICB & CSIR.
- Organises IICB Summer Training Programme for the Post Graduate students of different Universities, Institutions and Colleges for partial fulfilment of their degrees and involves in different Out-reach Programme.
- Organises different innovative Training Programme / Workshop of consistently high stands for IICB members, Research Fellows & Research Associates.
- Extends training to the external students/faculty through demonstration of methodology/ techniques used in IICB as well as through practical courses, workshops and conferences.
- Recommends name of suitable Scientists/Officers for their nomination in different R&D training programme /workshop organized by CSIR, HRDC and other national level institutes/organizations.

PhD Programme:

Objective: CSIR-IICB offers exciting opportunities to highly motivated and talented students with a keen sense of scientific enquiry for pursuing advanced career for research in the frontier areas of Chemical Biology, Modern Biology or Chemistry leading to PhD on a specific topic.

The major objective of the programme is to generate adequate human resources in the different fields of Biology, Chemistry and related research areas. The duration of this programme is generally five years.

Eligibility Criteria: CSIR-NET qualified candidates / UGC-NET/ ICMR Fellows/ DBT Fellows and subject to clearance of the entrance interview.

Junior Research Fellowship for GATE qualified engineering graduates (CSIR-JRF-GATE):

CSIR has introduced a new research fellowship in 2002 for the GATE qualified candidates with B.Tech. / B.Pharm / degree to pursue research leading to PhD. Each CSIR laboratory engaged in biological/biochemical research can have maximum 10 such JRF-GATE Fellows.

Besides the ad-hoc fellowship, IICB advertises for recruiting research fellows to work in grant-in-aid projects and different research schemes.

At a Glance:

Number of existing (Up to March 2011) Research Fellows/Associates is 274 from various funding agencies (CSIR/UGC/DST/DBT/ICMR/TLP)

Number of Project Assistants: 70

Learning and Instructional Support: Course Work / Training

PhD Course Work

To educate and train in multidisciplinary areas, CSIR-IICB offers a mandatory PhD course work for the Research Fellows in their first year, taught by faculty members of in-house as well as from other Institutes/Universities. The main objective of these courses is to make the students acquainted with modern Biological Sciences, Chemistry and Chemical Biology along with Statistical Analysis, Instrumental Analysis and Basic Computer courses.

The existing CSIR-IICB PhD course-work programme constitutes basic and advanced courses. The basic course is for bridging the gap between M.Sc. and PhD. The advanced course comprises of frontline areas of research and covers research methodology and review of current literature. Trainings are also provided for development of effective communication and writing skill (scientific) and on bioethics & laboratory safety.

The course comprises of two major disciplines, namely **Basic Course** with [a] Computer Applications; [b] Instrumental Analysis; [c] Statistical Analysis; [d] Basic Biology (for Chemistry students); and [e] Basic Chemistry (for Biological Sciences students); and **Advanced Course** with [a] Advanced Biology (for students engaged in Biological Sciences Laboratory) and [b] Advanced Chemistry (for Chemistry Laboratory students). In addition to this, introduction to some interdisciplinary topics viz. System Biology; Synthetic Biology; Cell Tissue Engineering; Chemical Biology etc. are taught in advanced courses.

Incentives to students: Depending on the academic performance several incentives are offered to meritorious students. These include cash awards to the PhD course work students based on marks, best thesis award etc.

Total number of Course work students for 2010: 63

Summer Training / Project Work / Dissertation Work

As per CSIR mandate, CSIR-IICB provides an excellent environment for training the next generation

of researchers towards partial fulfillment of postgraduate degrees. Its mission is to provide students with opportunities to acquire hands on knowledge in biological/chemical sciences and chemical biology research.

IICB has imparted training in the state-of -the-art techniques to several summer students from different Universities & Institutes. The aim is to let young minds feel the thrill and excitement of science by working on a project requiring application and critical appreciation of scientific principles. It also aims at active participation in the learning process through experimentation and putting into practice the knowledge acquired in the classrooms.

The summer program is primarily designed to encourage students from, first-generation college/university students by providing them the opportunity to do basic research in top-notch research institution, in a supportive learning environment with plenty of interaction with graduate students and faculty. The programme provides a unique opportunity for students who do not have access to top-notch research facilities at their own institution to conduct supervised research in state-of-the-art research facilities. Besides, we also try to accommodate students from disadvantaged backgrounds for pursuing a career in research.

Guidelines: Detailed guidelines can be available in CSIR-IICB website at HRG site. Under this programme the Institute conducts training of short duration in various disciplines and is absolutely free of any cost. . The courses comprise both lectures and practical with emphasis on practical R&D aspects in a particular discipline. The duration of this training programme / Project Work is generally two- three months and maximum six months duration during **March and August** every year.

Number of Summer Trainee/Project Trainee (2010-11): 124

Training & Workshop (Inter & Intra)

[A] Training programs organized by HRG-IICB:

- Administrative staff members (40 nos.) have participated in "LIVING IN EXCELLENCE-2" Motivational Training Programme held on 19th May, 2010, at IICB.

[B] Training Programme: Nominated/recommended for participation:

- Sri R. N. Das, Sr. Stenographer and Sri Sankar Santra, Sr. Stenographer have been nominated for their participation in the "**Orientation Programme for Sr.PS/PS/PA**" during the period form 24th to 26th May, 2010 at CSIR-HRDC, Ghaziabad.
- Sri S. M. Roy nominated for participation to the Training Programme on "**Competency Development for Technical Officers**"- organized by CSIR-HRDC, Ghaziabad during 28th September to 1st October,2010.
- Sri A. K. Jha, S. O. (F&A) and Sri A. K. Tiwary, S.O. (F&A) nominated for their participation

in "**Refresher Programme for Section Officer (F&A)**" - organized by CSIR -HRDC during August 16th - 21st , 2010.

- Dr. Siddhartha Majumdar, Head, HRG participated in a one day Workshop on "**Working with EQ**" conducted by the British Council, Kolkata, on 2nd December, 2010.
- Sri S. K. Das, F&AO, Sri Abhimanyu Kr. Tiwary, S.O.(F&A) & Sri Asit Kr. Roy, Assistant (F&A), nominated for "**2 days Workshop on new Accounting Software**" Training Programme held on 28.02.2011 & 01.03.2011, at CSIR-HRDC, Ghaziabad.
- Dr. Suman Khowala, Scientist was nominated for participation in the program "**Plan your life after retirement**" during March 28 - 30th, 2011, held at CSIR-HRDC, Ghaziabad.

Members:

Ms. Lily Das, Ms. Debasree Roy; Md. Ayub Shah, Sri B. Nayak.

SCIENTIST VISITORS

No.	Date	Speaker	Title of Seminar
1.	26.04.2010	Dr. Sanjay Dutta UCSD, USA	"Targeting RNA with Small molecules".
2.	26.05.2010	Dr. Dwaipayan Bharadwaj IIGB, New Delhi	"Dissecting the Complexity of Type2 Diabetes In North Indians."
3.	04.06.2010	Dr. Arindam Talukdar Prudue University, USA	"Stereoselective synthesis of anti-asthamatic drug candidate; and design and synthesis of enzyme inhibitors as antimicrobial agents".
4.	23.06.2010	Dr. Tuhin Das University of Pittsburgh, USA	"Role of Profilin-1 in Phospholipid signalling in breast cancer".
5.	23.06.2010	Dr. Somnath Bhattacharjee Michigan State University, USA	"Regio and chemo selective catalysis by metal nanoparticles soy protein polymer conjugate for commercial use homologative ring expansions for heterocycle synthesis".
6.	24.06.2010	Dr. Panchanan Maiti Deptt. of Neurology, UCLA	"Molecular aspect of amyloid beta protein assembly, toxicity and drug design."
7.	27.07.2010	Dr. Javed Agrewala IMTECH, Chandigarh	" Promiscuous peptide of 16 kDa antigen linked to Pam2Cys protects against M. tuberculosis by evoking enduring memory T cell response".
8.	13.08.2010	Dr. Tapas K. Hazra University of Texas, USA	"Transcription Coupled Repair of Oxidative DNA Damage".
9.	23.08.2010	Mr. S P Gon Choudhury Managing Director, WBGEDCL	"National Solar Mission".
10.	02.09.2010	Dr. Sathivel Ponniah Biomedical Res. Council, Singapore	"Animal Facility Management : It takes to Tango".
11.	17.09.2010	Dr. Dominik Schwudke Na. Cntr for Bio. Sc. Bangalore	"What insights Lipidomics can deliver in Neurodegeneration."
12.	21.10.2010	Dr. Changotra Harish Louisiana Stata University, USA	"Murine Norovirus - 1 : a model system to study pathobiology".
13.	26.11.2010	Dr. Saibal Chatterjee Basel Switzerland	"From miRNA turnover to maintenance of active miRISC."
14.	26.11.2010	Dr. Christian Engwerda Queensland, Australia	"Improving T cell responses during experimental visceral leishmaniasis."
15.	07.12.2010	Dr. Cheng-Ming-Chiang University of Texas, USA	"Epigenetic Control of Chromatin- Development Transcription".
16.	08.12.2010	Prof Ananda M Chakraborty University of Illinois, Chicago, USA	"Technology transfer from bench to beside - future generation drugs".

No.	Date	Speaker	Title of Seminar
17.	16.12.2010	Dr. Bhabatosh Das CNRS, Gif Sur Yvette, France	"Acquisition and dissemination mechanisms of mobile genetic elements integrated at the CTXΦ attachment sites in the Vibrio cholerae chromosomes."
18.	16.12.2010	Prof. Ayusman Sen Penn State University, USA	"Chemo and Phototactic Nano/Microbots."
19.	21.12.2010	Dr. Apurba Kumar Sau. National Inst. of Immunology. Delhi	"Regulation of GTP Hydrolysis in Interferon -gamma induced GTP - binding proteins."
20.	23.12.2010	Dr. Subhajit Biswas University of Cambridge, England	"Drug-resistant Mutations in Herpes Simplex Virus Helicase-Primase Complex: Effects on Virus Growth and Pathogenicity."
21.	29.12.2010	Prof. Shrikant Anant Kansas School of Medicine, USA	"RNA Binding Proteins : Novel Purveyor of Cancer."
22.	07.01.2011	Dr. Ritesh Tandon Emery School of Medicine, USA	"Viral tegument proteins and host factors in human cytomegalovirus maturation."
23.	11.01.2011	Dr. Rupasri Ain Head NCBSc, Bangalore	"Decording cell - cell communication at the maternal-fetal interface."
24.	17.01.2011	Prof. Sankar Mitra University of Texas, Galveston	"Endogenous Oxidative Stress and Cell Survival."
25.	18.01.2011	Dr. Amitabha Majumdar Cornell University, USA	"Interactions between microglia and Alzheimer's amyloid beta peptide."
26.	28.01.2011	De. Sovan Sarkar Whitehead Inst. for Bio. Res. Res USA	"Role of autophagy in Neurodegenerative diseases."
27.	31.01.2011	Prof. D. K. Mitra AIIMS, New Delhi	"Tregs cells suppress local immune response in Kala Azar."
28.	03.02.2011	Dr. Suresh C. Scientist & JSPS - fellow	"Computational studies on mechanisms of organic transformations."
29.	17.02.2011	Dr. Baibaswata Nayak Univversity of Maryland , USA	"Reverse Genetics of RNA viruses : a strategy for developing novel vaccine."
30.	18.02.2011	Dr. Pravin Nair Sloan Kettering Cancer Centre, USA	"Mechanistic insights to DNA ligases through biochemical and structural studies."
31.	24.02.2011	Dr. Indubhusan Deb Rutegrs University, USA	"Redox Neutral Reaction Cascades : Alfa-functionalization of amines."
32.	28.02.2011	Dr. Durba Sengupta Uni. of Groningen, Netherlands	"What Happens when a bee : Insight into the action of antimicrobial peptides."

No.	Date	Speaker	Title of Seminar
33.	02.03.2011	Dr. Dipyaman Ganguly Columbia University, USA	"A Sense of the Self and its Consequences."
34.	04.03.2011	Dr. Vinod Kumar Uni. of Colorado, Denver, USA	"Therapeutic targets in prostate cancer : What we can do more ?"
35.	08.03.2011	Prof. James A. Yorke Univ. of Maryland, USA	"Whole Genome Assembly : New Challenges."
36.	22.03.2011	Dr. Subhrangsu Chatterjee Univ. of Alberta, Edmonton, Canada	"Differential, species specific unfolding of Prion proteins."
37.	24.03.2011	Dr. Anup Banerjee Saint Louis University, USA	"Viral-Host interaction : Mechanism for HCV persistence and liver disease progression."

Colloquium Lecture

1.	12.08.2010	Dr. W M Busing, Director FEI Company, Netherlands	Application of Transmission Electron Microscopy in Structural and Cellular Biology.

IICB EVENTS

Date	Salient Details
April 23, 2010	IICB, Kolkata organized its 54th Foundation Day celebration. Prof. Indranil Manna, Director, CGCRI, Kolkata was present as Guest-in-Chief and Prof. Kanury V.S. Rao, Senior Scientist & Head, Immunology Group. ICGEB, New Delhi delivered the 22nd JC Ray Memorial Lecture.
April 30, 2010	A Cell Biology & Physiology Research Festival was organized by Cell Biology & Physiology Division of IICB, Kolkata. This festival was a new initiative to foster close interactions amongst the scientists and scholars.
May 19, 2010	HRG, IICB organized a workshop entitled 'LIVING IN EXCELLENCE' where Dr. S. Mukherjee delivered lecture to motivate the Administrative Staff members.
June 11, 2010	Mentor IICB, Kolkata organized First Convocation of NIPER, Kolkata. The convocation was presided over by Sri Asoke Kumar, Secy., Dept. of Pharmaceuticals, GOI and Prof. S.K. Brahmachari, DGSIR, was the Guest-in-Chief. In this First Convocation of NIPER, Kolkata, 29 (twenty-nine) students received their M.S. (Pharm.) Degree scrolls.
September 14, 2010	Hindi day was observed at CSIR-IICB auditorium. The chief guest of the day was Prof. Amarnath Sharma. Head of Hindi Department, Calcutta University and Sri Ramnarayan Saroj, Deputy Director of Hindi teaching scheme, also graced the occasion.
September 26, 2010	IICB celebrated the CSIR Foundation Day. On this occasion, Prof. Ajoy Kumar Ray, Vice-Chancellor, Bengal Engineering & Science University, Shibpur was invited as Guest-in-Chief. The Foundation Day lecture was delivered by Prof. Amitabha Chattopadhyay, Scientist 'H', CCMB, Hyderabad.
November 24-26, 2010	Twenty-seventh Annual Convention of the Society for Information Science & Conference on 'Open Access Gateway to Open Innovation' was organized by IICB-CSIR in association with Bose Institute, Kolkata. Prof. Sibaji Raha, Director, Bose Institute, presented the Welcome Address. Dr. Krishan Lal, President Elect, INSA, New Delhi and former Director, NPL, New Delhi inaugurated the symposium. Dr. Naresh Kumar, President, SIS presented a brief report on the activities of SIS followed by addresses from the Guest-in-Chief, Prof. Ajoy Kumar Roy, Vice-Chancellor, BESU and Guest of Honour, Prof. Dhrubajyoti Chattopadhyay, Pro Vice-

Date	Salient Details
	Chancellor (Academic), University of Calcutta. The meeting was attended by knowledge resource personnel nationwide from different institutions and libraries and also personnel from different international publishers.
December 11-12, 2010	First National Conference on Animal, Microbial, Plant Toxins & Snakebite Management on a title "Biotoxins in Health & Disease" was jointly organized by IICB, Kolkata and KPC Medical College & Hospital, Kolkata. Prof. P. Gopalakrishnakone, Dept. of Anatomy & Venom and Toxin Research Programme, National University of Singapore was the Guest-in-Chief and Prof. Alan L. Harvey of Strathclyde Institute of Pharmacy & Biomedical Sciences, University of Strathclyde, Glasgow, UK was present as International Guest.
December 29-30, 2010	IICB celebrated the CSIR Programme on Youth for Leadership in Science (CPYLS-2010). Prof. Bikash Sinha, Homi Bhabha Professor, Variable Energy Cyclotron Centre, Kolkata was present as Guest-in-Chief.
February 06-09, 2011	The year 2011 is the Platinum Jubilee Year of CSIR-IICB. As a part of this celebration, 30th Annual Convention of Indian Association for Cancer Research and International Symposium on "Signaling Network and Cancer" were organized at CSIR-IICB campus. Scientists and clinicians from different countries, namely UK, USA, Japan, Canada, Australia, Singapore, Korea and India participated in the conference. Prof. Siddhartha Roy, the Director, IICB delivered the welcome address. Dr. Rita Mulherkar, the President of IACR in her address said a few words about the organization and activities of IACR in brief and extended her heartfelt congratulation and wishes in celebration of 75 years of IICB. Dr. Tanuja Teni, Secretary, IACR focused on the organizational structure of IACR and its activities in details. The inaugural session ended with vote of thanks from Dr. Susanta Roychoudhury, Scientist, IICB and Secretary, Organizing Committee.
March 08 - 11, 2011	The 19th IEEE International Workshop on Nonlinear Dynamics of Electronic System (NDES 2011) was held in CSIR-IICB jointly with Saha Institute of Nuclear Physics, Kolkata. The different issues of nonlinear dynamics with an emphasis on electronic system were discussed in the meeting. Some of the relevant topics to IICB were cardiac models, neurodynamics, and synthetic biology.

Computer Division

Dr. Asoke Kr. Dasgupta, Mr. Sujit K. Majumdar, Mr. Prahlad Das

Technical Support

1. Maintain the Local and Wide Area Network.
2. Maintenance of server applications and hardware.
3. Maintain Computational facilities.

The I.T. facilities of IICB has extended it's service to 800 users with 100 Mbps ILL connection from NKN. At present the IICB Network facility management system has been upgraded with latest technology like radius Server, webmail, Bandwidth Management, RFID Technology, NMS Open View etc. Besides these, 200 Desktop PCs, Laptops and Printers have been procured and distributed to the staff members including Scientists, Technical & Administrative Staffs . The WIFI Technology has been introduced at IICB Campus as well as at NIPER Office and NIPER Hostel with 6.8 GHz RF link. About 350 users are having the facility of using WIFI technology throughout its range. More than 14 high end Switches, routers have been installed for IICB Network and WIFI Network. Recently, IICB IT division has been fabricated with 20 TB SAN and IBM servers for ERP application introduced by CSIR.

In House Maintenance

The division looks after about 500 Nodes with various problems, like Hardware, Software and Network problems. IICB Website has been modified from time to time on regular basis. Intrarnet website has been introduced for internal use, which includes various types of official work, Administrative matters, Office Memos, News etc. The Intra Website is updated from time to time on regular basis.

Academic Activities

i) Dr Asoke Kr Das Gupta has been nominated as a Member of the NIPER , Kolkata advisory committee.

ii) Dr Asoke Kr Das Gupta has been nominated as a faculty member of NIPER, Kolkata & IICB PhD course work for the year 2009-2010.

