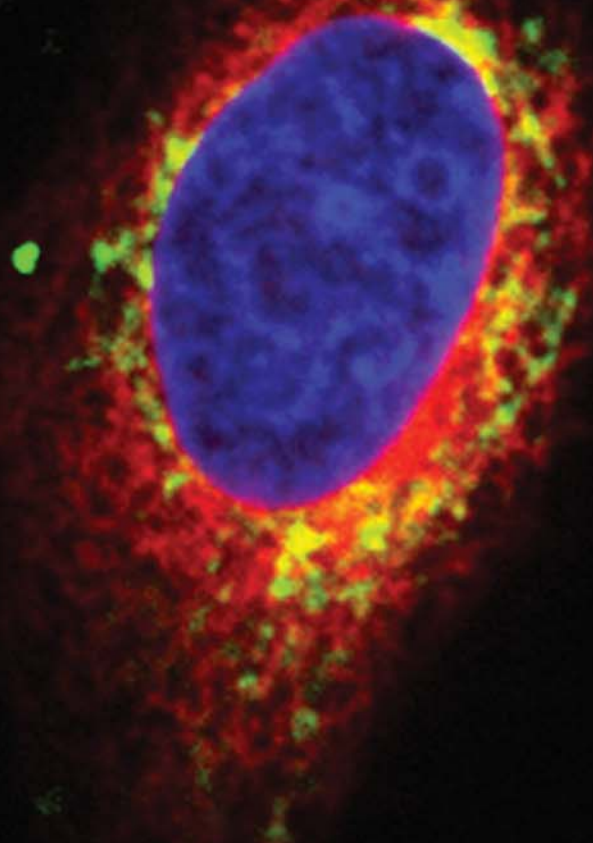
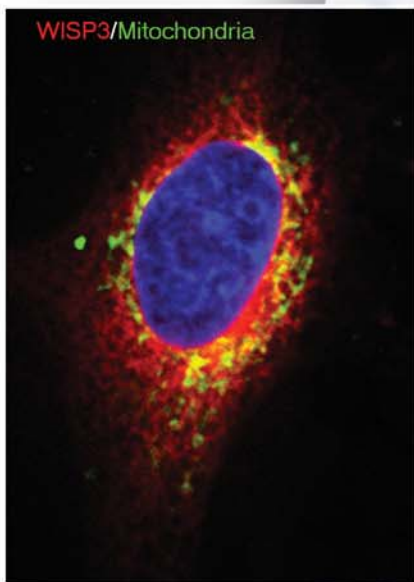


CSIR-IICB

सी एस आई आर
भारतीय रासायनिक जीवविज्ञान संस्थान
CSIR-Indian Institute
of Chemical Biology

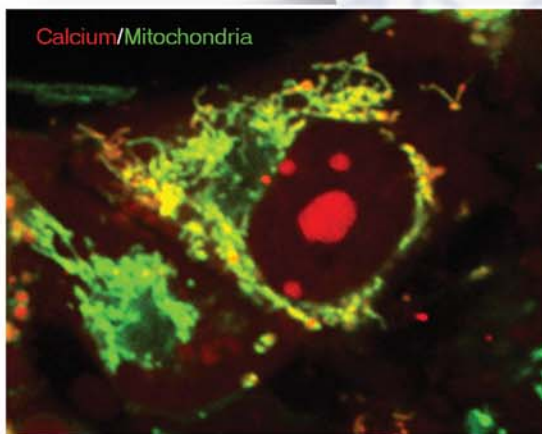


वार्षिक प्रतिवेदन
Annual Report 2015-16



Front Cover

Confocal microscopy of WISP3-myc transfected chondrocyte line depicts co-localization (yellow) of mitochondria (mitotracker green FM: green) with WISP3-myc (red).



Back Cover

Confocal microscopy depicts mitochondrial Ca^{2+} uptake estimated by co-localization (yellow) of Ca^{2+} (Rhod2: red) with mitochondria (Mitotracker green FM: green) in a WISP3 depleted chondrocyte line.