Library & Documentation Division

Mr. N. C. Ghosh, Mrs. P. Chatterjee, Mr. S. Bhakta, Mr. S.K. Naskar, Mrs. S. Ganguly, Mr. M. Halder, Mr. S. Nath & Mr. Asoke Ram

Library & Documentation Division (Knowledge Resource Centre) has been marked for the gradual growth in respect of collection development (print documents and electronic resources), systems and services to the S&T personnel, research scholars and outside walk-in users. It has been developing progressively its holdings containing books (texts & references), journals (print & online), serials, monographs, technical reports etc. As per the instructions of the Official Language Implementation Committee (OLIC), the Centre has been also developing a variety of collection in Hindi. ADONIS, (CD-ROM databases) containing about 743 academic journals in full text approximately from 1991 to 2002 in the biomedical, chemical and pharmaceutical disciplines. In addition the inter-library loan and resource sharing facilities have also been utilized for addressing the users' requirements.

Collections	Upto 31.03.2011
Books (including Hindi)	13851
Journals (print + online) including Indian titles	190
Bound volumes	32504
ADONIS (CD-Rom Database)	743 journals covered full text (1991-2002)
Annual Reports	3881
Thesis (CDs)/online	137

National Knowledge Resource Consortium (NKRC), formerly CSIR E-Journal Consortium is a CSIR Network Project under 10th Five Year Plan being implemented by CSIR-NISCAIR providing access to full text for thousands of exceptional STM Journals and online databases like Web of Science, 'Thomson Innovation' to the CSIR & DST Institutions including CSIR-IICB- Knowledge Resource Centre. The collection includes major publishers like Thomson Reuters, RSC, ACS, Wiley Blackwell, Springer, OUP, CUP, Emerald, Sage, NPG, Taylor & Francis and others. Access to NKRC (CSIR-DST E-journals Consortium) is available at **http://124.124.221.7/**

Services:

Reading Room - a well furnished centrally air-conditioned separate part of the division exclusively used for reading printed documents. During this period a large number of readers and other high dignitaries came to visit the division for reading daily newspapers, printed journals, current journals and other technical reports etc.

E-Journal Access - E-Journal access corner has been established inside the Reading Room of the division. 30 nos. of personal computer placed for surfing internet and accessing online journals/data bases subscribed by CSIR-IICB and available through National Knowledge Resource Consortium (NKRC). It has enhanced the access a lot.

Literature Search - Literature search is one of the very important services provided by the division to its scientists, research scholars and other users engaged in research activities from CSIR-IICB. The outside walk-in users also have been received a lot of such service during this period under review.

Circulation Service - about 688 documents have been issued / returned by the users during the period under review.

ADONIS is an offline electronic data base available in CDs containing full text articles of about 743 high impact factors journals since 1991-2002. About 44 print outs were delivered to the researchers on the basis of requisitions submitted to the division during this period.

Photocopy service - Photocopying is another major area of services in the division. During this period 8500 number of pages has been copied from bound volumes of printed journals, book chapter and from other printed documents to satisfy the user's requirement. Photo copying service has also been extended to the external users against minimum fees as photocopy charges.

Resource sharing is another significant service of the division which has been carried out on a regular basis during this period through efficient sharing of scholarly literature among like minded institutes to alleviate the users need optimally. For this purpose the division used the online union catalogue services offered by NUCSSI (**http://nucssi.niscair.res.in**) and ICAST (**http://www.icast.org.in**) / UCAT and JCCC (**http://instirc.jccc.in**).

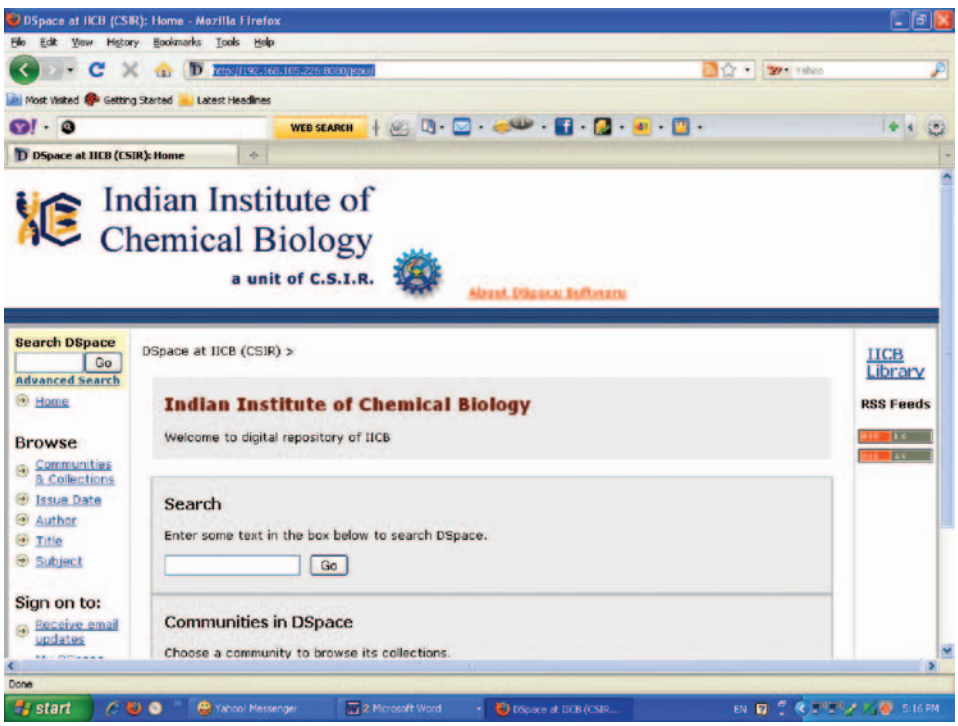
Online Public Access Catalogue (OPAC) is available on internet round the clock for providing information related to library holdings along with hyperlinked URL of the subscribed digital content. The OPAC is available at **http://14.139.223.107:8080/webopac/html/SearchForm** . So far a huge number of users from the institute as well as the outside world have been accessed the holding details of the library.

Two Users Awareness cum Training Programs have been arranged on E-Resources for maximizing its utilization and enhancing learning and research skills among the users.

Reference and Referral services have also been rendered adequately to its users (internal and external) during this period under review.

The **Newspaper Section** has been maintaining 9 nos. of daily newspapers in English, Hindi and Bengali.

Institutional Repository (IR) has been established using D-Space - open source software with an aim to provide online access to mostly pre-print of CSIR-IICB Research Articles, Thesis in full text, Annual Reports, New Letters etc. Under this period only a few thesis are uploaded in the system and can be viewed in intranet at: http://192.168.105.226:8080/jspui/



NIPER- Knowledge Resource Centre has also been functioning in the library premises; CSIR-IICB is the mentor of NIPER, Kolkata. During this period a higher quantity of books (text & references) on Medicinal Chemistry, Pharmaco-informatics and Natural Products have been included to its collection. About 100 students and members of faculty have been served by the centre during this period.

SciFinder (single user) also subscribed by the centre during the period under review.

Conference / Seminar / Symposium Organized

Mr. N. C. Ghosh

27th Annual Convention of the Society for Information Science (SIS) & Conference on 'Open Access: Gateway to Open Innovation', was organized as convenor.

Central Instrumentation

Dr. S. K. Dana, Tapan K. Mukherjee, Surojit M. Roy, Ajoy K. Pramanik, Tarak P. Nandi, M.Vignesh

The Central Instrumentation Division takes care of repair and maintenance of scientific instruments of the institute. The division is actively involved in maintaining the basic infrastructure and amenities for major scientific of the institute. It supports central facility of Centrifuge, Ultracentrifuge, UV/VS spectrophotometers and Lyophilizer. Maintenance has been provided to small but many most essential instruments, which are of high demand like fraction collector, electrophoresis apparatus, high voltage power supplies, voltage stabilizer and high vacuum systems, shaker, high-magnification microscope. The division operates the audio-visual systems, video conferencing system of the institute. In addition, the division initiated R&D efforts on developing new biomedical equipments. This division also carried out investigations on experimental chaos synchronization in electronic circuits under external funding from DST and DAE. Training on experimental nonlinear dynamics is provided to young students from different universities and researchers from India and abroad.

A group of scientists, technical officers and technical assistant support the operation, repair and maintenance of scientific instruments. A few research scholars and project assistants are working towards Ph.D. degrees on nonlinear dynamics using experiments in electronic circuit.

Research and Development

Research and development have been initiated in the division with a purpose of developing new apparatus for biological research. An important R&D initiative is related to develop new understanding of dynamical behaviors in biological and physical systems and to search for their applications. Nonlinear dynamical approach is mainly adopted for understanding living systems' behaviors like cardiac rhythm, neuronal interaction in the brain under pathological condition. The focus of our research is to investigate some of these aspects using mainly experiment on chaotic electronic circuits and with appropriate numerical studies of paradigm models. The basic idea is to set a trend of interdisciplinary research bringing together the knowledge of physics, electronic and biology to explore complex dynamics of natural systems.

A novel electronic circuit of synthetic genetic networks and investigated coupled dynamics of two such oscillators in experiment. A variety of dynamical features is observed as predicted in theory and reported by others. This is a very promising result for designing biological functions using modules of synthetic genetic networks. Another initiative is undertaken using radio-telemetric EEG/ECG measurement and data analysis to understand rat's brain function under drug-induced condition in collaboration with the neurobiology group of the institute.

Collaboration with many national and international institutions has been established. Some of the premier institutions in the country like Presidency University, Kolkata, Department of Physics and Astronomy, Delhi University, Institute for Plasma Research, Gandhinagar and Physical Research

Laboratory, Ahmedabad; Centre for nonlinear dynamics, Bharathidadsan Unviersity, Trichy are participating in the joint research. Institutions from abroad are also collaborating such as the Potsdam Institute of Climate Impact Research, Postdam, Germany; Elizabeth State University, North Carolina, USA; University of North Carolina, Greensboro, USA; Lebedev Physical Institute, Moscow, Russia; Oldenburg University, Germany have started collaboration.

Research Students

Mr. Ranjib Banerjee, Senior Research Fellow

Mr. Sourav K. Bhowmick, Seniro Research Fellow

Mr. Chittaranjan Hens, Project Assistant

Extramural Research Activities

(1) Project Title: *Chaos Synchronization: Exploring technology prospects*
Funding Agency: Department of Atomic eneegy, Board of Research in Nuclear Sciences, Mumbai.
Fund: 15.47 lakh (Duration: 2009-2012)

Principal Investigator: **Dr. Syamal Kumar Dana**

Co-Investigators:

E. Padmanaban, IICB, Kolkata

Dr. Prodyot K. Roy, Department of Physics, Presidency University, Kolkata

Prof. Abhijit Sen, Institute for Plasma Research, Gandhinagar, Gujarat

Dr. Gautam C. Sethia, Institute for Plasma Research, Gandhinagar, Gujarat

Invited Lectures

(1) Plenary Speaker, 11th Experimental Chaos Conference, University of Lille, Lille, France, May 2010.

(2) Plenary Speaker, 18th IEEE Int.Workshop, Nonlinear Dynamics of Electronic Systems, Technical University of Dresden, Dresden, Germany, June, 2010.

(3) Invited Talk, University of Oldeburg, Germany, July, 2010.

(4) Invited Speaker, International Conference Applications of Nonlinear Dynamical systems, Lake Louise, Calgary, Canada, September, 2010.

(5) Invited talk, University of North Carolina, Greensboro, USA, October, 2010.

(6) Invited Talk, Johns Hopkins University, USA, October, 2010.

(7) Invited talk, University of Maryland, USA, October, 2010.

(8) Resource Person, 3-day Hands-On Workshop on experimental nonlinear dynamics, University Agriculture, Abeokuta, Nigeria, November, 2010.

(9) Invited Talk, University of Ibadan, Nigeria, November, 2010.

(10) Invited Talk, University of Lagos, Nigeria, November, 2010.

Honours and Awards

Reviewer of Journals: CHAOS, Physica D, Physics Letters A, European Journal of Physics.

Conference organized

Convener, 19th IEEE International Workshop on Nonlinear Dynamics of Electronic Systems, March, 2011.

Division of Laboratory Animal Sciences

Dr. A. Konar, Dr. H. N. Ray, Mr. S. S. Verma, Mr. A. Das Mr. R. Sarkar, Mr. A. Sardar. Mr. J. Middya, Mr. P. Middya, Mr. T. Sarkar, Mr. Lalu Sardar, Mr. G. Sardar, Mr. S. Midya

IICB with its CPCSEA registered animal facility (Registration No 147/1999/CPCSEA, Date: 22. 07. 1999) is a podium for biomedical research going on in this institute, required for improvement of the quality of human life. This improvement stems in part from progress in ameliorating human disease and disability, in part from advances in animal health and veterinary medicine, and in part from the enlargement of our understanding of complex and intricately connected biological systems of human and animal physiology and its disorders. Besides that, work with living animals is vital to continue progress in many areas of clinical and basic research. Though there are alternatives in the form of cell and tissue culture, lower animal study or computer simulation, the use of whole animal is irreplaceable. The mission of the IICB animal facility is to provide animals of required specification for research projects of this Institute as well as to carry out a continuous research on laboratory animals. Through research on these animals, scientists are in search of cures and preventions for a number of human and animal ailments. The other major responsibility of this facility is to ensure the persuasion of 3Rs of animal experimentation and the ethical principles of animal use are followed as per CPCSEA guidelines.

The facility maintains a colony of mice (Balb/C), rats (Sprague-Dawley), hamster (Golden), rabbits (New Zealand) and guinea pigs (English). Two new strains (Swiss albino and C57BL/6) have been introduced in the breeding facility. The in-house breeding colony provides animals for the institutional research projects and housing facility for the experimental animals. Moreover, some other research institutes who have their CPCSEA registration, also collect animals from the facility for their IAEC approved research projects.

At any given point of time, IICB Animal house maintains about 4000 Rats, 4500 mice, 2200 hamsters, 225 rabbits and 100 Guinea Pigs. The animals are maintained in a conducive environment (i.e. Room Temp. 24 , ±2 °C ; relative humidity 55 - 60%; light and dark schedule 12:12 hrs; illumination 350 - 400 lux at 1 mt above the floor). The animals are provided ad libitum with balanced and sterilized diet in pelleted form, produced in-house.

A brief account of animal produced/supplied from the animal house in during this period is given in the following table :

Table: Statement of Production and Utilization of Animals during 2010-2011

Species	Stock on 1st April 2010	No. of animals		Total (A)	No. of animals issued				Total (B)	Stock (A-B) on 31st March, 2011
		Produced	Purchased		Produced	Purchased	Died in stock	Supplied to other institutes		
Mouse	1552	5742	456	6198	5444	456	0	20	5020	1178
Rat	1943	3077	0	5020	3403	0	0	0	3403	1617
Hamster	342	852	0	1194	818	0	0	0	818	376
Rabbit	86	99	0	185	33	0	0	50	83	102
Guinea pig	76	15	0	91	06	0	0	0	06	85

Engineering Services Unit

Dr. A. K. Sen, Mr. U. K. Barua, Mr. S. Saha, Mr. B. Jayakumar, Mr. S. Ray, Mrs. N. Bage, Mr. D. Banik, Mr. M. B. Malakar, Mr. P. K. Chanda, Mr. G. Malik, Mr. S. Basak, Mr. S. N. Mondal, Mr. S. Pradhan, Mr. S. Biswas, Mr. S. R. Tudu, Mr. S. Nath, Mr. S. Mazumder, Mr. Ujjal Roy, Mr. A. Karmakar, Mr. A. Pal, Mr. S. K. Ghosal, Mr. B. Das

The Engineering Services Unit (ESU) is comprised of the civil engineering, electrical engineering and air-conditioning & refrigeration sections.

Electrical Engineering Section

The electrical engineering section renders essential services and infrastructure support to R&D activities and other public utilities of the Institute. The section maintains and supplies steady power supply through the 6.6 MVA power sub-station of the institute and monitors for uninterrupted power supply system from the CESC source. The section also supplies emergency power through available DG Sets and conducts its operation & maintenance.

List of major works completed during the year:

- Renovation of LT power distribution system of sub-station under IRR.
- Renovation of Electrical installations of Room Nos. 17, 239, 235, 206, library etc.
- AMC for internal & external electrification works of Electrical installations.
- Installation of 2x500 KVA new DG-sets for Emergency power at IICB.
- Installation of capacitor bank.
- Feeder connections of LT cubicle panels and other allied works of the power substation.
- Renovation of electrical lines and power distribution system of several laboratories.
- Documentation of the existing electrical distribution system of IICB including layout and schematic diagrams.

The works that are under progress:

- Renovation of the electrical lines and power distribution system of selected laboratories.
- AMC for internal & external electrification works of Electrical installations.
- Maintenance & service overhauling of 6.6 KV HT power supply system.
- Maintenance of 2x500 KVA DG Set.

- Installation testing and commissioning of existing 1x62.5 KVA silent type DG Set at the Scientist apartment cum NIPER hostel campus.

Air-conditioning and Refrigeration Section

This section looks after the AC facility in all the laboratories, the library, the auditorium, the administrative wings and most importantly the animal house. It also takes care of the refrigerators and deep freezers in the laboratories, maintains the cold rooms and constant temperature rooms and is also responsible for the maintenance of the lifts.

List of major works in the past one year:

- Annual maintenance of window and split AC units.
- Annual maintenance of 2x80 TR AC plant for animal house.
- Maintenance of cold rooms & constant temperature rooms.
- Construction of a class 10000 Clean Room for the Protein Micro Array facility.

The following works are in progress:

- Renovation and refurbishing of the central AC plant is in progress to cater for the library and auditorium.
- Installation of two Modular Cold room.
- Annual maintenance of AC's, Lifts, AC power plant etc.
- Installation of state-of-the-art materia culture room.

Civil Engineering Section

The Civil Engineering Section renders services in the broad areas of infrastructure development, renovation of laboratories and common facilities, maintenance of campus, sewerage and drainage systems, cleaning and house-keeping work.

List of major works carried out during this period:

- Repair, renovation and up-gradation of different laboratories and offices.
- Repair and renovation of buildings and services (AMC).
- Repair and renovation of tissue culture rooms and laboratories.
- Repair, renovation and up-gradation of the CSIR hostels on Prince Anwar Shah Road.
- Construction of a new meeting room.

The following works are in progress:

- Renovation of the auditorium and several laboratories.
- Overall beautification of the campus and interior.
- Planning of extension of the IICB laboratory building and construction of the new Animal House through PMC.
- Repair and renovation of buildings and services through AMC.
- Repair and maintenance of the CSIR Scientists' Apartment Complex at Prince Anwar Shah Road.
- General cleaning and house-keeping of the CSIR Scientists' Apartment Complex at Prince Anwar Shah Road.
- Construction of new IICB campus at Salt Lake, Kolkata.
- Planning of construction of additional 4 stories at Salt Lake Campus.

Administration

GENERAL ADMINISTRATION

A wide range of functions are carried out by General Administration which cater to the life cycle of an Officer of the Scientific, Administrative and Technical Cadre encompassing manpower planning, cadre management, recruitment, role definition / allocation, skill assessment, workplace learning, career advancement, transfer, employee benefits, retirement, performance assessment etc. In addition Administration is also responsible for arrangement of all logistics and managing the day to day affairs of the Institute.