वार्षिक प्रतिवेदन
Annual Report
2015-16

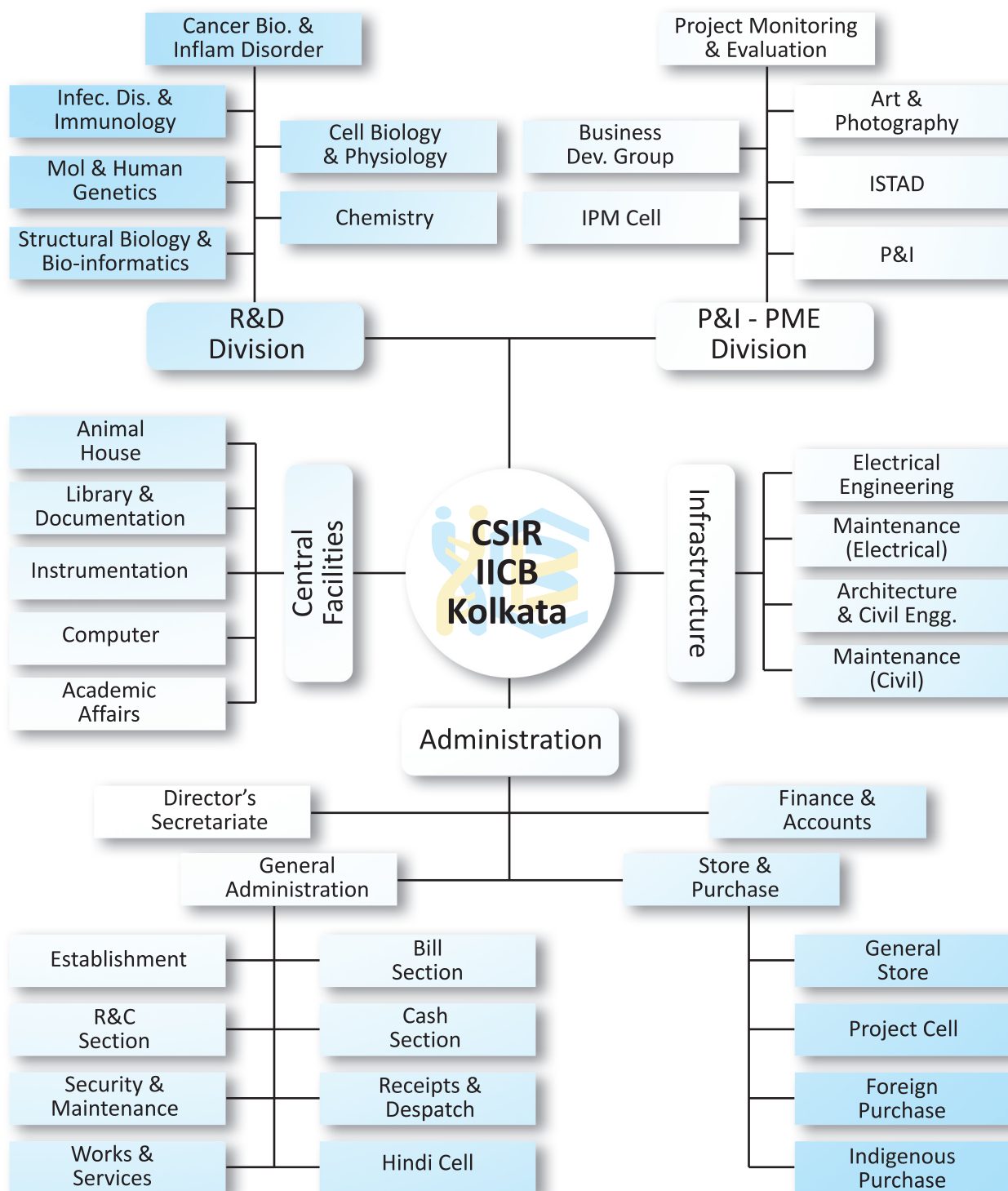


Jadavpur Campus

Salt Lake TRUE Campus



सी एस आई आर-भारतीय रासायनिक जीवविज्ञान संस्थान
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Contents