Officers in General Administration

- Mr. S.K. Chaudhuri, Administrative Officer
- Mr. K. Bhattacharjee, Section Officer
- Mr. Siddhartha Dey, Section Officer
- Ms. Shampoo Sengupta, Section Officer
- Mr. P.K. Saha, Section Officer
- Mr. Ashok Putatunda, Section Officer

COA & AO's Secretariat

- Mr. Sankar Kr. Santra

Sections in General Administration & Associated Staff

[i] Recruitment, Committee & CR

Mr. Siddhartha Dey, Ms. Indira Kundu, Mr. Tapan Das, Mr. Raju Pal, Mr. Ranjit Debnath, Mr. Saugata Das

[ii] Establishment - I

Ms. Shampoo Sengupta, Mr. Kanu Mondal, Ms. Anjana Mandi, Ms. Sanhita Ganguli, Mr. R. N. Hansda

[iii] Establishment - II

Mr. K. Bhattacharjee, Mr. D.K. Kisku, Mr. Prem Singh, Mr. Alok Ray, Mr. Atanu Moitra, Mr. Paresh Sarkar, Mr. Jayanta Pal, Mr. Suresh Balmiki, Mr. Kailash C. Nayek, Mr. TK Sinha Roy, Mr. Nandalal Routh

[iv] Establishment - III

Mr. P.K. Saha, Ms. Monalisa Bhattacharya, Md. Mukhtar Ahmed

[v] Receipt & Issue

Mr. A. Putatunda, Mr. Saibal Giri.

FINANCE & ACCOUNTS

This wing of administration is mainly concerned with keeping record of budgetary requirements, controlling & monitoring the expenditure and preparing budget for the Institute regarding plan & non-plan expenditure, which is about Rs.67-72 crores per annum. Keeping track of progressive expenditure of budget for every month, keeping financial records for 17 Networked Projects, externally funded projects, disbursement of pension to pensioners, accounting and auditing files routed through Establishment, Purchase and other scientific decisions. TO Seek grant from outside bodies, i.e. UGC, ICMR, DBT etc., monthly remittance of P. Tax, I. Tax, Service Tax, etc. and incorporating entire vouchers of the Institute in IMPACT software. Through IMPACT entry, our Annual Accounts and Balance Sheet is generated for onward transmission to CSIR,HQ.

Functional hierarchy of Finance & Accounts wing is follows:

Shri S.K. Das (F&A Officer), Shri A.K. Jha (S.O. F&A), Shri A.K. Tiwary (S.O. F&A), Shri Sanjoy Mukhopadhyay, Shri Anil K. Chanda, Smt. Banani Dutta, Smt. P.L. Saha, Shri Asit Kr. Roy, Shri Mihir Kr. Dutta & Shri Vishal Agarwal.

Stores & Purchase

The Stores & Purchase Division caters to the research and other requirement of IICB. The annual procurement budget of IICB is about Rs 500 million annually comprising of research consumables like chemicals, glass wares, plastic wares etc and various capital items. After successful implementation of online procurement and stores systems since 2007, the division had introduced web based ordering system from last year and continued successfully in the reporting year for Sigma products, Vendor Managed Inventory program, stock of consumable of companies like Fisher, SRL, Spectrochem, Merck, RFCL, JT Baker, Tarson, Axygen, Fermenta, Thermo, BD falcon, Invitrogen, Takara-clontech, MN, Gilson & Eppendorf Pipettes, Computer cartridges of HP, Corning and so on. The division assists scientists and other users to utilize their budget grant within the project deadlines. The division also undertakes the issue of total logistic chain of items from anywhere in the world to IICB that are either purchased by IICB or being sent as free gifts or samples. It also undertakes customs clearance with concessional customs duty within demurrage free clearing time from Kolkata Airport and Sea port. Adjustment of OB, replies to audit and other statutory authorities, assistance to accounts for bank re-conciliation are other activities performed by the division.

The division is manned by the following personnel

Shri US Das, COSP, Shri NK Saha, SPO, Shri R Bage, SO(S&P), Shri TK Mitra, SO(S&P), Shri P Naskar, Shri ABS Roy, Shri R Roy, Shri B Das, Smt B Pal, Shri A Sen, Shri P Sarkar, Shri RP Gorh, Shri S. Banik, Smt. Somadevi, Shri RN Jana, Shri UN Mandi.

Official Language Activities of the Institute

This year in accordance with the official language act, the compliance has been successfully made in the Institute with special reference to implementation of various practical usage of official language in the daily activities like day to day translation, Hindi word writing and displaying etc. including but not limited to preparation of official memos, general orders, issuance of notices, tenders, etc in bilingual form which is in accordance to rule 3(3) of the official language act.

IICB observed Hindi week from 9-14 September 2010. On the 13th of September Hindi debate competition was held in the Institute. The topic of the debate competition was 'Reservation is a must for ladies in public service commission'. Dr. Sidhartha Majmudar Technical Officer & P. Paliwal, Sr. Hindi Officer (CGCRI) were the judges of this competition.

At 2.30 pm same day a Hindi workshop was held, This workshop was conducted by Sri P.Paliwal Senior Hindi officer, CGCRI. He spoke on Hindi scientific and technical vocabulary and the use of correct vocabulary and use of vocabulary for different purpose. He also spoke on the solutions the aspects of different Hindi technical words.

Hindi day was observed on 14th September, 2010. The Chief guest of the day was Prof Amarnath Sharma, Head of Hindi dept of Calcutta University. Sri Ramnarayan Saroj, Deputy Director Hindi teaching scheme, Kolkata also graced the occasion. Senior scientists Dr. Adya, & Dr. T. K. Dhar were present in the occasion. They delivered their messages in Hindi and inspired the participants and audience to work in Hindi. 50 prizes were kept for writing Hindi correct word. Dr. Sidhartha Majumdar, technical officer & Sri Vijay Shankar Mishra Hindi teacher were the Judges of Hindi competitions held like Hindi elocution, Hindi debate, extempore.

The vote of thanks was given by Sri S.K.Chowdhury, Administrative Officer and the programme was organised by Smt. A. Nag, Senior Hindi translator.

Extramural Research Activities

INFECTIOUS DISEASES AND IMMUNOLOGY

Invited Lectures

Dr. H. K. Majumder

Topic : Topology of DNA governed by DNA topoisomerase of *Leishmania*.
Venue : DBT workshop on "PCR based Advanced DNA Fingerprinting" at Assam University, Silchar.
Date : April 21-May 5, 2010.

Topic : Targeted therapeutics and kDNA based diagnostics of *Leishmania*.
Venue : Assam University, Silchar.
Date : April 21-May 5, 2010.

Topic : Development of diagnostics and therapeutics against Leishmaniasis.
Venue : One day seminar lecture series on Basic and Applied Microbiology, Dept. of Microbiology, Burdwan University.
Date : May 14, 2010.

Topic : A journey with *Leishmania* DNA topoisomerases.
Venue : Institute for Microbial Technology, Chandigarh.
Date : May 06, 2010.

Topic : *Leishmania* DNA topoisomerases: Fascinating story behind.
Venue : Arhus University, Dept. Of Molecular Biology, Denmark.
Date : September 29, 2010.

Topic : Targetted therapeutics against *Leishmania* parasites.
Venue : Kalyani University on its Golden Jubilee Celebration.
Date : August 17, 2010.

Topic : Chikitshya Bigyane Anabic jeeb bidyar proyog.
Venue : Gopal Chandra-Sarala Ganguly Memorial Oration Lecture at Ramkrishna Mission, Golpark.
Date : May 14, 2010.

Topic : A journey on DNA topoisomerases of *Leishmania.*
Venue : Delhi University, South Campus (UDSC).
Date : September 03, 2010.

Topic : DNA topoisomerase inhibitors induced apoptosis in *Leishmania*.
Venue : International conference on "Cell Signalling and Diseases" at School of Biotechnology, KIIT University, Bhubaneswar.
Date : October 29, 2010.

Topic : Leishmanisis, a threat to tropical countries: Diagnostics and prevention.
Venue : UGC sponsored symposium on Resurgent vector borne diseases and climate change: A threat to mankind at Maharaja Uday Chand Mahatab Womens College, Burdwan.
Date : December 15, 2010.

Topic : Tyrosyl DNA phosphediesterase from *Leishmania*.
Venue : Guha Research Conference-2010 at Aurangabad.
Date : December 16-21, 2010.

Dr. Chitra Mandal

Topic : "9-O-acetyl sialic acids: A promise for future therapy and management of childhood acute lymphoblastic leukemia" in the Hematological malignancies.
Venue : NCBS-SJMC at NCBS, Bangalore.
Date : August 2-3, 2010.

Topic : Modulation of sialic acid regulating enzymes crucially drives the fate of Leukemic cells and their correlation with disease status in leukemia.
Venue : Potsdam, Potsdam, Germany at 13th International Conference on Biology and Chemistry of Sialic Acids (Sialoglyco 2010).
Date : August 21 - 26, 2010.

Topic : Herbal medicine as an alternative approach for leukemia therapy and its signalling pathway.
Venue : Swabhumi in Kolkata.
Date : September 11-12, 2010.

Topic : Neutral sphingomyelinase-ceramide cascade mediated Synergistic activation of JNK and p38MAPK in leukemia by a steroidal lactone.
Venue : Estuary island resort, Trivandrum, Kerala, India in the 9th International Symposium Roles of Eukaryotic Cell SurfaceMacromolecule (Founded by late Biochemical Prof. B. K Bachawat).
Date : January 27-31, 2011.

Topic : Functional role of sialic acid regulating enzymes in acute lymphoblastic Leukemia.
Venue : CSIR-Indian Institute of Chemical Biology, Kolkata.
Date : February 6-9, 2011.

Topic : Cell signaling and cancer.
Venue : Dept. of Molecular Endocrinology, National Institute for Research in Reproductive Dept Health, Parel, Mumbai.
Date : March 12, 2011.

Topic : Exploration of Indian potential herbal sources for future new drugs: A promise for treatment of a variety of cancers.
Venue : Manipur University.
Date : March 28-29, 2011.

Topic : Sugar plays mysteries role in diagnosis and therapy of leukemia patients.
Venue : Imphal, Manipur University.
Date : March 28-29, 2011.

Dr. Pijush K. Das

Topic : Mechanisms by which *Leishmania* parasites establish infection within macrophages of human host: cyclic nucleotide signaling.
Venue : 150 years Celebration Symposium of Ashutosh College, Calcutta University .
Date : September 03, 2010.

Topic : Macrophage biology in relation to disease pathogenesis using leishmaniasis as the model macrophage disease.
Venue : Aarhus University, Aarhus, Denmark, Department of Molecular Biology.
Date : September 30, 2010.

Topic : From cells to signaling cascades: Manipulation of macrophage defense by a Model intracellular pathogen, *Leishmania donovani*.
Venue : National Symposium on Molecular Signaling in Biology, North-Eastern Hill University, Shillong .
Date : March 25, 2011.

Topic : Cyclic nucleotide signaling in the establishment of *Leishmania* infection in macrophages. Symposium on Cell Biology, St. Xavier's College, Kolkata.
Venue : Symposium on Cell Biology, St. Xavier's College, Kolkata.
Date : March 23, 2011.

Dr. Syamal Roy

Topic : Poor stability of peptide-MHC Complex may specify defective cellular immunity in Leishmaniasis.
Venue : Federal Drug Administration (FDA)/CBER.
Division of Emerging and Transfusion Transmitted Diseases.
Dept. of Health and Human Services, Bethesda, MD, USA.
Date : September 1, 2010.

Topic : A new way to look at defective cellular immunity in Leishmaniasis.
Venue : University of Connecticut, CT, USA.
Date : September 7, 2010.

Topic : Membrane biology of Leishmania infection.
Venue : Tufts University School of Medicine, Boston, MA, USA.
Date : September 10, 2010.

Dr. Nahid Ali

Topic : Potentiating effects of MPL on DSPC bearing cationic liposomes promote recombinant gp63 vaccine efficiency: impressive immunogenicity and protection.
Venue : 37th Annual Conference of Indian Immunology Society, Jammu.
Date : February 7-9, 2011.

Topic : Visceral Leishmaniasis: Disease pathogenesis and control.
Venue : Research Council meeting. IICB, Kolkata.
Date : March 10, 2011.

Dr. Rupak Bhadra

Topic : The stringent response related gene dksA is involved in pleiotropic regulation in *Vibrio cholerae.*
Venue : Indo-Sweden International Symposium on Molecular and Pathophysiological Research on Enteric Pathogens held in Kolkata during January 27-29, 2011.
Date : January 27, 2011.

Topic : Nutritional starvation stress related genetic circuit in *Vibrio cholera*.
Venue : National Seminar cum Workshop' on "Application of Advance Techniques in Bio- Medical Laboratory Science" (DST and UGC sponsored) held during 25-29 March, 2011.
Date : March 26, 2011.

Dr. Tripti De

Topic : National Symposium on Trends in Cellular Biochemistry and Biophysics .
Venue : University of Kalyani, Kalyani.
Date : 5-6 October, 2010.

Dr. Uday Bandopadhyay

Topic : Role of mitochondrial pathology and apoptosis in gastric mucosal cell during Non-steroidal anti-inflammatory drugs (NSAIDs)-induced gastropathy. (Section Regulation of biochemical and cellular process in diverse systems).
Venue : SBC(I) Annual meeting , I.I.Sc.Bangalore.
Date : December 13-15, 2010.

Dr. Malini Sen

Topic : Evaluating Wnt and WISP: A Molecular Approach.
Venue : SBC Symposium.
Date : June 11, 2010.

Chairing a Session

Dr. H. K. Majumder

Chaired a session on Ist National Conference on Animal, Microbial Plant toxins and snake bite Management "Biotoxin in Health & Diseases" at Dept. of Biochemistry, KPC Medical College & Hospital, Kolkata on December 11, 2010.

Chaired a session In the 30th Annual Convention of Indian Association for Cancer Research & International Symposium on "Signalling Network and Cancer" at Indian Institute of Chemcial Biology during February 6-9, 2011.

Inaugurated workshop on Intellectual Property Rights at BCET, Durgapur on 30.03.2011 as Working Chairman of West Bengal State Counicl for Science & Technology.

Dr. Chitra Mandal

Chairing a Session "New Frontiers of Hematology and Oncology" during September 12th, 2010 held at Swabhumi in Kolkata.

Chairing a Session 9th International Symposium Biochemical Roles of Eukaryotic Cell Surface Macromolecule (Founded by late Prof. B. K Bachawat) during January 27-31, 2011, Estuary island resort, Trivandrum, Kerala, India.

Chairing a Session 30th Annual Meeting of the Indian Association for Cancer Research and International symposium on signaling network and cancer during 6-9 February 2011, at CSIR-Indian Institute of Chemical Biology, Kolkata.

Chairing Technical Session & Invited Lecture (IL3) of 18th West Bengal State Science and Technology Congress during 28th February- 1st March 2011 held at Narendrapur College Campus.

Dr. Pijush Das

Chaired a session on National Symposium on Molecular Signaling in Biology, North-Eastern Hill University, Shillong on March 25, 2011.

Academic performance: Teaching, Examining and Training

Dr. H. K. Majumder

Guest Professor, Department of Biophysics, Molecular Biology and Genetics, Calcutta University.

Guest Faculty Member, National Institute of Pharmaceutical Education and Research, (NIPER) Kolkata.

Member, Board of Studies in Biotechnology, St. Xaviers College, Kolkata.

Member, Board of Studies in Microbiology, Lady Brabourne College, Kolkata.

Member, Advisory cum Monitoring Committee under "University with Potential for Excellence" Scheme of UGC, Calcutta University.

External Examiner of the Ph.D. thesis submitted to Hyderabad University and Jawaharlal Nehru University, New Delhi.

Lead Guest Editor of the Special Issue on "Target Identification and Intervention Strategies against Kinetoplastid Protozoan Parasites" for the journal Molecular Biology International, SAGE- Hindawii Press USA, 2011.

Dr. Pijush K. Das

Guest Professor, M.Sc. (Biophys & Mol. Biol), M.Sc. (Biotechnology), M.Sc. (Microbiology), M.Sc. (Genetics) of Calcutta University, M.Tech (Biotech) of Jadavpur University and M.Tech (Biotech) of West Bengal University of Technical Education for teaching Biochemistry and Cell Biology.

Examiner in the M.Sc. (Biochemistry), M.Sc. (Biophysics & Molecular Biology), M.Sc. (Biotechnology), M.Sc. (Microbiology), M.Sc. (Genetics) at Calcutta University and M.Tech. (Biotech) at Jadavpur University.

Member, Board of Studies, North-Eastern Hill University.

Dr. Chitra Mandal

Teaching at NIPER, Kolkata, as a Guest faculty member.

Training Summer students selected by Indian Academy of Science, Bangalore.

Appointed as the external examiner to examine thesis and conduct viva voce examination of a few Ph.D thesis submitted to (i) Jadavpur University, Kolkata; (ii) J.N.U, New Delhi; (iii) National Institute of Immunology (NII), New Delhi.

Member of Project review committee of ICMR.

Reviewer of many project proposals submitted for funding to CSIR, DST, DBT, ICMR.

Reviewer of many manuscripts submitted to several International and National journals.

Dr. Syamal Roy

Teaching Post graduate students in Bioengineering at Jadavpur University, Kolkata700032.

Dr. Nahid Ali

Lead Guest Editor, special issue on Immunity to Visceral Leishmaniasis, Journal of Tropical Medicine, Hindawi Publishing Corporation, 2011.

Reviewer of FEMS Immunology and Medical Microbiology, Journal of Microencapsulation, Journal of Controlled Release, Vaccine, Experimental Parasitology, BMC Immunology, Expert Reviews,

Journal of Food Biotechnology, Molecular Pharmaceutics, International Journal of Integrative Biology Chemotherapy.

Reviewer, projects submitted for financial assistance to DST, CSIR, ICMR and Wellcome Trust.

Supervised the project work of three students of M.Sc and M.Tech, working as summer trainees Reviewer for Expert Opinion for Drug Delivery, Journal of Parasitology, BMC Immunology, Nanomedicine, New Technology, Biology and Medicine, Scholarly Research Exchange, International Journal of Integrative Biology, etc.

Dr. Rukhsana Chowdhury

Examiner, M.Sc. (Biotechnology) Calcutta University.

Member of Ph.D committee, West Bengal University of Health Sciences.

Jt. Secretary, Proteomics Society (India).

Dr. Rupak Bhadra

Acted as an external examiner of Ph.D. viva voce examination of Jadavpur University, Kolkata.

Served as an M.Sc. examiner of Department of Microbiology, Bijoygarh College.

Served as an external reviewer for research proposals submitted to DST, DBT, CSIR etc.

Acted as a reviewer for Elsevier, SGM, BMC Series, Wiley-Blackwell etc.

Teaching of M.Pharm. students of NIPER, Kolkata.

Taking course work classes of the students enrolled in Ph.D. at IICB.

Teaching of M.Sc. Physiology students of Presidency College, Kolkata.

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Dr. Uday Bandopadhyay

Teaching, examining and training: Examiner, Department of Biochemistry, CU; NIPER, Kolkata.

Dr. Malini Sen

Immunology (IICB) and Selected topics of Metabolism (NIPER) .

Dr. Aparna Laskar

Demonstration of instruments is provided all year long, whenever initiated by the institute and on specific CSIR initiated open house programmes.

Invited as a guest faculty at the CME organized by the academic/ research department of Cancer

Centre Welfare Home & Research Institute (CCWH&RI), Thakurpukur, Kolkata.

Deputation Abroad

Dr. H. K. Majumder

Visited the laboratory of Professor Birgitta R. Knudsen, Department of Molecular Biology, Aarhus University, Aarhus, Denmark during September 27-October 04, 2010 in connection with developing a collaborative programme between Indian Institute of Chemical Biology and Aarhus University, Denmark on infectious diseases.

Dr. Chitra Mandal

Attended 13th International Conference on Biology and Chemistry of Sialic Acids (Sialoglyco 2010) at Potsdam, Germany during August 21 - 26, 2010 and deliver an Invited talk.

Dr. Pijush K. Das

Visited the laboratory of Professor Birgitta R. Knudsen, Department of Molecular Biology, Aarhus University, Aarhus, Denmark during September 27-October 04, 2010 in connection with developing a collaborative programme between Indian Institute of Chemical Biology and Aarhus University on infectious diseases.

Dr. Syamal Roy

Visited Federal Drug Administration (FDA). Department of Health & Human Services, Bethesda, MD, USA, during 21-08-2010 to 20-09-2010.

Visited Pasteur Institute, Paris for Mid-term Evaluation of European Commission Funded Project, during 21-09-2010 to 25-09-2010.

Papers/Abstract presented in the Conference

Dr. Chitra Mandal

National Conference: Ten (10) numbers.

Syamal Roy

National Conference: Two (02) numbers.

Dr. Rupak Bhadra

National Conference: One (01) number.

Dr. Mridula Misra

National Conference: One (01) number.

Dr. Mita Chatterjee Debnath

National Conference: Two (02) numbers.

Dr. Krishna Das Saha

National Conference: Two (02) numbers.

Conference/Symposia/Workshops organized

Dr. Chitra Mandal

Joint Convenor of 30th Annual Convention of Indian Association for Cancer Research and International Symposium during 6-9th February 2011 at CSIR-IICB.

Dr. Rupak Bhadra

Served as a member and organized the 30th Annual Convention of Indian Association For Cancer Research & International Symposium on 'Signalling Network and Cancer' plus celebration of 75th year of IICB.

Dr. Mridula Misra

As convener of Radioactive, Chemical Safety and Bio-Safety Committee a "Training Programme and Workshop on Laboratory Safety" (Chemical Safety, Radioactive Safety and Bio-Safety) has been organized on 30th September 2010 at IICB, Kolkata for the students and staff of IICB, Kolkata.

Major Infrastructural facilities

Dr. Rupak Bhadra

Maintenance of Scanning Electron Microscope (Tescan, Model VEGA II LSU) facility.

MOLECULAR AND HUMAN GENETICS

Invited Lectures

Dr. S. Adhya

Topic : Physiological effects of mitochondrion-targeted RNAs on rat muscle function.
Venue : International Conference on Mitochondrial Research and Medicine, Katra, India.
Date : 12-13 November, 2010.

Dr. Kunal Ray

Topic : A perspective on pigmentation and albinism in Indian context.
Venue : Biotechnology Department, Calcutta University.
Date : April 9. 2010.

Dr. Keya Chaudhuri

Topic : Association of DNA repeated sequences in the XRCC5 gene with susceptibility to oral cancer.
Venue : Symposium on DNA structure, function and applications organized by the DNA Society of India and Jadavpur University, Kolkata held at Jadavpur University.
Date : July 7, 2010.

Topic : IICB-Library: the knowledge resource centre.
Venue : 27th Annual Convention and Conference on "Open Access Gateway to Open Innovation" of Society for Information Science (SIS), jointly organized by IICB & Bose Institute at Bose Institute, Kolkata.
Date : 24th November, 2010.

Topic : Cholera toxin associates with Vibrio cholerae outer membrane vesicles and are internalized by human intestinal epithelial cells.
Venue : 1st National Conference on Animal, Microbial, Plant Toxins & Snakebite Management, organized by KPC Medical College and Hospital & Indian Institute of Chemical Biology, held at KPC Medical College, Kolkata.
Date : 11th December, 2010.

Topic : Role of intracellular signaling cascade and epithelial cell-dendritic cell cross talk in the initiation of inflammatory response in host following Vibrio cholerae infection.
Venue : International Symposium on Molecular and Pathophysiological Research on Enteric Pathogens organized by National Institute of Cholera & Enteric Diseases, Kolkata on the occasion of Centenary & golden Jubilee Celebration of ICMR & NICED respectively, held at Peerless Inn, Kolkata.
Date : 28th January, 2011.

Dr. Susanta Roychoudhury

Topic : Novel Role of Spindle Assembly Checkpoint Protein Cdcc20 in Transcription Regulation: A New Insight into the Genomic Instability in Human Cancer.
Venue : 79th Annual Meeting of Society of Biological Chemists, IISc, Bangalore.
Date : December 13-16, 2010.

Dr. Ashok K. Giri

Topic : Arsenic Contamination in Ground Water and its Health Effects and Genetic Susceptibility, Route of Exposure and Mitigation.
Venue : 2nd Westlake Conference on Translational Medicine, Hangzhou, China.
Date : December 1, 2010.

Topic : Arsenic Contamination in Groundwater: Health Effects, Genetic Susceptibility, Route of Exposure and Mitigation.
Venue : INSA Panel Discussion on Hazardous metal pollution in India sources toxicity and management at the Indian National Science Academy.
Date : December 1, 2010.

Topic : Arsenic Induced Toxicity and Carcinogenicity: Genetic and Genomic Approaches to Identify Susceptible Individuals.
Venue : 30th. Annual Conference on Society of Toxicology which was held at the Jamia Hamdard Universty, New Delhi.
Date : December 9-11, 2010.

Topic : Arsenic Contamination in Ground Water: Health Effects, Genetic Susceptibility and Its Mitigation.
Venue : 2nd Asian Conference on Environmental Mutagens which was held at Pattaya, Thailand.
Date : December 15-18, 2010.

Topic : Ground water arsenic contamination and its health effects: Evaluation of genetic susceptibility and route of exposure for mitigation.
Venue : Environmental Mutagen Society Meeting which was held at the Vellore Institute of Technology, Vellore.
Date : Feb. 4-6, 2011.

Topic : Genetic and Genomic Approaches to Decipher Arsenic Toxicity and Susceptibility.
Venue : DST-INSPIRE Internship Program at School of Biotechnology, KIIT University, Bhubaneswar.
Date : February 11, 2011.

Chairing a Session

Dr. Kunal Ray

Chaired a session on Community Ophthalmic Genetics (October 31, 2010) in International Symposium on Community Ophthalmology organized by the Indian Association of Community Ophthalmology, Science City, Kolkata (October 30 & 31, 2010).

Chaired a session on Neurobiology (December 7, 2010) in International Symposium organized by Dept of Biophysics, Molecular Biology and Genetics, University of Calcutta, Kolkata.

Dr. Keya Chaudhuri

Chaired a session in the symposium on New Frontiers on Haematology and Oncology organized by Netaji Subhas Chandra Bose Cancer Research Institute, Sept 11-12, 2010.

Chaired a session in the 1st National Conference on Animal, Microbial, Plant Toxins & Snakebite Management, organized by KPC Medical College and Hospital & Indian Institute of Chemical Biology, held at KPC Medical College, Kolkata on 11-12th December, 2010.

Chaired a session in the 30th Annual Convention of Indian Association for cancer Research & International Symposium on "Signaling Network and Cancer", at CSIR-IICB, Kolkata, 6-9 February, 2011.

Dr. Ashok K. Giri

Chaired a session at the 2nd Asian Conference on Environmental Mutagens which has held at Pattaya, Thailand from December 15-18, 2010.

Papers/Abstract presented in the Conference

Dr. Suvendra Bhattacharyya

National Conference: Six (06) numbers.
International Conference: One (01) number.

Dr. Kunal Ray

National Conference: Three (03) numbers.
International Conference: One (01) number.

Dr. Keya Chaudhuri

National Conference: Ten (10) numbers.

Dr. Susanta Roychoudhury

National Conference: Eight (08) numbers.

Dr. Ashok K. Giri

International Conference: One (01) number.

Academic Performance: Teaching, Examining & Training

Dr. S. Adhya

Lectures on Cell Biology to Calcutta University students.

Dr. Suvendra Bhattacharyya

Served as a guest lecturer at the Dept. of Biophysics and Molecular Biology, University of Calcutta.

Dr. Kunal Ray

An honorary lecturer and examiner of the M. Sc. (Biotechnology), M. Sc. (Genetics), and M. Sc. (Neuroscienes), Calcutta University.

An honorary lecturer and examiner of NIPER at IICB.

Deliver lectures in the UGC sponsored courses in Calcutta University.

Member (External Expert) of a committee to perform function of Postgraduate Board for M.Sc. course in Genetics and Neurosciences in Calcutta University.

Member (External Expert) of a committee to perform function of Postgraduate Board for M.Sc. course in Biotechnology in Presidency University.

Member of Monitoring Committee for National Fund for Basic & Strategic Research (NFBSRA).

Evaluate research proposals submitted to DST, DBT, CSIR etc. for funding.

Supervised eight students in the mandatory project work as part fulfillment of their various degrees like BTech, MSc and MTech.

Associate Editor, Journal of Genetics (published by Springer).

Reviewed papers for (i) Molecular Vision, (ii) BMC Genetics, (iii) BMC Molecular Biology, (iv) Archives of Ophthalmology, (v) Journal of Biosciences, (vi) Journal of Investigative Dermatology, (vii) Journal of Genetics (viii) Clinical Genetics etc.

Dr. Keya Chaudhuri

Supervised students from WBUT-Bioinformatics, Presidency College, Bengal College of Eng & Tech, Durgapur, Biochemistry C.U., NIT-Rourkela Orissa, NIPER-Kolkata, St. Xavier's College in dissertation work for the partial fulfillment of their M.Sc, M.Tech, M.Pharm degrees.

Lecturer and Examiner of NIPER, Kolkata.

Lecturer, Examiner of Ph.D. Course Work, IICB.

Dr. Susanta Roychoudhury

Teacher in Cell Biology course in M.Sc. (Biophysics, Molecular Biology & Genetics), Calcutta University.

Teacher in Cancer Genetics course in M.Sc. (Biotechnology), Calcutta University.

Teacher in Cancer Genetics course in integrated Ph.D., West Bengal University of Technology, Kolkata.

Teaching Genomics in graduate program for Ph.D. students of Indian Institute of Chemical Biology, Kolkata.

Teaching Recombinant DNA technology, mutation and DNA-protein interaction in M.S. (Pharma), NIPER, Kolkata.

Dr. Ashok K. Giri

Working as a Teacher and also as an Examiner at the Genetic Department, Centre of Advanced Study, Department of Botany, University of Calcutta.

Teaching NIPER Students at IICB.

Trained 15 Fogarty trainee at the Fogarty Monthly meeting at IICB in the session 2010 to 2011.

Deputation Abroad

Dr. Suvendra Bhattacharyya

Deputation under Indo-Swiss Joint research Program (ISJRP) to Friedrich Miescher Institute, Basel, Switzerland during the month of March-April, 2011.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Invited Lectures

Dr. Aparna Gomes

Topic : Anticancer Zootherapy from the folk to modern science with special reference to snake and scorpion venom.
Venue : National seminar on scope & Recent development of natural products Iswarchandra Vidyasagar College, Belonia, Tripura.
Date : 12th November, 2010.

Dr. Pratap K. Das

Topic : Molecular nano motors of living cells.
Venue : National Institute of Technology, Rourkela.
Date : 5th April, 2010.

Dr. Snehasikta Swarnakar

Topic : Matrix metalloproteinases gene polymorphism and the risk of gastric cancer.
Venue : Thakurpukur Cancer Hospital, Kolkata, West Bengal.
Date : 18th July, 2010.

Topic : Association of MMPs with inflammation marker in gastric cancer.
Venue : New frontiers in hematology and oncology, Kolkata, West Bengal.
Date : 11th-12th Sep, 2010.

Topic : Matrix metalloproteinases as key regulator to arrest gastric ulcer: A new challenge.
Venue : Guha Research Conference, Aurangabad.
Date : 16th-21st Dec, 2010.

Topic : Eradication of Helicobacter pylori infection by curcumin via Matrix metalloproteinase-9 and -3.
Venue : SFRR-India, Madras.
Date : 9-11th Jan, 2011.

Topic : Association of matrix metalloproteinases and their inhibitors with inflammation marker in gastric ulcer.
Venue : Havana Redox-2011, Havana, Cuba.
Date : 27-29th Jan, 2011.

Topic : Functional importance of limulin: A sialic-acid binding lectin from American horseshoe crab, *limulus polyphemus*.
Venue : Bioactiva 11, Trichy, Tamilnadu.
Date : 10-11th Feb, 2011.

Topic : Recent Advances in Biomedical Research.
Venue : 150th Birth Anniversary of Dr. Kadambini Ganguly, Krishnagar, West Bengal.
Date : 26th Feb, 2011.

Dr. Suman Khowala

Topic : Lignocellulolytic enzymes production by low cost agro wastes by an edible fungus *Termitomyces clypeatus*.
Venue : International Biotechnology Symposium 2010, Rimini, Italy.
Date : 14-18th September, 2010.

Topic : Molecular chaperone-like properties of an extracellular low size sucrase from filamentous fungus *Termitomyces clypeatus.*
Venue : Madurai Kamraj University.
Date : 12-14th November, 2010.

Topic : Microbial enzymes.
Venue : Kalaslingam University, Krishnankoil.
Date : 15-16th November, 2010.

Dr. Sharmila Chattopadhyay

Topic : Subtracted cDNA library construction and EST analysis from methyl jasmonate induced cell suspension culture of *Podophyllum hexandrum*.
Venue : MINAS, Bikaner.
Date : 4-6th February, 2011.

Topic : Defense signaling mechanism to combat biotic stress.
Venue : University of Calcutta.
Date : 3rd March, 2011.

Chairing a Session

Dr. Tarun Kumar Dhar

Chaired a session in 30th Annual Convention of Indian Association for Cancer Research and International Symposium on 'Signaling Network and Cancer', CSIR-IICB, Kolkata, 2011.

Dr. Snehasikta Swarnakar

Chaired a session in New Frontiers in Hematology and Oncology, 11-12th Sep, 2010, Kolkata, West Bengal.

Chaired a session in SFRR-India, 2011, Madras, 9-11th Jan, 2011.

Chaired a session in Havana-Redox 2011,Havana, Cuba 27-29th Jan, 2011.

Chaired a session in Bioactiva 11, Trichy, 10-11th Feb, 2011.

Academic Performance/Teaching

Dr. Tarun Kumar Dhar

Invited by ChemBioChem to review the book entitled 'Assay Development-Fundamentals and practices" by Ge Wu, Willey 2010.

Reviewer of several papers to be published in Analytica Chimica Acta, J. Science Food & Agriculture, Mycotoxin Research.

Evaluated research proposal submitted to Indo-US Science & Technology Forum and CSIR.

Dr. (Mrs.) Aparna Gomes

Supervised thesis of MS, Pharm., NIPER,Guwahati; B. Tech., HIT, Haldia; MS, Biotechnology, KIT School of Biotechnology, Kharagpur.

Acting as the Chairman Human Ethical Committee, Presidency College, Kolkata.

Reviewer of Indian Journal of Pharmacology, Indian Journal of Biotechnology, Toxicology, Phytotherapy Research, Journal of Ethnopharmacology, Protein and peptide letter, Chinese Journal of Physiology.

Selection committee member, Dept of Biotechnology and molecular biology, Kalyani University.

Evaluated Research Proposals submitted to ICMR, DST.

Dr. Pratap K. Das

Visiting Faculty and examiner in the Department of Bioscience & Engineering, Jadavpur University.

Dr. Snehasikta Swarnakar

Acted as examiner of M.Sc. of the Department of Biochemistry, Environmental Science and Microbiology, Calcutta University.

Editorial Board member of International Journal of Biomedical Sciences.

Reviewer of paper published in Journal of Ethnopharmacology, International Journal of Biochemistry and Cell Biology, Free Radical Biology and Medicine, Food and Nutrition Science, World Journal of Surgical Oncology, China.

Reviewer of external projects under CSIR, DBT and DST.

Board member of SFRR-ASIA.

Adjunct faculty of Department of Environmental Sciences, University of Calcutta.

Examiner of Ph. D viva at Jadavpur University.

Evaluated Research Proposals submitted to ICMR, DST.

Member of Academic Council, Dept of Biotechnology, St Xaviers College, Kolkata.

Convenor of Divisional Journal club, IICB, Kolkata.

Dr. Suman Khowala

Ph.D. Examiner Agharkar Research Institute, Pune; Acharya Nagarjuna University, Guntur; Anna Malai University, Chidamabaram; Madurai Kamraj University. Bidhan Nagar College, Salt Lake, Kolkata. National Institute Interdisciplinary Scinece & Technology, Trivandrum; Guru Nanak Dev University, Amritsar.

Reviewer of paper published in Journal of Bioresource Technology, Food Research International, Applied Biochemistry and Biotechnology, Chemical Engineering Journal, Current Microbiology, Biotechnology progress, Electronic journal of Biotechnology, Current Trends in Biotechnology and Pharmacy, International journal of Association of Biotechnology and Pharmacy, International Journal of Biomedical Science.

Reviewing projects from DBT and CSIR, Govt. of India.

Dr. Sharmila Chattopadhyay

Conducted Ph.D. viva-voce University of Kalyani.

Reviewer of several papers to be published in Planta, Plant Science, Food Chemistry.

Evaluated Research Proposals submitted to ICMR, CSIR.

Invited to write a chapter in a book entitled "Genetic Transformation", inTech Open Access Publisher; to contribute on Reactive Oxygen Species in Plants; Transgenic Plants in Journal of Botany, Hindawi Publishing Corporation.

Papers/Abstracts presented in the Conference

Dr.(Mrs.) Aparna Gomes

National Conference: Seven (07) numbers.

Dr. Snehasikta Swarnakar

National Conference: One (01) number.

Dr. Anil K. Ghosh

National Conference: Three (03) numbers.

Dr. Suman Khowala

National Conference: Five (05) numbers.
International Conference: One (01) number.

Dr. Sharmila Chattopadhyay

National Conference: Five (05) numbers.
International Conference: One (01) number.

Conference/symposia/Workshop Organised

Dr. Aparna Gomes acted as an organising secretary in a national conference "1st National Conference on Animal Microbial and Plant Toxin (AMPTOX) held in KPC Medical College from 11-12th December, 2010.

Upgradation of Major Infrastructural Facilities

Establishment of Transgenic Plant Facility.

CHEMISTRY

Invited Lectures

Dr. G. Suresh Kumar

Topic : Isoquinoline alkaloids as potential RNA binding natural products.
Venue : National Conference on New Arena in Photosciences, Jadavpur University, Kolkata.
Date : August 28, 2010.

Topic : Thermoanalytical investigations of natural product-DNA interactions for drug design.
Venue : IMA Center at the International Congress on Analytical Science 2010, IMA Center, Kochi.
Date : November 24-27, 2010.

Topic : Protoberberine plant alkaloids: unique nucleic acid binding properties as the basis of potential therapeutic action.
Venue : Sambalpur University, Sambalpur, Orissa at the International Conference on Plant Science in Post Genomic Era (ICPSPGE-2011).
Date : February, 17-19, 2011.

Dr. Partha Chattopadhyay

Topic : The synthesis of benzannulated medium ring heterocycles in drug design.
Venue : Dept of Chemistry, Tripura University.
Date : 12-14th January, 2011.