Director's Report	005
Cell Biology and Physiology Division	009
Infectious Diseases and Immunology Division	035
Cancer Biology & Inflammatory Disorders Division	053
Organic and Medicinal Chemistry Division	087
Molecular and Human Genetics Division	121
Structural Biology & Bioinformatics Division	127
Network Projects in 12th Five-year Plan (2012-17)	155
Publication & Information and Planning, Monitoring & Evaluation Division	161
Performance at a Glance	184
Central Facilities	193
Engineering Services Unit (ESU)	204
Administration	206
National Institute of Pharmaceutical Education and Research (NIPER - Kolkata)	209
Publication Highlights	214
Doctorates From CSIR-IICB	227
Staff List as on March 31, 2016	231

From Director's Desk



Every year the Institute publishes its Annual Report to disseminate a brief account of our research activities and accomplishments, published works and intellectual properties, to our friends, well wishers and scientific community. It's my pleasure to present the Annual Report for the period from April 2015 to March 2016. This report presents an account of our growth. Apart from the scientific contributions, it also includes critical information on 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 several years. I am happy to present that our stride for progress has continued unabated towards excellence and in the last few years we have taken major steps to translate its research results into products for societal benefit. We are doing well in terms of technology transfer. Drugs like 'Asmon' and 'Prostalyn' developed by us from Indian medicinal plants are now in the market.

The role of CSIR-IICB in 'Affordable healthcare through modern science' is well recognized since its early days. We have sustained progress in the current period by enhancing the quality of science. The new campus, CSIR-IICB Translational Research Unit of Excellence (CSIR-IICB TRUE) has started functioning as a productive platform for successful industry-institute tie-up for



translating previously achieved and ongoing biomedical discoveries by CSIR-IICB scientists into deliverables for societal benefit. The institute is continuing to function as the mentor institute for National Institute of Pharmaceutical Education and Research (NIPER), Kolkata. We can expand here about the teaching and training of about 100 students every year and prepare them for the future career as Indian budding scientists.

CSIR-IICB now has seven major scientific divisions: Cell Biology & Physiology, Infectious Diseases & Immunology, Cancer Biology & Inflammatory Disorders, Chemistry, Drug Development, Diagnostics & Biotechnology, Molecular & Human Genetics and Structural Biology & Bioinformatics. The institute embodies a symbiosis between chemistry and biology that translates to a commitment to higher standards of health for all. The chemists are tirelessly making tools to harness and redefine biological phenomena and the biologists are constantly working on understanding physiological processes and diseases. Scientists are continuing their efforts to unravel the molecular basis of cancer, altered immune responses during chronic infection and inflammation, and the pathophysiology of several metabolic and neurodegenerative disorders such as diabetes and Parkinson's disease. This year four scientists were promoted to the position of Chief Scientist and four new scientists have been recruited. We have paid substantial attention in developing drugs from our indigenous and natural resources like native Indian medicinal plants. The successful implementation of the human genome project has raised new hopes of identifying genes responsible for complex human diseases at a

much faster rate than ever. Accordingly, a project has been initiated to identify risk alleles accountable for susceptibility to oral and cervical cancers.

During this period thirty one extramural projects from different funding agencies were executed by the scientists of CSIR-IICB, which includes one from Wellcome Trust, London. Eleven new projects have been sanctioned. Based on the expertise of our scientists, CSIR-IICB was assigned with nineteen Planned Projects in the Twelfth Five Year Plan of which five are Nodal Network Projects others Partner Network Projects. The progresses of these projects have been highly appreciated by the Research Council. These projects networked with other CSIR labs, will exploit and project the high potential of CSIR-IICB scientists.

We celebrated our 59th Foundation Day on April 10, 2015. Prof. Siddhartha Roy, Dean of Studies, Bose Institute, Kolkata and former Director, CSIR-IICB was the Chief Guest. Prof. Peter Walden, Department of Dermatology, Charité', Humboldt University, Berlin, Germany was present as Special Guest at the occasion. Prof. C. P. Thakur, Chairman, Balaji Utthan Sansthan, Kala-azar Research Centre, Patna and Hon. member of the parliament (Rajyasabha) and also former Cabinet Minister, Govt. of India delivered the 27th J. C. Ray Memorial Lecture. Prof. Subhash C. Basu, University of Notre Dame, Indiana, USA delivered the 1st B. K. Bachhawat Memorial Lecture.