Dr. Asish Kumar Sen

Topic : Structure and synthesis of biologically important carbohydrates with special reference to lipopolysaccharides from Vibrio cholerae.
Venue : XXV Carbohydrate Conference, Department of Chemistry HP University, Shimla, Himachal Pradesh.
Date : 11-13th November, 2010.

Chaired a Technical Session

Dr. Asish Kumar Sen

XXV Carbohydrate Conference, Department of Chemistry HP University, Shimla, Himachal Pradesh, November 11-13th, 2010.

Academic Performance / Teaching

Dr. S. B. Mandal

Guest faculty member, NIPER, Kolkata and PhD Course work of IICB.

Acting as a coordinator to help NIPER students for their placement.

Reviewer of Organic Letters, Carbohydr. Res., J. Org. Chem. (ACS), J. Ind. Chem. Soc.

Dr. Partha Chattopadhyay

Honorary guest faculty member for Post Graduate Teaching, Department of Chemistry, Scottish Church College, Kolkata.

Honorary guest faculty member, NIPER- Kolkata.

Reviewer of J. Org. Chem. (ACS), Tetrahedron, Tetrahedron Lett., Bioorg. Med. Chem. Lett (Elsevier Science).

PhD Thesis Examiner of Acharya Nagarjuna University and Osmania University.

Dr. S. Mukhopadhyay

Honorary Lecturer in Postgraduate Teaching in Chemistry Department, Calcutta University.

Guest faculty member, NIPER, Kolkata.

Dr. G. Suresh Kumar

Guest faculty member of NIPER, Kolkata and PhD course work of IICB.

PhD thesis examiner of Pune University, Jadavpur University, AIIMS, Cochin University of Science and Technology.

Reviewer of J. Am. Chem Soc. (ACS), J. Phys. Chem. B (ACS), Biomacromolecules (ACS), Mol. BioSyst. (RSC), Biophysical Chemistry (Elsevier), Biochim. Biophys. Acta (Elsevier), J. Chem. Thermodyn. (Elsevier), Biophys. Chem. (Elsevier) J. Pharmaceut. Biomed. Anal. (Elsevier), Fitoterapia. (Elsevier), Talenta (Elsevier), J. Biomol. Struct. Dyn. (Adenine Press), DNA Cell Biol, Indian J. Biochem. Biophys, Indian J. Exptl. Biology.

Dr. A. K. Banerjee

Reviewer of Org. Lett., J. Org. Chem. (ACS).

Member of the Board of Examiners in Chemistry for M. Sc. Part-II, Calcutta University.

Acted as an examiner in Chemistry for M. Sc. Part-II, Jadavpur University.

Dr. P. Jaisankar

Guest faculty member of NIPER, Kolkata and Ph. D. Course work, of IICB, Kolkata.

Acting as Reviewer of Org. Lett. (ACS), Eur. J. Med. Chem.., Syn. Commun.

External examiner of Ph. D. thesis of Madras, Jadavpur and Osmania universities.

Dr. Chinmay Chowdhury

Reviewer of Bioorg. Med. Chem. Lett., RSC-Advances.

Served as Ph.D. thesis examinar of Osmania University.

Taught the Ph.D. Course-work of IICB, Kolkata.

Dr. R. C. Yadav

Expert member in the selection committee meetings for the Scientists and Technical Officers in Central Mechanical Engineering Research Institute (CMERI), Durgapur and also in the Indian Association for the Cultivation of Science (IACS), Kolkata.

Dr. Asish Kumar Sen

Ph.D. thesis examiner Burdwan University and CFTRI, Mysore.

Seven Lectures at NIPER, Kolkata centre.

Honours and Awards

Dr. G. Suresh Kumar

Secretary, DNA Society of India (2009-2014).

Member, National Executive Council of Indian Biophysical Society (2009-2011).

Member, Editorial Advisory Board, "The Open Natural Product Journal" (Bentham Sciences).

Member Editorial Advisory Board, "International Journal of Physical Sciences" (Academic Journal).

Member, Editorial Advisory Board, "African Journal of Biochemistry Research" (Academic Journal).

Dr. P. Jaisankar

Awarded Raman Research Fellowship by CSIR to visit Nagoya University, Japan, 2010 on deputation.

Dr. Partha Chattopadhyay

Member of the Editorial Board of Referees, ARKIVOC, USA from 2008-onwards.

Dr. A. K. Banerjee

Acting as Project Director of NIPER, Kolkata.

Member of the Steering Committee, Dept. of Pharmaceuticals, Ministry of Chemicals & Fertilizers, Govt. of India.

Member of Joint Counselling Committee for the Master program in NIPER, Mohali, Punjab.

Member, Committee constituted to formulate rules, service conditions, etc. of NIPER staff, constituted by Dept. of Pharmaceuticals, Govt. of India.

Member Secretary of State Level Co-ordination Committee, Govt. of West Bengal, constituted by Dept. of Pharmaceuticals, Govt. of India.

Dr. Asish Kumar Sen

Received ACCT(I) Life Time Acheivement Award-2010.

Elected as Hon. President of the Association of Carbohydrate Chemists & Technologists (India) 2010-12.

Member of the Advisory Committee of NIPER-Kolkata.

Chairing a Session

Dr. G. Suresh Kumar

Chaired one scientific session at the 7th Asian Biophysics Association Symposium, Habitat Center, New Delhi during January 30-Feb 03, 2011.

Chaired one scientific session at the International Conference on Plant Science in Post Genomic Era (ICPSPGE-2011), Sambalpur University, Sambalpur, Orissa during February 17-19, 2011.

Chaired one scientific session at the National Symposium on DNA Structure, Function and Applications, Jadavpur University, Kolkata on July 7, 2010.

Papers/Abstracts presented in the Conference

Dr. G. Suresh Kumar

National Conference: Twelve (12) numbers.

Dr. N. B. Mondal

National Conference: One (01) number.

Dr. Partha Chattopadhyay

National Conference: Three (03) numbers.

Dr. Chinmay Chowdhury

National Conference: Two (02) numbers.

Dr. P. Jaisankar

National Conference: Three (03) numbers.

Dr. Asish Kumar Sen

National Conference: Four (04) numbers.

Conferences/Symposium/Workshop Organized

Dr. Asish Kumar Sen

Convener, CPYLS-2010 Programme of CSIR.

STRUCTURAL BIOLOGY & BIOINFORMATICS

Invited Lectures

Dr. Chitra Dutta

Topic : Genomic imprints of adaptive evolution in extremophilic microbes.
Venue : DBT Bioinformatics Centre, North Bengal University.
Date : April 24, 2010.

Dr. Debasish Bhattacharyya

Topic : 'Loose unstable assembly of Bovine Serum Albumin'.
Venue : Indian Spectrophysics Association, Chennai.
Date : 10th - 12th February, 2011.

Dr. Subrata Adak

Topic : 'Ascorbate peroxidase from Leishmania major controls the differentiation of promastigotes by regulating oxidative stress'.
Venue : Department of Molecular biology, University of California, Irvine, USA.
Date : 17th Feb, 2010.

Dr. Krishnananda Chattopadhyay

Topic : .
Venue : Center for Physics in living Cells, University of Illinois at Urbana Champaign, USA.
Physics Colloquium, Department of Physics, Emory University, USA.
Date :

Chairing a Sessions

Dr. Debasish Bhattacharyya

At the National Conference on Recent Advances in Molecular Physics (NCRAMP '11) held at the Department of Physics, Queen Mary's College, Chennai, 10-11th February, 2011.

At National Conference on Animal, Microbial, Plant Toxins and Snake Bite Management (AMPTOX 2011) held at KPC Medical College, Kolkata on 11-12th December 2010.

Academic Performances

Dr. M. C. Bagchi

Acted as a Guest Faculty Member, Paper setter and Examiner in Biostatistics for the M.S.(Pharm) course of National Institute of Pharmaceutical Education and Research (NIPER), Kolkata.

Served as a reviewer for Current Computer Aided Drug Design, Journal of Enzyme Inhibition & Medicinal Chemistry, SAR & QSAR in Environmental Research, Medicinal Chemistry Research, Chemical Biology and Drug Design, Indian Journal of Biochemistry and Biophysics journals.

Acted as an external member of AICTE project of the Department of Pharmaceutical Technology, Jadavpur University.

Acted as a coordinator of Statistics course for Ph.D. students of IICB.

Acted as an external expert for selection of Research Associate and Research Scholars in the Theoretical Physics Department of the Indian Association for the Cultivation of Science, Kolkata.

Evaluated projects submitted to Indo-US Science & Technology Forum, New Delhi & Department of Science & Technology, New Delhi for funding.

Guided students for the award of Ph.D. degree in Pharmacy from Jadavpur University and M. Tech degree of West Bengal University of Technology.

Acted as an examiner of Ph.D. thesis of Rajasthan University, Jaipur.

Dr. Chitra Dutta

Guest faculty, paper-setter & examiner (Bioinformatics) at the post-graduate level of NIPER, Kolkata.

Guest faculty, Departments of Genetics, Neuroscience, Microbiology & Biotechnology, Calcutta University.

Paper-setter in CSIR-UGC NET Exam. 2011.

Referee of manuscripts submitted to Nucl. Acids Res., Bioinformatics, DNA Res., BMC Genomics, BMC Evol. Biol., Microbiology, J. Mol. Evol., Virus Res. etc.

Reviewer of Project proposals submitted to CSIR, DST & DBT, Govt. of India.

Dr. Debasish Bhattacharyya

Served as a guest lecturer at the Department of Biotechnology, Jadavpur University, Calcutta (M.Sc. Semester I.).

Served as a guest lecturer at the Department of Biochemistry, University of Calcutta for Ph.D. course work.

Served as a lecturer of theoretical and practical classes of NIPER, Calcutta.

Served as a member of Board of Studies of Calcutta University (B.Sc, Biochemistry)

Dr. Nanda Ghoshal

Acted as examiner for viva-voce examination for Ph.D. (Pharm.) Degree of J. U. held on April 16, 2010 at Pharmaceutical Technology Div., J.U.

Teaching at Niper, Kolkata, as a guest faculty member (for the academic year 2010-11).

Acted as examiner for M.Pharm. Final (thesis and corresponding oral) examination, J.U., held in June, 2010 at Pharmaceutical Technology Div., J.U.

Evaluated two research project proposal submitted to CSIR for funding entitled:

Molecular modeling, dynamics and docking studies of human p-glycoprotein for the identification of hotspots for ligand binding.

Identification of critical residues in protein folds using graph theoretic approaches.

Dr. Krishnananda Chattopadhyay

Four lectures on Protein Folding, M.Sc. special classes in the Department of Biochemistry, University of Kolkata.

Dr. Jayati Sengupta

Acted as external examiner for project thesis of MS (Pharm) students, NIPER, Kolkata.

Took Basic and Advance Electron Microscopy classes under the Ph.D. course work program conducted by IICB, Kolkata.

Provided summer training for M.Sc. students.

Deputation Abroad

Prof. Siddhartha Roy

Visited Hokkaido University, Japan from 26.10.10 to 30.10.2010 to deliver a series of lectures at Hokkaido University.

Dr. Debasish Bhattacharyya

Participated as an invitee at the SBCN 2010 (Society of Biochromatography and Nanoseparation) at Lyon, France held 19-22 October, 2010.

Invited oral presentation entitled 'Isolation of protein componet from Russell's viper venom that destabilizes □-amyloid aggregate *in vitro*' was offered by Ms Payel Bhattacharjee (JRF) at SBCN 2010 at Lyon, France held 19-22 October, 2010.

Invited oral presentation was offered by Dr. Piyali Datta Chakraborty, on deputation from Albert David Ltd. at SBCN 2010 at Lyon, France held 19-22 October, 2010.

Dr. Krishnananda Chattopadhyay

Visiting Faculty, Department of Physics, University of Illinois at Urbana Champaign, USA, July-Oct, 2010.

Honours and Awards

Dr. M. C. Bagchi

Received the VLifeScience Best Publication Award for the year 2010.

Dr. Chitra Dutta

Member, Editorial Board, International Journal of Soft Computing & Bioinformatics.

Member, Advisory Board, NIPER (Kolkata).

Member, PG Board of Studies, Department of Genetics, Calcutta University.

Dr. Debasish Bhattacharyya

Selected as a member of the editorial board of the 'Journal of Chromatography B' for 3 years term (2008-2011).

Awarded 'Member of honor of the SBCN' at Lyon, France 2010 (DB).

Awarded Indian Spectro-physics Association (ISPA) Prize 2009 at Chennai in 2011.

Dr. Nanda Ghoshal

Reviewer of manuscripts for J. Med. Chem., J. Bioorg. Med. Chem., J. Mol. Graph. Mod., Chemical Biology & Drug Design, Eur. J. Med. Chem., J. Chem. Info. Model.

Papers/Abstracts presented in the Conferences

Dr. Debasish Bhattacharyya

National Conference: Five (05) numbers.

Dr. Krishnanda Chattopadhyay

International Conference: One (01) number.

Dr. Jayati Sengupta

National Conference: One (01) number.

Dr. Subrata Adak

National Conference: Three (03) numbers.

Dr. Nakul Maiti

National Conference: One (01) number.

Conference/Symposium/Workshops Organized

Dr. Debasish Bhattacharyya

Served as Treasurer of the national conference AMPTOX 2010 held at KPC Medical College in collaboration with IICB in December, 2010.

CELL BIOLOGY & PHYSIOLOGY

Invited Lectures

Dr. K. P. Mohanakumar

Topic : A novel protective compound for Parkinson's disease.
Venue : Sandler Medical Center, University of Kentucky, Lexington, USA.
Date : October 29, 2010.

Topic : Plenary Lecture: Ayurvedic medication for Parkinson's disease: Two sides of a coin.
Venue : 15th Indian Society of Chemists & Biologists International Conference (Commemorating 2011 as the International Year of Chemistry) on "*Bridging Gaps in Discovery and Development: Chemical and Biological Sciences for Affordable Health, Wellness and Sustainability*" at Saurashtra University, Rajkot.
Date : February 6, 2011.

Topic : Neurochemistry of dopamine in denervated and innervated striata of animals following long-term L-DOPA treatment: Causes and corrections.
Venue : *Cellular and Molecular Basis of Brain Plasticity & Repair Mechanisms* at Local Chapter of Society for Neuroscience (SfN) first meeting in India, Defence Institute of High Altitude Research, Leh, Ladakh.
Date : September 4, 2010.

Topic : Sunlight delight for Parkinson's disease.
Venue : Sree Sankara College, Kalady, (MG University), Alwaye.
Date : October 7, 2010.

Topic : Rat Brain Stereotaxic Surgery, *in vivo* Brain Microdialysis & Neurotransmitter Analyses.
Venue : Neurocon-2011 Workshop, Institute of Postgraduate Medical Education & Research, Kolkata.
Date : January 24, 2011.

Topic : Regenerative therapy for Parkinson's disease.
Venue : International Conference on "Neuron: Degeneration, Regeneration and Proliferation" organized by Department of Biochemistry, Institute of Post Graduate Medical Education and Research in collaboration with the Cell Biology and Physiology Division, IICB.
Date : January 30, 2011.

Topic : Vitamin D3 helps in treating Parkinson's disease.
Venue : *International Conference on Molecular Medicine 2011 with key focus on metabolic disorders and Aging,* at the Charusat University, Anand, Gujarat jointly organized by Indian Institute of Technology, Madras, India, The Swinburne University, Australia, University at Buffalo (The State University of New York), USA and the Laila Pharmaceuticals Pvt. Ltd., Chennai.
Date : January 10, 2011.

Dr. Arun Bandyopadhyay

Topic : Extracellular Matrix and Accelerated Collagen Degradation Cause Ventricular Dysfunction in Hyperthyroid Rat Heart.
Venue : 98th Indian Science Congress, SRM University, Chennai.
Date : January 3 -7, 2011.

Dr. S. N. Kabir

Topic : Acaciaside B-enriched fraction of *Acacia auriculiformis*: a dual action topical microbicide with wide safety margin.
Venue : BIT Life Sciences' 1st World Congress of Virus and Infections-2010.
Date : July 31-August 3, 2010, Busan, South Korea.

Topic : Experimental hyperhomocysteinemia in rats: a laboratory model to explore the molecular cues to polycystic ovary syndrome.
Venue : 6th Singapore Association for Laboratory Animal Science, Singapore.
Date : December 2-3, 2010.

Topic : Microbicides: Empowering women to protect their reproductive health.
Venue : National Seminar on "Women's health: Recent research & trends", Vidyasagar University, Medinipore.
Date : March 17, 2011.

Topic : Experimental hyperhomocysteinemia in rats: a laboratory model to explore the molecular cues to polycystic ovarian syndrome.
Venue : 98th Science Congress, SRM University, Chennai.
Date : January 3-7, 2011.

Dr. Mrinal Kanti Ghosh

Topic : Signalling Crosstalks: Implications in Cancer: Mentor Talk.
Venue : B. C. Guha Symposium for Young Investigators-2010 at Puri.
Date : April 09-11, 2010.

Topic : Signaling crosstalk between EGFR and Wnt/β-catenin pathways in human cancer.
Venue : 30th Convention of Indian Association for Cancer Research 2011 at CSIR-IICB, Kolkata.
Date : February 06-09, 2011.

Topic : Mechanistic understanding of crosstalk between EGFR and Wnt/β-catenin signalling in brain cancer.
Venue : Neurocon 2011 at CGCRI, Kolkata.
Date : January 29-31, 2011.

Dr. Sib Sankar Roy

Topic : Free fatty acid and insulin resistance.
Venue : Texas A & M Health Science Center, Temple, Texas.
Date : August 18, 2010.

Topic : Molecular studies on metabolic disorders.
Venue : Department of Reproductive Medicine, University of California, San Diego.
Date : September 9, 2010.

Topic : Mitochondrial dysfunction and Type 2 Diabetes.
Venue : UGC sponsored International Seminar on Diabetes at Kanailal Bhattacharya College, Howrah.
Date : December 17, 2010.

Dr. Tushar Chakraborty

Topic : Natural History of the Genes (Professor N Subrahmanian Endowment Lecture 2010-2011).
Venue : Institute of Historical Studies, Kolkata.
Date : March 4, 2011.

Topic : Of Plants, People and Profit: Impact of GM Technology in Food and Agriculture.
Venue : Ramkrishna Mission Institute of Culture, Golpark, Kolkata arranged by the Vivekananda Science Circle.
Date : March 24, 2011.

Topic : GM Technology : The Informed Dissent.
Venue : Presidency University Science Club, Kolkata.
Date : January 18, 2011.

Dr. S. R. Dungdung

Topic : Identification of key molecules involved in the regulation of sperm motility during epididymal transit.
Venue : 98th Session of Indian Science Congress at SRM University, Chennai.
Date : January 5, 2011.

Dr. Tuli Biswas

Topic : 4-hydroxynonenal-mediated ROS dependent initiation of apoptotic signals in erythrocytes during chronic exposure to arsenic.
Venue : International Conference on Recent Trends in Therapeutic Advancement of Free Radical Science & 10th Annual Meeting of the Society for Free Radical Research, India, at Chennai.
Date : January 09 -11, 2011.

Chairing a session

Dr. K. P. Mohanakumar

The Session : "Health & Wellness by Natural Products and Neutraceuticals".
The Meeting : 15th Indian Society of Chemists & Biologists International Conference (Commemorating 2011 as the International Year of Chemistry) on "*Bridging Gaps in Discovery and Development: Chemical and Biological Sciences for Affordable Health, Wellness and Sustainability*".
Venue : Saurashtra University, Rajkot.
Date : February 6, 2011.

The Session : "Herbal remedies for neurological disorders".
The Meeting : International Symposium on Cellular and Molecular Basis of Brain Plasticity & Repair Mechanisms and Annual meeting of Society for Neuroscience (SfN).
Venue : Defense Institute of High Altitude Research, Leh, Ladakh.
Date : September 4, 2010.

Dr. S. N. Kabir

Chaired a session in the International Conference on Frontiers in Reproductive Biotechnology and 20th Annual Meeting of the Indian Society for the Study of Reproduction and Fertility, February 9-11, 2011, University of Rajasthan, Jaipur.

Dr. Tuli Biswas

Chaired a session in the International Conference on Recent Trends in Therapeutic Advancement of Free Radical Science & 10th Annual Meeting of the Society for Free Radical Research, India, held at Chennai on January 09 -11, 2011.

Dr. Tushar Chakraborty

Chaired a session on Environmental Ethics, in one day symposium organized by the Pavlov Institute, Kolkata on February 26, 2011.

Academic Performance: Teaching, Examining and Training

Dr. K. P. Mohanakumar

Appointed as the external examiner to conduct the viva voce examination in respect of the research scholar, Mr. K. S. Vinaykumar of Centre for Research, Anna University, Chennai.

Supervised the project work of five Post graduate students working as Summer Trainee.

Reviewed 21 manuscripts for J. Neurochem., Cell. Mol. Neurobiol., Neurosci. Res., Neurotoxicology, Neurosci. Lett., Hippocampus, J. Chem Neuroanat., Behav. Brain. Res., and Nitric Oxide.

Taught for one month (April - 28, 2009) at IISER Thiruvananthapuram.

Evaluated and prepared reports on 8 CSIR-EMR, 3 DST and 2 DBT projects submitted by various institutions.

Trained 3 summer students, and 2 graduate students from outside organization.

Trained 16 young scientists and graduate students from the Asia Pacific Region on stereotaxic applications, dissection of brain regions, and micropuch technique for isolating discrete brain nuclei and HPLC.

Dr. S. N. Kabir

Guest Teacher and Examiner, M.Sc., Physiology, Calcutta University.

Guest Teacher and Examiner, M.Sc., Physiology, Vidyasagar University.

Guest Teacher, M.Sc., Physiology, Krishnath College, Kalyani University.

Guest Teacher and Member of the Expert committee, M.Sc., Physiology, Rammohan College, Kolkata.

Guest Teacher, Examiner, and Member of the Board of Examiners in Physiology M.Sc., Presidency University.

Examiner, M.Sc., Physiology, Burdwan University.

Dr. Sib Sankar Roy

Appointed as UGC Visiting Teacher at Tripura University, Agartala, to teach a course to M.Sc. Life Science students.

Paper setter of M.Sc. (Human Physiology) Examination at Tripura University, Agartala.

External Examiner for Ph.D., Jadavpur University.

Dr. Sumantra Das

Delivered a course of lectures on Neurobiology as part of curriculum (Special paper) for second year M.Sc. students of the Department of Biochemistry as well as first year M.Sc. students of the Department of Neuroscience, Calcutta University.

Lecturer and Examiner of NIPER, Kolkata.

Supervised the project work of two M.Sc. students working as Summer Trainee.

Dr. Tuli Biswas

Examiner of Ph.D. thesis and viva-voce of Calcutta University and Jadavpur University.

Research guide of four pre-doctoral students and one project fellow.

Supervised the project work of two M.Sc. students working as summer trainee.

Evaluated scientific and technical of research proposals submitted for funding to CSIR and DST, Govt.of India.

Dr. Tushar Chakraborty

Teaching Basic Mechanisms of Replication, Transcription and Translation in NIPER, Kolkata. Also acted as Paper setter & Examiner.

Resource Person & Lecturer on M.Sc. Course in Science Communication conducted by the National Council of Science Museum.

Served as a reviewer for the Science Communication Journal, Propagation, published by NCSM.

Dr. Mrinal Kanti Ghosh

Teaching on "Signal Transduction: Signaling in Cancer and Stem Cells" in the course work offered to Ph. D. students of IICB, Kolkata.

Lecturers on "Drug Metabolism and Toxicity and Metabolic Disorders (2 Credits)" and Examiner of M. Pharm, NIPER, Kolkata.

Deputation abroad

Dr. K. P. Mohanakumar

Visited University of Kentucky, Lexington, at the Chandler Medical Centre, Spinal Cord and Brain Injury Research, USA for a period of 15 days w.e.f. 29.10.2010 to 12.11.2010.

Visited San Diego, California to attend the Annual Meeting of the Society for Neuroscience from November 13-17, 2010.

Dr. Sibsankar Roy

Visited University of California, San Diego from April-September, 2010 with CSIR Raman Research Fellowship to work in the area of transcriptional regulation of genes associated with metabolic syndrome.

Conference/Symposium/Workshop organized

Dr. Mrinal Kanti Ghosh

Convener: International conference on "Signaling Networks & Cancer", 30th IACR & 75th Anniversary of IICB (CSIR) during February 6-9, 2011, Kolkata.

Papers/Abstract presented in the conference

Dr. K. P. Mohanakumar

National Conference: Five (05) numbers.

Dr. Arun Bandyopadhyay

National Conference: One (01) number.

Dr. S. N. Kabir

National Conference: Three (03) numbers.
International Conference: Two (02) numbers.

Dr. Mrinal Kanti Ghosh

National Conference: Five (05) numbers.

Dr. Padma Das

National Conference: Five (05) numbers.

Dr. Sib Sankar Roy

National Conference: Two (02) numbers.

Dr. Tuli Biswas

National Conference: Three (03) numbers.

Dr. S. R. Dungdung

International Conference: Three (03) numbers.
National Conference: Six (06) numbers.


বিশ্বকবি রবীন্দ্রনাথ ঠাকুরের

External Funding

INFECTIOUS DISEASES AND IMMUNOLOGY

Projects sanctioned in 2010-2011

Sl. No.	Principal Investigator	Project Title	Funding Agency	Total Fund (Rs. in lakhs)	Duration
1.	Dr. Aditya Konar **(Animal House Division)**	Nanotechnology based drug delivery system for prevention of cataract: Proof of concept in a Rabbit Model	DBT, Govt. of India	6.28 (1st year)	27.09.10 - 26.09.13
2.	Dr. Krishna Das Saha **(Infectious Diseases & Immunology)**	Study on Leishmanial integral membrane proteins(s) induced growth inhibition of melanoma cells with exploration of the mechanism involved and characterization of the bioactive protein component(s)	ICMR, Govt. of India	11.36 (1st year)	13.10.10 - 12.10.13
3.	Dr. Padma Das **(Cell Biology & Physiology)**	Studies of anticarcinogenic functiions of compounds isolated from the edible mushroom	DBT, Govt. of India	19.42	04.03.11 - 03.03.14

Projects completed in 2010-2011

Sl. No.	Principal Investigator	Project Title	Funding Agency	Total Fund (Rs. in lakhs)	Duration
1.	Dr. M. C. Bagchi **(Structural Biology & Bioinformatics)**	Anti-tubercular drug design by calculated molecular descriptors: A QSAR approach	DBT, Govt. of India	12.07	27.09.06 - 26.09.10
2.	Dr. Debasish Bhattacharya **(Structural Biology & Bioinformatics)**	Regulation of activity and assembly of multi-meric proteins	DST, Govt. of India	21.49	31.10.06 - 30.10.10
3.	Dr. Soumen Dutta **(Structural Biology & Bioinformatics)**	Structural Insights into the Type III Secretion System (TTSS) of Pathogenic Bacteria	DST, Govt. of India	22.51	23.03.07 - 22.09.10

Sl. No.	Principal Investigator	Project Title	Funding Agency	Total Fund (Rs. in lakhs)	Duration
4.	Dr. Sib Sankar Roy **(Cell Biology & Physiology)**	Isolation, Molecular characterization and biological evaluation of anti-diabetic principles(s) from a few Indian medicinal plants	DST/ Biswa-bharati	20.26	01.03.07 - 31.12.10
5.	Dr. S. R. Dungdung **(Cell Biology & Physiology)**	Purification and characterization of sperm motility inhibiting protein factor from goat epididymal plasma and fertility management	ICMR, Govt. of India	7.20	08.05.07 - 07.05.10
6.	Dr. Sib Sankar Roy **(Cell Biology & Physiology)**	Characterization of anti-cancer and anti-inflammatory molecules from Piper betel leaf extract and identification of their targets by proteomics	NICHOLAS PIRAMAL PVT. LTD.	30.00	18.10.07 - 17.10.10
7.	Dr. Sib Sankar Roy **(Cell Biology & Physiology)**	The role of Pitx2 homeodomain transcription factor to regulate ovarian function	DST, Govt. of India	23.54	10.11.07 - 09.11.10
8.	Dr. Tripti De **(Infectious Diseases & Immunology)**	Protective efficacy of purified constituents of Centella asiatica leaf extract in an experimental model of visceral leishmaniasis	DBT, Govt. of India	6.58	25.02.08 - 24.02.11
9.	Dr. Mrinal K. Ghosh **(Cell Biology & Physiology)**	Regulation of Stat: Understanding Mechanisms to Counteract Prostate Cancer	DST, Govt. of India	5.43	24.08.09 - 23.08.10

Projects ongoing in 2010-2011

Sl. No.	Principal Investigator	Project Title	Funding Agency	Total Fund (Rs. in lakhs)	Duration
1.	Dr. M. C. Bagchi **(Structural Biology & Bioinformatics)**	Anti-tubercular drug design by calculated molecular descriptors: A QSAR approach	DBT, Govt. of India	12.07	27.09.06 - 26.09.10
2.	Dr. Debasish Bhattacharya **(Structural Biology & Bioinformatics)**	Regulation of activity and assembly of multi-meric proteins	DST, Govt. of India	21.49	31.10.06 - 30.10.10
3.	Dr. Soumen Dutta **(Structural Biology & Bioinformatics)**	Structural Insights into the Type III Secretion System (TTSS) of Pathogenic Bacteria	DST, Govt. of India	22.51	23.03.07 - 22.09.10

Sl. No.	Principal Investigator	Project Title	Funding Agency	Total Fund (Rs. in lakhs)	Duration
4.	Dr. Sib Sankar Roy **(Cell Biology & Physiology)**	Isolation, Molecular characterization and biological evaluation of anti-diabetic principles(s) from a few Indian medicinal plants	DST-Biswabharati	20.26	01.03.07 - 31.12.10
5.	Dr. S. R. Dungdung **(Cell Biology & Physiology)**	Purification and characterization of sperm motility inhibiting protein factor from goat epididymal plasma and fertility management	ICMR, Govt. of India	7.20	08.05.07 - 07.05.10
6.	Dr. Sib Sankar Roy **(Cell Biology & Physiology)**	Characterization of anti-cancer and anti-inflammatory molecules from Piper betel leaf extract and identification of their targets by proteomics	Nicholas Piramal Pvt. Ltd.	30.00	18.10.07 - 17.10.10
7.	Dr. Sib Sankar Roy **(Cell Biology & Physiology)**	The role of Pitx2 homeodomain transcription factor to regulate ovarian function	DST, Govt. of India	23.54	10.11.07 - 09.11.10
8.	Dr. Tripti De **(Infectious Diseases & Immunology)**	Protective efficacy of purified constituents of Centella asiatica leaf extract in an experimental model of visceral leishmaniasis	DBT, Govt. of India	6.58	25.02.08 - 24.02.11
9.	Dr. Partha Chattopadhyay **(Chemistry)**	Synthesis of Benzannulated Medium Ring Heterocycles by using, Intramolecular Buchwald Hartwig reaction and their Binding studies to Nucleic acids and Proteins	DST, Govt. of India	18.77	26.06.08 - 25.06.11
10.	Dr. Sharmila Chattopadhyay **(Cell Biology & Physiology)**	Phyllanthus amarus - a novel source of antileishmanial drug	ICMR, Govt. of India	28.50	16.10.08 - 15.10.11
11.	Dr. S. R. Dungdung **(Cell Biology & Physiology)**	Further Studies On Upgrading The Recently Developed Computerized Spectrophotometric Sperm Motility Analyzer And Its Application For Assessing Sperm Fertility Potential	DST, Govt. of India	20.94	02.07.08 - 01.07.10
12.	Dr. Malini Sen **(Infectious Diseases & Immunology)**	Role of Wht 5a signaling in Inflammation in Rheumatoid Arthritis	DBT, Govt. of India	52.85	11.08.08 - 10.08.11

Sl. No.	Principal Investigator	Project Title	Funding Agency	Total Fund (Rs. in lakhs)	Duration
13.	Dr. Malini Sen **(Infectious Diseases & Immunology)**	Role of WISP3 (Wnt Induced Secreted Protein 3) in Cartilage Maintenance	DST, Govt. of India	26.23	18.09.08 - 17.09.11
14.	Dr. Nirup Bikash Mondal **(Chemistry)**	Active targeting of nanoparticles grafted with ligands to cells of the reticuloendothelial system by receptor mediated endocytosis and their application against macrophage-associated diseases	DBT, Govt. of India	11.27	17.10.08 - 16.10.11
15.	Dr. Nahid Ali **(Infectious Diseases & & Immunology)**	A comparative evaluation of the potency and durability of leishmanial donovani gp63 DNA - and protein-based vaccines against experimental visceral leishmaniasis	DST, Govt. of India	23.23	27.10.08 - 26.10.11
16.	Dr. Snehasikta Swarnakar **(Drug Development, Diagnostics & Biotechnology)**	Prevention of Gastric ulceration Black Tea: An insight into Extracellular Matrix Remodeling of gastric tissues	NTRF, Govt. of WB	6.28	11.12.08 - 10.12.11
17.	Dr. Susanta Roychowdhury **(Molecular & Human Genetics)**	Chemical and Biological studies of indigenous medicinal and aromatic plants	DST, Govt. of WB	21.40	28.11.08 - 27.11.11
18.	Dr. Mridula Misra **(Infectious Diseases & Immunology)**	Tyr3 -Octreotide derivatives: Synthesis, Radiolabelling and Application as Tumor Targeted Radiopharmaceuticals	DAE, Govt. of India	17.55	18.03.09 - 17.03.12
19.	Dr. Tripti De **(Infectious Diseases & Immunology)**	Lipid immunity to vaccine generation:Identification, protective efficacy and mechanism of action of Leishmanial Glycolipid in the Murine model of Visceral Leishmaniasis	DST, Govt. of India	19.75	16.03.09 - 15.03.12
20.	Dr. Suvendra Bhattacharya **(Molecular & Human Genetics)**	Role of the ELAV Protein HuR in micro-RNA-mediated Gene Regulation in Normal and Transformed Human Cells	DST-(Swiss) ISJRP	27.55	13.03.09 - 31.01.12

Sl. No.	Principal Investigator	Project Title	Funding Agency	Total Fund (Rs. in lakhs)	Duration
21.	Dr. Chitra Mondal **(Infectious Diseases & Immunology)**	The influence of O-acetylated cell surface-expressed sialoglycans of bone marrow associated leukemias	ICMR-German	39.86	30.06.09 - 29.03.12
22.	Dr. Syed Nazrul Kabir **(Cell Biology & Physiology)**	Characterization of anti-HIV properties of Acaciaside-B and pre-clinical studies towards its development as a potential microbicide-spermicide formulation	DBT, Govt. of India	36.87	23.07.09 - 22.07.12
23.	Dr. Mrinal K Ghosh **(Cell Biology & Physiology)**	Regulation of Stat: Understanding Mechanisms to Counteract Prostate Cancer	DST, Govt. of India	5.43	24.08.09 - 23.08.10
24.	Dr. Suvendra Bhattacharya **(Molecular & Human Genetics)**	Effects of celluar microenvironment on post-transcriptional gene regulation in mammalian cells	HFSPO, France	$ 300000	01.03.08 - 28.02.11
25.	Dr. Syamal Roy **(Infectious Diseases & Immunology)**	New tools for monitoring drug resistance and treatment response in Visceral Leishmaniasis in the Indian subcontinent	DST-European Union	¤ 288,000	Sept, 09 - Aug, 13
26.	Dr. Syamal Roy **(Infectious Diseases & Immunology)**	Development of a DNA vaccine for visceral leishmaniasis	DST-European Union	¤ 65,250	Sept, 09 - Aug, 12
27.	Dr. Krishna Das Saha **(Infectious Diseases & Immunology)**	Effect of the membrane proteins of attenuated Leishmania donovani on the growth of cancer cell	ICMR, Govt. of India	11.36 (1st year)	01.07.09 - 30.07.12
28.	Dr. Mita Chatterjee Debnath **(Infectious Diseases & Immunology)**	Physicochemcial and biological evaluation of transition metal chelates of some sulfur containing amino acids	ICMR, Govt. of India	3.10	21.10.09 - 20.10.12
29.	Dr. Shyamal K Dana **(Instrument Division)**	Chaos Synchronization: Exploring Technology prospects	DAE, Govt. of India	15.74	22.10.09 - 21.10.12
30.	Dr. Mita Chatterjee Debnath **(Infectious Diseases & Immunology)**	Evaluation of 99mTc-tricarbonyl chelates fluoroquinolones, nitrofuryl carbazones and nitrofuryl thiosemicarbazone for detecting sites of infection	DAE, Govt. of India	16.04	07.12.09 - 06.12.12

Sl. No.	Principal Investigator	Project Title	Funding Agency	Total Fund (Rs. in lakhs)	Duration
31.	Dr. Chinmay Chowdhury **(Chemistry)**	Chemical & Biological evaluation of selected Indian medicinal plants for anti-cancer activities	DST, Govt. of India	16.22	08.02.10 - 07.02.13
32.	Dr. Aditya Konar **(Animal House Division)**	Nanotechnology based drug delivery system for prevention of cataract: Proof of concept in a Rabbit Model	DBT, Govt. of India	6.28 (1st year)	27.09.10 - 26.09.13
33.	Dr. Krishna Das Saha **(Infectious Diseases & Immunology)**	Study on Leishmanial integral membrane proteins(s) induced growth inhibition of melanoma cells with exploration of the mechanism involved and characterization of the bioactive protein component(s)	ICMR, Govt. of India	11.36 (1st year)	13.10.10 - 12.10.13
34.	Dr. Nahid Ali **(Infectious Diseases & Immunology)**	Intellectural and infrastructural facilities and manpower for the project run by Lifecare Innovations Pvt. Ltd.	Lifecare Innovations Pvt. Ltd.	6.38	6 months
35.	Dr. Suvendra Bhattacharya **(Molecular & Human Genetics)**	Mechanism of mRNA compartmentalization in the cyloplasm of mammalian cells	Wellcome Trust, London	472,118 GBP	Sept., 09 - Sept., 14
36.	Dr. Padma Das **(Cell Biology & Physiology)**	Studies of anticarcinogenic functiions of compounds isolated from the edible mushroom	DBT, Govt. of India	19.42	04.03.11 - 03.03.14

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Mookherjee S., Banerjee D., Chakraborty S., Banerjee A., Mukhopadhyay I., Sen A. & Ray K. 2010. Association of IL1A and IL1B loci with primary open angle glaucoma. BMC Medical Genetics **11:** 99.