The institute observed 73rd Foundation Day of CSIR on September 26, 2015 with Prof. Samir Bhattacharya, Emeritus Professor, Centre for Advance Studies in Zoology, School of Life Sciences, Visva-Bharti, Santiniketan and former



Director of CSIR-IICB as the Guest-in Chief. Dr. Amit Ghosh, Emeritus Scientist, National Institute of Cholera & Enteric Diseases, Kolkata delivered the Foundation Day lecture.

Sri Y. S. Chowdary, Hon'ble Union Minister of State for Science & Technology and Earth Sciences visited CSIR-IICB on December 29, 2015. In his day long stay he interacted with scientists, reviewed the recent technologies developed in the institute, appreciated the work of CSIR-IICB and gave suggestions and guidance to achieve further excellence and translate science into products of societal benefit.

CSIR-IICB has organized a training programme for 2015 batch of 18 IAS Officers Trainees on January 22, 2016 for Winter Study Tour under their 'Bharat Darshan' programme.

On February 08, 2016 the second campus, CSIR - IICB Translational Research Unit of Excellence (TRUE), at Salt Lake, Kolkata was inaugurated by Dr. Harsh Vardhan, Hon'ble Union Minister for Science and Technology and Earth Sciences and Vice President of CSIR. This unit, includes an Incubation Centre conceived as a productive platform for successful industry-institute cooperation for translating previously achieved and ongoing biomedical discoveries by CSIR-IICB scientists into biomedical deliverables with a view to contribute country's startup movement. Dr. Rabiranjan Chattopadhyay, Minister in Charge for Science & Technology, Biotechnology, Govt. of West Bengal was present in the occasion as a Distinguished Guest. The programme was followed by an Exhibition regarding Industry-Institute partnership where the products rolled out from CSIR-IICB were exhibited by Industries

and the most promising technologies in pipeline were exhibited by the scientists and students of the institute.

The institute signed a MoU on February 08, 2016 with National Research Development Corporation (NRDC) to promote entrepreneurship. The MoU was signed in the presence of Dr. Harsh Vardhan, Union Minister of Science & Technology and Earth Sciences and West Bengal Minister for Science, Technology & Biotechnology, Dr. Rabiranjan Chattopadhyay.

During this period CSIR-IICB organized and hosted several scientific and other programmes among which the followings are most important:

A one-day National Seminar on "Recent Advances in Biotechnology" on 17th April 2015; 3rd Annual Research Festival on 5th June 2015 and India-EMBO Partnership Symposium on 5th February, 2016.

During this period a number of scientists of our institute received many national honors and awards which includes Fellowship of The World Academy of Sciences (TWAS), Indian National Science Academy (FNA), National Academy of Sciences (FNASc), West Bengal Academy of Science and Technology (FAScT), NASI Scopus Young Scientist Award in Biological Sciences, Innovators Award by FICCI, Sir J. C. Bose fellowship, National Women Bio Scientist Award, Swarna Jayanti Fellowship and many others.

A large number of scientists and technologists of national and international repute visited our institute, delivered lectures and held discussions with different research groups during this period. Notable visitors were Prof. Brett Tyler from Oregon State University, USA.; Prof. Peter



Walden, University of Berlin, Germany; Prof. Bruce P. Lanphear of Simon Fraser University, Vancouver, Canada; Prof. Florian Hollfelder, University of Cambridge, UK; Dr. Rajarshi Choudhury, University of North Carolina, USA.; Dr. Christophe Len, UTC, France; Dr. Dipankar Bhandari, Max Planck Institute for Developmental Biology, Tübingen, Germany; Prof. V. S Parmar, University of Massachusetts, USA; Dr. Debashis Mitra, National Centre for Cell Science, Pune; Prof. Dieter Bromme, Dept. of Biochemistry and Molecular Biology, Vancouver, Canada; Dr. Andrew Peterson, Genentech, California; Dr. Angshumoy Roy from Baylor College of Medicine, Texas, USA and Dr. Sanjoy Samanta of University of Massachusetts Medical School, Worcester, USA. More than eighty six students from different Universities and Institutes of India participated in summer training and other training programmes at CSIR-IICB. A large number of Scientists of CSIR-IICB were involved in teaching and training programmes of NIPER and neighboring universities and institutes.

In this period Scientists published research works mostly in reputed international journals and the notable among them are in Nature Communications, EMBO Reports, Angewandte Chemie, Chemical Communications, Journal of Biological Chemistry, Scientific Reports. A steady number of quality publications in journals of high impact factors are the hallmark of the Institute's progress in research. In 2015 the total numbers of publications were 203. I feel proud that the average impact factor of research publications was 3.52 during this year and CSIR-IICB is ranked fifth in the Nature Index list among

Indian Institutes in Life Sciences category.

CSIR-IICB filed three international patents related to bioactive formulations to combat neurodegenerative disease, kala-azar and biomarker for leishmaniasis. Nine patents have been granted among which eight are in abroad.

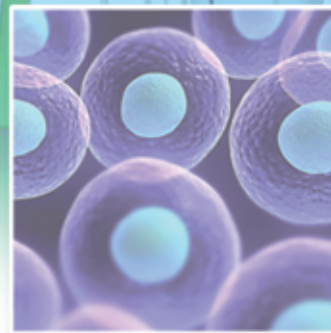
CSIR-IICB has always remained as a centre of choice for promising researchers with ambition to work in biological and chemical fields. This year the institute has attracted a large number of bright, young research fellows and research associates from all over the country in the different fields of chemical and biological sciences for engaging in cutting edge research. During 2015-16 around 290 Research fellows and associates worked in doctoral & post-doctoral programs. During this period five foreign guests and students, one foreign collaborator also worked or received training in the institute. We have commissioned a number of high end equipments like a high-resolution mass spectrometry analyzer, Orbitrap to further improve the quality of our research. We have a modern Animal House which includes mice, rat, hamster, guinea pig and rabbit with facility to breed. The aadhaar enabled biometric attendance system (AEBAS) has been introduced and it is functioning well.

I extend my gratitude to all the staff members of our Institute and students for their sincere activities 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 new heights in the coming days.

Dr. Samit Chattopadhyay

CSIR-IICB, Kolkata

Cell Biology and Physiology Division



Dr. K.P. Mohanakumar, Dr. Sumantra Das (Head), Dr. Syed N. Kabir, Dr. Arun Bandyopadhyay, Dr. Sib Sankar Roy, Dr. Sandhya R. Dungdung, Dr. Tushar Chakraborty, Dr. Subhas C. Biswas, Dr. Rupasri Ain and Dr. Partha Chakrabarti

The Division of Cell Biology and Physiology comprises an interactive group of eight independent laboratories. The scientists of this division are dedicated to understanding the complex mechanisms governing cell function in the context of tissues, organs, and whole organisms so as to decipher the molecular and cellular mechanisms underlying the pathophysiology of human diseases. Mechanistic studies are being undertaken to understand the various pathophysiology of disease states employing cellular and animal models. Neurodegenerative diseases, cardiac hypertrophy, obesity, diabetes, drug addiction, uteroovarian dysfunction, ovarian development, developmental neurobiology, placental morphogenesis, sperm motility are the major areas of interest for the group. Another hallmark of the division is its culture of collaboration, both at the intra- as well as at the inter-institutional levels. Many of the members of the division actively participate in postgraduate teaching at various Universities in addition to mentoring Ph.D. students and summer trainees. 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 nature of research carried out in the individual laboratories of the division is detailed here.

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Studies on the signal transduction pathways underlying DHA induced differentiation of astroglial cells

Participants

Tuhin, Subhra Banerjee, Moitreyi Das

Tecnician : P. C. Deuri

Background

Role of omega-3 polyunsaturated fatty acid, docosahexaenoic acid (DHA) on neuronal development

Evolution of the high order brain function in humans is being increasingly attributed to the intake of poly unsaturated fatty acids (PUFAs) of which the omega-3 polyunsaturated fatty acid, docosahexaenoic acid (DHA) has special significance. DHA is not only an essential prerequisite in every steps of neuronal development but has also been shown to promote astrocyte differentiation in our earlier studies.