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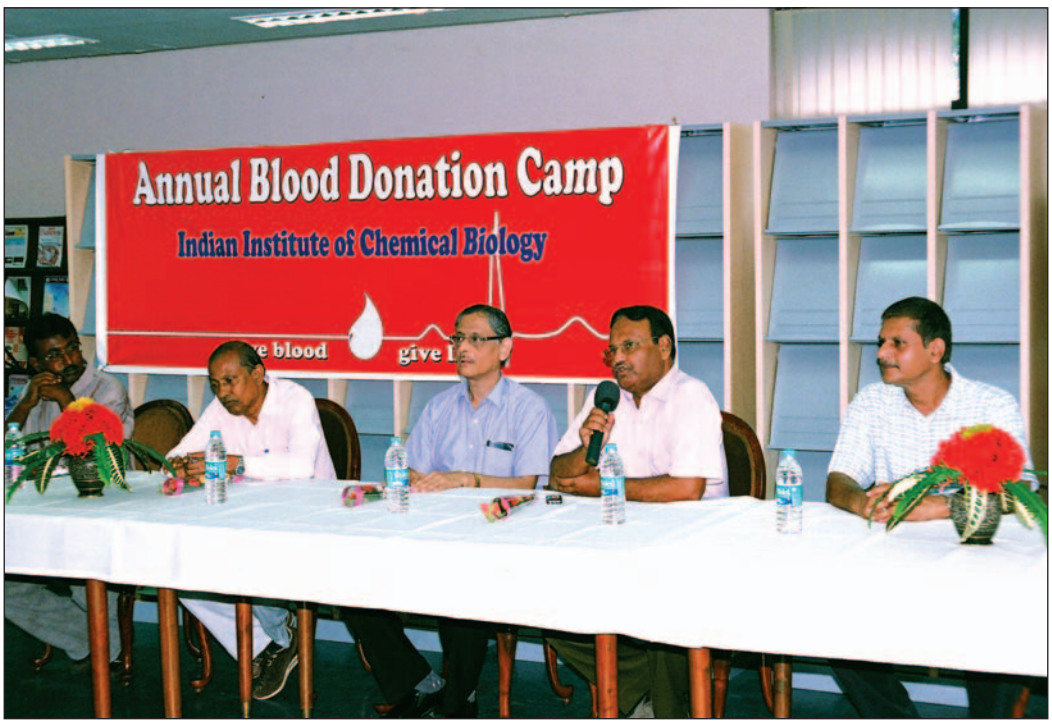
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Indian Institute of Chemical Biology

Doctorates from the Institute

No.	Recipient's Name	Title of Thesis Date of	University/ Name Award	Supervisor's	Scientific Division
1.	Dr. Sreetama Sen	Molecular pathways involved in 3-nitropropionic acid model of Huntington's Disease	J.U.	Dr. K. P. Mohanakumar	Cell Biology & Physiology
2.	Dr. Sumita Mishra	Localisation of Annexin A6 in cardiomyocytes and its involvement in cardiac hypertrophy	J.U. / Dec. 2010	Dr. Arun Bandyopadhyay	Cell Biology & Physiology
3.	Dr. Priyanka De	Functional Significance of Gene Expression Profile in Glucocorticoid-Induced Hypertrophied Heart	J.U. / Dec. 2010	Dr. Arun Bandyopadhyay	Cell Biology & Physiology
4.	Mr. Anupom Borah	Contribution of dopamine in dopaminergic neurodegeneration	J.U. / 2010	Dr. K.P. Mohanakumar	Cell Biology & Physiology
5.	Dr. Debabrata Biswas	Studies on the mechanism of hemolysis in chronic arsenic toxicity	J.U. / Dec. 2010	Dr. Tuli Biswas	Cell Biology & Physiology
6.	Dr. Sandip Kumar Hota	Synthetic studies in organised and homogeneous media	J.U. / July 2010	Dr. Partha Chattopadhyay	Chemistry
7.	Dr. Maidul Hossain	Biophysical Studies on the interaction of some intercalating and groove binding molecules with deoxyribonucleic acids	J.U. / Dec. 2010	Dr. G. Suresh Kumar	Chemistry
8.	Dr. Priyankar Paira	Synthesis and bio-evolution of anilido quinolines and fused quinolines	J.U. / Dec. 2010	Dr. N.B. Mandal & Dr. S. Banerjee	Chemistry
9.	Dr. Abhijit Hazra	Synthesis of bioactive polynuclear heteroaromatics mainly based on indoles and quinolines	J.U. / Dec. 2010	Dr. N.B. Mandal & Dr. S. Banerjee	Chemistry
10.	Dr. Aparajita Ghosh	Tissue Targeted Drug Delivery in Cellular Disorders in Animal Model	J.U. / Aug. 2010	Dr. Nirmalendu Das	Drug Dev., Diag. & Biotechnology
11.	Dr. Anindita Banerjee	Evaluation of a medicinal plant - Phyllanthus amarus and its improvement at the genetic level	J.U. / Sep. 2010	Dr. Sharmila Chattopadhyay	Drug Dev., Diag. & Biotechnology
12.	Dr. Dhananjay Soren	Secretion and purification of xylan hydrolase from Termitomyces clypeatus	J.U. / Dec. 2010	Dr. A. K. Ghosh & Dr. S. Sengupta	Drug Dev., Diag. & Biotechnology
13.	Dr. Ajanta Saha	A study on the genetic elements of acidophilic bacteria of mine origin	J.U. / 2011	Dr. A.K. Ghosh	Drug Dev., Diag. & Biotechnology

No.	Recipient's Name	Title of Thesis Date of	University/ Name Award	Supervisor's	Scientific Division
14.	Dr. Sumit Paul	Studies on the extracellular matrix remodeling in endometriosis: Involvement of matrix metalloproteinases	J.U. / Dec. 2010	Dr. Snehasikta Swarnakar	Drug Dev., Diag. & Biotechnology
15.	Dr. Laishram Pradeep Kumar Singh	Role of matrix metalloproteinases in ethanol-induced gastric ulcer and diabetic gastric ulcer: Effects of antioxidants	J.U. / Dec. 2010	Dr. Snehasikta Swarnakar	Drug Dev., Diag. & Biotechnology
16.	Dr. Shakuntala Ghorai	Co-aggregation of sucrase with cellobiase in the regulated secretory pathway of filamentous fungus Termitomyces clypeatus	J.U. / Dec. 2010	Dr. Suman Khowala	Drug Dev., Diag. & Biotechnology
17.	Dr. Swagata Pal	Studies and characterization of intracellular cellobiase in the secretory pathway of filamentous fungus Termitomyces clypeatus in presence of 2-deoxy-D-glucose	J.U. / Dec. 2010	Dr. Suman Khowala	Drug Dev., Diag. & Biotechnology
18.	Dr. Bijoylaxmi Banerjee	Molecular & biochemical characterization of DNA topoisomerases and repair enzymes from Leishmania donovani towards search for possible therapeutic targets	J.U. / 2011	Dr. H. K. Majumder	Infectious Diseases & Immunology
19.	Dr. Susmita Chandra	Development of new radiopharma-ceuticals for nuclear brain imaging pharmacokinetics and mechanism of action	J.U. / 2011	Dr. Mridula Misra	Infectious Diseases & Immunology
20.	Saumyabrata Mazumdar	A comparative evaluation of the potency and durability of DNA & protein based vaccines against visceral Leishmaniasis	J.U. / 2011	Dr. Nahid Ali	Infectious Diseases & Immunology
21.	Dr. Arunima Biswas	Host-parasite interaction: Modulation of signaling pathways in macrophage and Leishmania and its impact on parasitic infectivity	J.U. / Nov. 2010	Dr. Pijush K. Das	Infectious Diseases & Immunology
22.	Dr. Gunjan Dhar	Characterization of a tRNA interacting component of the Leishmania mitochondrial tRNA import complex	J.U. / Dec. 2010	Dr. Samit Adhya	Molecular & Human Genetics
23.	Dr. Suddhasil Mookherjee	Molecular and Functional Analysis of Glaucoma: A Study Based on Indian Patients	J.U. / Dec. 2010	Dr. Kunal Ray	Molecular & Human Genetics

No.	Recipient's Name	Title of Thesis Date of	University/ Name Award	Supervisor's	Scientific Division
24.	Dr. Mainak Sengupta	Molecular Genetic Basis of Albinism in Indian Patients	J.U. / Dec. 2010	Dr. Kunal Ray	Molecular & Human Genetics
25.	Dr. Taraswi Banerjee	Study of the regulation of spindle assembly checkpoint gene CDC20 and its role in genomic instability	J.U. / 2010	Dr. Susanta Roy Choudhury	Molecular & Human Genetics
26.	Dr. Mayukh Banerjee	Comparison of Genetic Damage, Biochemical Changes and Genetic Variants between Skin Symptomatic and Asymptomatic Individuals Exposed to Arsenic	J.U. / Dec. 2010	Dr. A.K. Giri	Molecular & Human Genetics
27.	Dr. Srijata Mukherjee	Study of structure, dynamics and interaction of gene regulatory proteins	J.U. / Dec. 2010	Prof. Siddhartha Roy	Structural Biology & Bioinformatics
28.	Dr. Paromita Raha	Study of conformation and dna binding specificity of transcription factors	C.U. / Dec. 2010	Prof. Siddhartha Roy	Structural Biology & Bioinformatics
29.	Dr. Savita Bhutoria	In silico Studies on Anticonvulsant Compounds for Designing Improved Drugs	J.U. / Sep. 2010	Dr. Nanda Ghoshal	Structural Biology & Bioinformatics
30.	Dr. M. Nahren Manuel	In-silico Studies on Anticancer Compounds: Targeting the Cell Cycle	J.U. / Dec. 2010	Dr. Nanda Ghoshal	Structural Biology & Bioinformatics


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National Institute of Pharmaceutical Education and Research (NIPER - Kolkata)

Honours and Awards

INFECTIOUS DISEASES AND IMMUNOLOGY

Dr. H. K. Majumder

- Member of the Institutional Ethical Committee, Institute of Post Graduate Medical Education & Research (IPGMER), Kolkata. 2007-till date.
- Member of the Research Advisory Committee of the Central Sericulture Research & Training Institute, Berhampur, Murshidabad, West Bengal.
- Member of the Selection Committee for SRF/RA of CSIR.
- Member of the Fellowship Scrutiny Committee of National Academy of Sciences, India (FNASc)
- Chairman of the NASI, Allahabad Kolkata Local Chapter (NASI), w.e.f. 31.12.2007.
- Member of the Senate of Indian Ibnstitute of Science, Education and Research, Kolkata (IISER-K).
- Chairman, Expert Committee for State Innovation Award, Govt. of West Bengal.
- Chairman, State Level Climatic Change Committee, Govt. of West Bengal.
- Working Chairman of the West Bengal State Council of Science & Technology-2004 onwards.

Dr. Chitra Mandal

- Received J.C. Bose Fellowship award by Department of Science and technology.
- A Member of Research Council (RC) of Institute of Genomics & Integrative Biology.
- A member of RAB.
- A member of a few CSIR head quarter committees.
- Reviewer of National and International journals.
- Reviewer of National and International projects for national and International funding.

Dr. Pijush K. Das

- Sir J.C. Bose National Fellowship Award from the Department of Science & Technology (DST) with effect from 16-09-2010 for outstanding contribution to Biological Science research in India.
- Nominated as a Member of the Board of Studies of North Eastern Hill University, Shillong since 2010.

MOLECULAR & HUMAN GENETICS

Dr. Suvendra Bhattacharyya

- International Senior Research Fellow of the Wellcome trust London, UK.
- Young Researcher award from the Lady Tata Memorial Trust.
- Selected as Associates of the Indian Academy of Sciences, Bangalore.

Dr. Keya Chaudhuri

- Reviewer of papers for (i) Antimicrobial Agents & Chemotherapy, ASM Press, USA (ii) Clinical & Vaccine Immunology, ASM press, USA (iii) Journal of Clinical Microbiology, ASM press, USA (iv) Applied & Environmental Microbiology, ASM Press, USA (vi) PLoS One, Public Library of Science; (viii) BMC Immunology, Biomed Central, London, UK; (ix) BMC Bioinformatics, Biomed Central, London, UK (x) Journal of Cellular Biochemistry, Wiley-Interscience, USA; (xi) Microbial Pathogenesis, Elsevier, The Netherlands; (xii) Apoptosis, Springer, Germany; (xiii) Journal of Medical Microbiology, SGM,UK (xiv) Food and Chemical Toxicology, Elsevier, The Netherlands (xv) European Journal of Immunology, Wiley-VCH; (xvi)Microbiological Research, Elsevier,Netherlands, (xvii) Nucleic Acids Research, Oxford University Press, (xviii)Journal of Public health & Epidemiology, Academic journals, Africa.

Dr. Ashok K. Giri

- Elected as a Member of the Executive Council (2011-2013) of the International Association of Environmental Mutagen Societies (IAEMS).

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Dr. Snehasikta Swarnakar

- Elected Fellow of West Bengal Academy of Science and Technology, Dec 2010.
- Elected Member of Guha Research Council, Dec 2010.
- Biographical record in Who's Who in the World 2011, by Marquis Publication, USA.

Dr. Suman Khowala

- Member of the management council of The Biotech Research Society, India (2009-11).
- General Secretary of Kolkata Chapter of IICB-Jadavpur University, The Biotech Research Society, India (2009-11).

CHEMISTRY

Dr. G. Suresh Kumar

- Secretary, DNA Society of India (2009-2014).
- Member, National Executive Council of Indian Biophysical Society (2009-2011).
- Member, Editorial Advisory Board, "The Open Natural Product Journal" (Bentham Sciences).
- Member Editorial Advisory Board, "International Journal of Physical Sciences" (Academic Journal).
- Member, Editorial Advisory Board, "African Journal of Biochemistry Research" (Academic Journal).

Dr. P. Jaisankar

- Awarded Raman Research Fellowship by CSIR to visit Nagoya University, Japan., 2010 on deputation.

Dr. Partha Chattopadhyay

- Member of the Editorial Board of Referees, ARKIVOC, USA from 2008-onwards.

Dr. A. K. Banerjee

- Acting as Project Director of NIPER, Kolkata.
- Member of the Steering Committee, Dept. of Pharmaceuticals, Ministry of Chemicals & Fertilizers, Govt. of India.
- Member of Joint Counseling Committee for the Master program in NIPER Mohali-Punjab
- Member, Committee constituted to formulate rules, service conditions, etc. of NIPER staff, constituted by Dept. of Pharmaceuticals, Govt. of India.
- Member Secretary of State Level Co-ordination Committee, Govt. of West Bengal, constituted by Dept. of Pharmaceuticals, Govt. of India.

Dr. Asish Kumar Sen

- Received ACCT(I) Life Time Acheivement Award-2010.
- Elected as Hon. President of the Association of Carbohydrate Chemists & Technologists (India) 2010-12.
- Member of the Advisory Committee of NIPER-Kolkata.

STRUCTURAL BIOLOGY & BIOINFORMATICS

Dr. M. C. Bagchi

- Received the VLifeScience Best Publication Award for the year 2010.

Dr. Chitra Dutta

- Member, Editorial Board, International Journal of Soft Computing & Bioinformatics.
- Memebr, Advisory Board, NIPER (Kolkata).
- Member, PG Board of Studies, Department of Genetics, Calcutta University.

Dr. Debasish Bhattacharyya

- Selected as a member of the editorial board of the 'Journal of Chromatography B' for 3 years term (2008-2011).
- Awarded 'Member of honor of the SBCN' at Lyon, France 2010 (DB).
- Awarded Indian Spectro-physics Association (ISPA) Prize 2009 at Chennai in 2011.

Dr. Nanda Ghoshal

- Reviewer of manuscripts for, J. Med. Chem., J. Bioorg. Med. Chem., J. Mol. Graph. Mod., Chemical Biology & Drug Design, Eur. J. Med. Chem., J. Chem. Info. Model.

CELL BIOLOGY & PHYSIOLOGY

Dr. K. P. Mohanakumar

- Awarded ICMR International Fellowship for Senior Indian biomedical scientists for the year 2010-11.
- Elected member of the Committee on Aid and Education in Neurochemistry (CAEN) of the International Society for Neurochemistry, UK.
- Appointed as Editorial Board Member of Neuroscience & Medicine www.scirp.org/journal/nm by NM Editorial Board, Scientific Research Publishing, Irvine, USA.
- Appointed as Editorial Board member of Anatomy and Cell Biology http://www.acbjournal.com, Incheon, South Korea.

- Editorial Board Member of Journal of Cell & Tissue Research http://www.tcrjournals.com/journal1.php, India.
- Appointed as a Member of Scientific Advisory Board by Parkinson's & Ageing Research Foundation, Bangalore, 2011.

Dr. Sib Sankar Roy

- Elected as Sectional Recorder of 'New Biology' section of Indian Science Congress for two years (2011 and 2012).
- Appointed as a UGC visiting teacher by Tripura University, Agartala.

Dr. S. N. Kabir

- Member, Sub-group on "Pre-clinical Research on Microbicides", ICMR.
- Member, Domain Expert Group on "Pre-clinical development of spermicide - S010-1255 as a vaginal contraceptive", NMITLI, CSIR.
- Chairman, Consortium Advisory Committee on "Genetic basis of inferior sperm quality and fertility of cross-bred bulls", ICAR.