Genetic epidemiology of addiction

As an ongoing collaborative projects with a psychiatric clinic, Baulmon, Kolkata as well as with Chittaranjan National Medical College, Kolkata, genetic epidemiological studies on opioid addiction are being carried out to develop anti-addiction compounds.

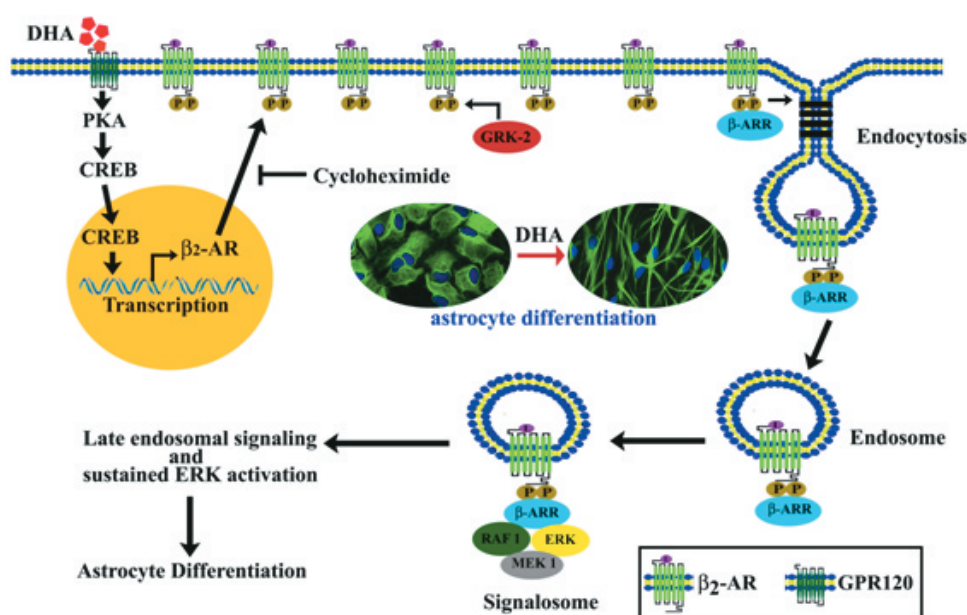
Development of potent morphine substitute

Morphine has been in use since the days of the ancient Sumerians (2100 BC) and is still the drug of choice, even today, for the treatment of chronic pain. However, there is a concerted effort, worldwide, to develop a suitable substitute of morphine, which unlike morphine, would be devoid of tolerance and dependence.

Work Achieved

Role of omega-3 polyunsaturated fatty acid, docosahexaenoic acid (DHA) on neuronal development.

We have explored the signaling mechanism underlying the astrocyte maturation process induced by DHA. It was observed that a sustained activation of extracellular signal-regulated kinase (ERK), after DHA treatment was critical for astrocytes differentiation. Such a activation was sensitive to different endocytic inhibitors, suggesting that this ERK activation was purely endosomal. The β_2 -Adrenergic receptor antagonist, ICI-118,551 selectively inhibited DHA-induced differentiation process, indicating a downstream involvement of β_2 -AR in the differentiation process.



DHA also caused an immediate induction of PKA activity followed by activation of the downstream cAMP response element binding protein (CREB). Taken together, the observations suggest that DHA upregulate β_2 -AR in astrocytes, which undergo endocytosis and initiate signals for sustained endosomal ERK activation that finally drive the differentiation process.

Genetic epidemiology of addiction

We wanted to identify the possible association of specific single nucleotide polymorphisms (SNP) of candidate genes in addiction using PCR-based RFLP as well as DNA sequencing analysis. It is well known that drugs of abuse cause elevated levels of brain-derived neurotrophic factor (BDNF), specifically in the reward centres of the brain. A study is continuing, to identify the SNPs in the BDNF gene which could be risk factors in heroin and alcohol addiction using DNA of blood samples from cases and controls.