Staff List of IICB as on March 31, 2011

Staff Strength at a Glance

Director			1
Scientist – Gr. IV	…	…	68
Engineer	…	…	4
Technical – Gr. III	…	…	52
Technician – Gr. II	…	…	39
Helper – Gr. I	…	…	17
Ministerial Officer	…	…	17
Ministerial Staff	…	…	44
Gr. D (Non-Technical)	…	…	14
Canteen Staff	…	…	10
TOTAL	**…**	**…**	**266**

Detailed Staff List

Scientific and Technical

Sl. No.	Employee's Name	Emp. ID	Designation
1.	Prof. Siddhartha Ray	489	Director
2.	Dr. Samit Adhya	37	Scientist H
3.	Dr. (Mrs.) Chitra Mandal	60	Scientist H
4.	Dr. H.K. Majumdar	23	Scientist Gr. IV(6)
5.	Dr. Pijush K. Das	40	Do
6.	Dr. S.B. Mondal	76	Do
7.	Dr. K.P. Mohanakumar	77	Do
8.	Dr. Tarun K. Dhar	63	Do
9.	Dr. A.K. Sen (Jr)	65	Do
10.	Dr. Anil K. Ghosh	68	Do

Sl. No.	Employee's Name	Emp. ID	Designation
11.	Dr. Syamal Roy	93	Scientist Gr. IV(6)
12.	Dr. (Mrs.) Keya Chaudhuri	83	Do
13.	Dr. Sumantra Das	87	Do
14.	Dr. S.B. Mukhopadhyay	80	Scientist Gr. IV(5)
15.	Dr. Santu Bandyopadhyay	97	Do
16.	Dr. Partha Chattopadhyay	81	Do
17.	Dr. Manish Ch. Bagchi	78	Do
18.	Dr. S.N. Kabir	90	Do
19.	Dr. (Mrs.) Chitra Dutta	95	Do
20.	Dr. Ashok Kumar Giri	402	Do
21.	Dr. Debashish Bhattacharya	96	Do
22.	Dr. Shyamal Kumar Dana	86	Do
23.	Dr. (Mrs.) Aparna Gomes	91	Do
24.	Dr. Nirmalendu Das	100	Do
25.	Dr. (Mrs.) Nahid Ali	103	Do
26.	Dr. Susanta Roychowdhury	98	Do
27.	Dr. U.S. Chowdhury	84	Do
28.	Dr. Kunal Ray	415	Do
29.	Dr. (Mrs.)Tuli Biswas	109	Do
30.	Dr. Sukdeb Bandopadhyay	102	Do
31.	Dr. Nirup Bikash Mondal	107	Do
32.	Dr. G. Suresh Kumar	105	Do
33.	Dr. (Mrs.) Rukhshana Chowdhury	115	Do
34.	Dr. Aparesh Bhattacharya	59	Scientist Gr. IV(4)
35.	Dr. (Miss) Moonmoon Bhowmik	110	Do
36.	Dr. Samir Kr. Dutta	111	Do
37.	Dr. Arun Bandyopadhyay	445	Do
38.	Dr. P. Jaisankar	112	Do
39.	Dr. Rupak Kr. Bhadra	124	Do
40.	Dr. (Mrs.) Nanda Ghoshal	119	Do
41.	Dr. Ram Chandra Yadav	154	Do
42.	Dr. Asish Kr. Banerjee	116	Do
43.	Dr. (Mrs.) Suman Khowala	118	Do

Sl. No.	Employee's Name	Emp. ID	Designation
44.	Dr. Tushar Kanti Chakraborty	99	Scientist Gr. IV(4)
45.	Dr. (Mrs.) S.R. Dungdung	120	Do
46.	Dr. Tanmoy Mukherjee	125	Do
47.	Dr. Sibsankar Ray	443	Do
48.	Dr. Aditya Konar	441	Do
49.	Dr. Pratap Kr. Das	62	Scientist Gr. IV(3)
50.	Sri U.K. Barua	464	Do
51.	Dr. (Mrs.) Padma Das	117	Do
52.	Dr. (Mrs.) Debjani Mondal	123	Do
53.	Mrs. N.V.M. Khalko	122	Do
54.	Dr. (Mrs.) Tripti De	433	Do
55.	Dr. Soumen Datta	503	Do
56.	Dr. Chinmay Chowdhury	520	Do
57.	Dr. Uday Bandopadhyay	521	Do
58.	Dr. K.N. Chattopadhyay	523	Do
59.	Dr. Mrinal Kanti Ghosh	524	Do
60.	Dr. (Mrs.) Malini Sen	527	Do
61.	Dr. (Mrs.) Jayati Sengupta	532	Do
62.	Dr. S.N. Bhattacharya	530	Do
63.	Dr. (Mrs) Sarmila Chattopadhyay	447	Do
64.	Dr. Subrata Adak	472	Do
65.	Dr. (Miss) Snehasikta Swarnakar	473	Do
66.	Dr. Biswadip Banerji	540	Do
67.	Dr. Subhas Ch. Biswas	547	Do
68.	Dr. Nakul Ch. Maiti	551	Do
69.	Dr. Saraswati Garai	528	Scientist Gr. IV(1)
70.	Dr. (Mrs.) Mridula Misra	142	Principal Technical Officer
71.	Dr. (Mrs.) Krishna Das Saha	143	Do
72.	Sri H.N. Roy	152	Do
73.	Dr. (Mrs.) S.E. Besra	145	Do
74.	Sri Tapan Kumar Mukherjee	140	Do
75.	Sri A.K. Das	151	Do
76.	Dr. (Mrs) Mita Chatterjee Debnath	432	Senior Technical Officer (3)

Sl. No.	Employee's Name	Emp. ID	Designation
77.	Sri S.K. Sahoo	163	Senior Technical Officer (3)
78.	Dr. S. Majumdar	164	Do
79.	Sri Chirantan Debdas	535	Do
80.	Sri Mohan Lal Jana	167	Do
81.	Dr. Prashanta Kr. Chakraborty	169	Do
82.	Dr. Kalidas Paul	168	Do
83.	Sri Shekhar Ghosh	467	Do
84.	Sri A.K. Bairagi	165	Do
85.	Sri Samir Kr. Roy	171	Do
86.	Dr. Ashok Kumar Dasgupta	172	Do
87.	Sri Sandip Saha	494	Supdt. Engineering Gr. III(6)
88.	Sri Susanta Ray	514	Asst. Exec. Engineer Gr. III(4)
89.	Sri B. Jayakumar	517	Do
90.	Mrs. Nirali Bage	466	Junior Engineer, Gr. I
91.	Sri Narayan Ch. Ghosh	499	Senior Technical Officer (2)
92.	Sri Surajit Mohan Roy	166	Do
93.	Sri Gautam Gupta	170	Do
94.	Sri Binayak Pal	448	Do
95.	Dr. (Mrs.) Aparna Laskar	449	Do
96.	Dr. Sankar Kumar Maitra	174	Do
97.	Dr. Ardhendu Kr. Mandal	175	Do
98.	Dr. Tapas Sarkar	177	Do
99.	Dr. (Miss) Subhagata Ghosh	179	Do
100.	Sri Arupesh Majumdar	180	Do
101.	Sri Sekhar Mukherjee	477	Do
102.	Sri R.N. Mandi	185	Do
103.	Dr. Ramdhan Majhi	184	Do
104.	Sri P. Gangopadhyay	186	Do
105.	Sri Asish Mullick	187	Do
106.	Mrs. Dipika Roy	188	Do
107.	Mrs. Purnima Chatterjee	173	Do
108.	Mrs. Banasri Das	176	Do
109.	Sri Diptendu Bhattacharya	178	Do

Sl. No.	Employee's Name	Emp. ID	Designation
110.	Sri Kshudiram Naskar	162	Senior Technical Officer (1)
111.	Sri E. Padmanaban	496	Do
112.	Sri Pratap Ch. Kayal	182	Do
113.	Sri Sandip Chowdhury	411	Technical Officer
114.	Mrs. Arti Khetrapaul	463	Technical Assistant
115.	Sri Swapan Kr. Mondal	465	Do
116.	Sri Jishu Mandal	495	Do
117.	Sri Debashis Banik	513	Do
118.	Sri Sandip Chakraborty	516	Do
119.	Sri T. Muruganandan	539	Do
120.	Sri Chinthapalli Balaji	545	Do
121.	Sri Karri Suresh Kumar	550	Do
122.	Sri Vigneshwaran M.	552	Do
123.	Sri Santu Paul	556	Do
124.	Sri Sandip Kundu	557	Do
125.	Miss Moumita Chakraborty	558	Do
126.	Sri Ajoy Kr. Pramanik	195	Senior Technician (2)
127.	Sri M.B. Malakar	219	Do
128.	Sri S.K. Basak	220	Do
129.	Sri Goutam Malik	224	Do
130.	Sri P.K. Chanda	236	Do
131.	Sri S.N. Mondal	237	Do
132.	Sri S.K. Prodhan	239	Do
133.	Sri S.C. Das	241	Do
134.	Sri S.R. Tudu	251	Senior Technician (1)
135.	Sri Swapan Kumar Naskar	244	Do
136.	Md. Ayub Shah	344	Do
137.	Sri Sheo Shankar Verma	242	Do
138.	Sri Tapas Chowdhury	246	Do
139.	Sri Pradip Mondal	383	Do
140.	Sri A.K. Sen	478	Do
141.	Sri Tarak Prasad Nandi	247	Do
142.	Mrs. Sutapa Ganguly	248	Do

Sl. No.	Employee's Name	Emp. ID	Designation
143.	Sri Sanjib Biswas	249	Senior Technician (1)
144.	Sri R.P. Gorh	250	Do
145.	Sri Sarit K. Sarkhel	245	Do
146.	Sri Nishikanta Naskar	252	Do
147.	Sri Pallab Mukherjee	253	Do
148.	Sri Ranjit Das	345	Do
149.	Sri Abhijit Paul	450	Do
150.	Sri Anirban Manna	410	Technician (2)
151.	Sri Samir Majumder	426	Do
152.	Md. M. Ahmed	360	Do
153.	Sri Paresh Sarkar	409	Do
154.	Sri Sujit Kr. Majumdar	416	Do
155.	Mrs. Mahua Bhattacharjee	419	Do
156.	Sri Prabir Kr. Das	418	Do
157.	Sri Atanu Maitra	417	Do
158.	Sri Tapan Das	460	Do
159.	Sri Ujjal Roy	529	Technician (1)
160.	Sri Arup Karmakar	534	Do
161.	Sri Soumalya Sinha	546	Do
162.	Nita Chakraborty Ms	553	Do
163.	Akash Gupta Sri	554	Do
164.	Samir Thami Sri	555	Do
165.	Sri R. Mahato	258	Laboratory Assistant
166.	Sri Sunil Nath	272	Do
167.	Sri R.N. Jana	274	Do
168.	Sri Prahlad Das	275	Do
169.	Sri Bhaskar Basu	440	Do
170.	Sri Shyamal Das	279	
171.	Sri Madan Halder	479	Do
172.	Sri Amerika Das	280	Laboratory Attendant (2)
173.	Sri Nimai Charan Prodhan	282	Do
174.	Sri Sambhu Raul	351	Do
175.	Sri Suresh Balmiki	353	Do

Sl. No.	Employee's Name	Emp. ID	Designation
176.	Sri U.N. Mandi	358	Laboratory Attendant (2)
177.	Sri Nandalal Routh	352	Do
178.	Sri S.K. Banik	361	Do
179.	Sri Ashoke Sardar	501	Laboratory Attendant (1)
180.	Sri Ram Kumar Sarkar	502	Do
181.	Sri Shyamal Nath	519	Do

Administration

Sl. No.	Employee's Name	Emp. ID	Designation
1.	Sri U.S. Das	515	Controller, Stores & Purchase
2.	Sri S.K. Chaudhuri	497	Administrative Officer
3.	Sri S.K. Das	498	F&A Officer
4.	Sri N.K. Saha	549	Stores & Purchase Officer
5.	Sri Subhas Ch. Dutta	290	Sr. Security Officer
6.	Sri Kausik Bhattacharjee	492	Section Officer (General)
7.	Sri Siddhartha Dey	485	Do
8.	Mrs. Shampoo Sengupta	525	Do
9.	Sri P.K. Saha	468	Do
10.	Sri Asok Putatunda	542	Do
11.	Sri Asim Kr. Jha	518	Section Officer (F&A)
12.	Sri Abhimanyu Kr. Tiwary	533	Do
13.	Sri Tapan Kumar Mitra	320	Section Officer (Stores & Purchase)
14.	Sri Ratan Bage	397	Section Officer (Stores & Purchase)
15.	Sri S.K. Chhatui	312	Private Secretary
16.	Sri Nilratan Biswas	538	Do
17.	Sri Debdas Guhathakurta	313	Do
18.	Sri Kanu Mondal	392	Assistant (General) Gr. I (Acp)
19.	Sri K.C. Das	302	Assistant (General) Gr. I (MACP)
20.	Sri D.R. Chakraborty	306	Do
21.	Mrs. Anjana Mandi	308	Do

Sl. No.	Employee's Name	Emp. ID	Designation
22.	Mrs. Sanhita Ganguly	427	Assistant (General) Gr. I (MACP)
23.	Mrs. Monalisa Bhattacharjee	428	Assistant (General) Gr. I
24.	Miss Lily Das	330	Do
25.	Mrs. Indira Kundu	331	Do
26.	Sri R.N. Hansda	334	Do
27.	Sri Prem Singh	335	Do
28.	Sri D.K. Kisku	340	Do
29.	Sri Alok Ray	396	Assistant (General) Gr. II (MACP)
30.	Sri Jayanta Pal	510	Assistant (General) Gr. II
31.	Sri Tarun Kr. Sinha Roy	508	Do
32.	Sri Raju Pal	507	Do
33.	Sri Ranjit Debnath	509	Do
34.	Sri Saugata Das	511	Do
35.	Sri Sukhendu Biswas	512	Do
36.	Sri A.K. Chanda	327	Assistant (F&A) Gr. I (MACP)
37.	Mrs. Banani Dutta	476	Assistant (F&A) Gr. I
38.	Sri Sanjoy Mukhopadhyay	343	Do
39.	Mrs. P.L. Saha	332	Do
40.	Sri Asit K. Roy	336	Assistant (F&A) Gr. II (MACP)
41.	Sri M.K. Dutta	338	Do
42.	Sri Vishal Agarwal	506	Assistant (F&A) Gr. II
43.	Sri Panchanan Naskar	322	Assistant (S&P) Gr. I (MACP)
44.	Sri A.B.S. Roy	328	Assistant (S&P) Gr. I
45.	Sri Rajib Ray	536	Do
46.	Sri Bisweswar Das	342	Do
47.	Mrs. Bula Pal	363	Assistant (S&P) Gr. II
48.	Sri Pradipta Sarkar	505	Do
49.	Sri Arnab Sen	504	Do
50.	Mrs. Ambalika Nag	321	Senior Hindi Translator
51.	Sri Nikhil Kumar Das	315	Senior Stenographer (MACP)
52.	Sri Sankar Prasad Dutta	316	Do
53.	Sri Dipak Kr. Guin	318	Do
54.	Sri Asim Roy	323	Senior Stenographer (ACP)

Sl. No.	Employee's Name	Emp. ID	Designation
55.	Mrs. Pratima Banerjee	324	Senior Stenographer (MACP)
56.	Sri Shankar Bhakta	325	Do
57.	Sri Rabindranath Das	393	Senior Stenographer
58.	Sri Saibal Giri	405	Do
59.	Sri Sankar Santra	490	Do
60.	Sri Gautam Saha	453	Junior Stenographer
61.	Smt Moumita Majumdar	491	Do
62.	Sri Ashok Ram	348	Gr-C (NT) (ACP)
63.	Sri Bideshi Nayak	349	Do
64.	Sri Kailash Chandra Nayak	365	Gr-C (NT) (Upgraded)
65.	Mrs. Gita Ghosh	364	Do
66.	Mrs Soma Devi Sharma	401	Do
67.	Sri Gopal Ch. Mandal	412	Do
68.	Sri Asit Mitra	413	Do
69.	Sri Janmanjoy Midya	431	Do
70.	Sri Pasupati Midya	430	Do
71.	Sri Shyamal Kr. Ghosal	423	Do
72.	Sri P.C. Dehury	414	Do
73.	Sri Manoranjan Adhikary	425	Do
74.	Sri Tapan Sarkar	424	Do
75.	Sri Dinesh Mahali	451	Group-C (NT)
76.	Sri Tarun Dutta	367	Asstt. Manager-cum-Store Keeper
77.	Sri Amal Dutta	369	Clerk
78.	Sri Balaram Panda	368	Halwai-cum-Cook
79.	Sri Sudhangshu Halder	373	Tea Maker
80.	Sri Bimal Das	372	Bearer
81.	Sri Ashok Sadhukhan	371	Bearer
82.	Sri Badal Haldar	370	Bearer
83.	Sri Jagabandhu Biswas	374	Wash Boy
84.	Sri Nirapada Halder	375	Sweeper
85.	Sri Mantu Das	376	Sweeper

Retirement List from April 01, 2010 to March 31, 2011

Sl. No.	Name of the Staff	Designation	Date of Retirement
1.	Shri T.K. Chakraborty	Tech.Officer	30.04.2010
2.	Mrs. Chaina Devi Nayak	Gr.C (Non-technical)	30.04.2010
3.	Dr. S.N. Chakraborty	Sct., Gr.IV(4)	31.07.2010
4.	Shri P. Dhank	Technician	31.08.2010
5.	Mrs. Ratnabali Adhikari	Assistant (G),Gr.I	31.08.2010
6.	Shri Ranjan Ghosh	SO(SP)	30.09.2010
7.	Dr. A.K. Sen (Sr)	Sct.,Gr.IV(4)	31.10.2010
8.	Shri S.C. Sil	Gr.I	31.10.2010
9.	Dr. R. Mukhopadhyay	Sct.,Gr.IV(4)	31.12.2010
10.	Dr. S.R. Sarkar	COA	31.12.2010
11.	Dr. S.B. Mukhopadhyay	Sct.,Gr.IV(5)	31.03.2011
12.	Shri G.C. Sarkar	Technician	VR wef. 07.12.2010

New Appointment from April 01, 2010 to March 31, 2011

Sl. No.	Name of the Staff	Designation	Date of Appointment
1.	Shri Karri Suresh Kumar	Tech.Assistant	20.05.2010
2.	Dr. Nakul Ch. Maiti	Senior Scientist	25.05.2010
3.	Shri Vigneshwarn	Tech. Assistant	26.07.2010
4.	Ms. Nita Chakraborty	Technician (1)	26.08.2010
5.	Shri Akash Gupta	-do-	26.08.2010
6.	Shri Samir Thami	-do-	01.09.2010
7.	Shri Santu Paul	Technical Assistant	20.10.2010
8.	Shri Sandip Kundu	-do-	21.10.2010
9.	Miss Moumita Chakraborty	-do-	21.10.2010

Name of Emeritus Scientists / Prestigious Fellowship Holders

Sl. No.	Name of Emeritus Scientists	Position
1.	Dr. Pradip Kumar Dutta	Emeritus Scientist
2.	Dr. Aloke Kumar Dutta	-do-
3.	Dr. Anup Bhattacharya	-do-
4.	Prof. Samaresh Mitra	Sr. Scientist
5.	Dr. Surajit Ghosh	Ramanujan Fellow
6.	Dr. Saikat Chakraborty	Ramalingaswamy Fellow

Name of Staff Resigned /Terminated / Transferred

Sl. No.	Name	Designation	Date
1.	Dr. G. Tripathi	T.O.	Resigned on 2.8.2010
2.	Shri Rajat Bandyopadhyay	Tech.Asstt.	Terminated on 25.04.2010
3.	Shri Sudip Ghosh	Jr. Steno	Transferred on 13.10.2010

OBITUARY

Dr. Mohammed Islam Khan, who began his career at IICB as a Research Scholar in 1978 and joined CSIR service as Scientist in May, 1990 at NCL, Pune, later transferred to IICB in October, 2009 as Scientist F and continued his career with good research work in the field of Chemistry & Structural Biology and sense of fairness and honesty on and off the course, passed away while in service on November 12, 2010 as a result of chronic renal failure.

Dr. M I Khan is survived by his wife and two daughters, his relatives and many friends both personal and professional.

CSIR-IICB Research Council, 2010-2011

Prof. M. Vijayan (Chairman)
Honorary Professor
Molecular Biophysics Unit
Indian Institute of Science
Bangalore - 560012

Dr. A. N. Bhisey (Member)
Former Director
Cancer Research Institute
7, Yug Prabhat Society
Naryan Pathara Marg, Mahim
Mumbai - 400 016

Prof. R. V. Hosur (Member)
National Facility for High Field NMR
Tata Institute of Fundamental Research
Homi Bhabha Road, Navy Nagar
Mumbai - 400 005

Prof. K. Muniyappa (Member)
Head, Department of Biochemistry
Indian Institute of Science
Bangalore - 560 012

Prof. B. Bhattacharyya (Member)
Department of Biochemistry, Bose Institute,
Centenary Building, P-1/12 C. I. T.
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Dr. Girish Sahni (Member from Sister Lab.)
Director
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Dr. Rajesh S. Gokhale (Cluster Director)
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Dr. Kunal Roy (Secretary)
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प्रबंध परिषद्

(1 जनवरी, 2010 से 31 दिसम्बर, 2011 तक)

Management Council

(For the period from 01.01.2010 to 31.12.2011)

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