Development of potent morphine substitute

As a part of a collaborative effort with the Indian Association for the Cultivation of Science, Kolkata, we had previously reported that an isoquinuclidine derivative of Benzofuran, was a potent antinociceptive agents for pain relief, comparable with morphine. An Indian Patent has also been

applied for (no. 946/KOL/2014 dated 16-09-2014). We further tested the compound for tolerance and physical dependence. Unlike in mice, chronically treated with morphine, animals treated chronically with the drug showed no signs of abstinence symptoms like stereotyped jumping or body weight lost, when subjected to naloxone precipitated withdrawal. There was negligible tolerance of the drug towards developing analgesia, as analysed in the hot plate test.during astrocytes differentiation. DHA interact with GPR120 leading to activation of PKA and downstream CREB. CREB, in turn, cause transcriptional activation of β_2 -AR. Increased β_2 -AR in the membrane then undergo endocytosis causing sustained ERK activation through endosomal signaling, thereby promoting differentiation.

PUBLICATIONS

Gharami K., Das M. and Das S. (2015) Essential role of docosahexaenoic acid towards development of a smarter brain *Neurochem Int* **89**, 51-62.

Das, M., Ghosh, M., and Das, S. (2015) Thyroid Hormone-Induced Differentiation of Astrocytes is Associated with Transcriptional Upregulation of β -arrestin-1 and β -adrenergic Receptor-Mediated Endosomal Signaling. *Molec. Neurobiol.* (Epub ahead of Print)

Banerjee ,T.S., Hazra, A., Mondal, N.B., and Das, S. (2015) The quinoline compound, S4 effectively antagonizes alcohol intake in mice: Possible association with the histone H3 modifications. *Neurochem. Internat* **87**, 117-127

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Molecular cues to the anti-implantation effect of nano-puerarin in rats

Participants

SRF: Ghungroo Saraswat, Kalyani Mondal

Background

Unintended pregnancy and population explosion are significant global problem with grave implications for the future. With the long term objective to develop a non-steroidal emergency contraceptive (EC) formulation, we have earlier demonstrated that puerarin intercepts implantation in rats, albeit at unacceptably higher doses. We, therefore, wanted to improve upon the efficacy of puerarin in terms of all parameters related to its development as potent contraceptive candidate.

Work Achieved

We developed poly lactic-co-glycolic acid-encapsulated nano-puerarin (PN) and mapped the molecular pathway underlying its anti-implantation effects. PN exerted a dose-dependent anti-implantation effect. As marked by attenuated expression of stromal cell desmin, alkaline phosphatase, insulin-like growth factor binding protein 1, and decidual prolactin-related protein, the anti-implantation effect of PN seemed secondary to compromised decidualization. Using in vivo (pregnant and pseudopregnant rats) and in vitro (endometrial stromal cell (ESC) culture) treatment models, we document that PN enforced inhibition of uterine expression of Hbegf and Hoxa10 and their downstream signaling molecules, Cyclin D3/CDK4. PN also efficiently ablated the Ihh-Coup-Tf2-Bmp2 signaling pathway and invited the loss of uterine potential for decidualization. There was a dose-dependent up-regulation of RHOA and its effector protein kinase, ROCK1, leading to the promotion of MLC phosphorylation and actin-myosin interaction. PN also down-regulated Hbegf-EGFR mediated stromal cell activation of ERK and expression of its target genes FOS and STAT3 and expression of MMP9. These effects acting together stabilized the stroma and inhibited the stromal cell migration. This study also suggests that PN-mediated anti-migratory



effects could be reversed in the presence of EGFR activator. Central to this array of events was the adversely altered endometrial expression of oestrogen receptor (ER) subtypes and repression of progesterone receptor (PR) that indulged endless proliferation of luminal epithelia and distorted the precisely choreographed stroma–epithelia crosstalk

that effectively hinders the implantation process to block the establishment of pregnancy. PN, therefore, is envisioned as a likely candidate molecule that deserves further exploration for the development of non-steroidal EC formulation. The following are some of the figures representing salient observations.

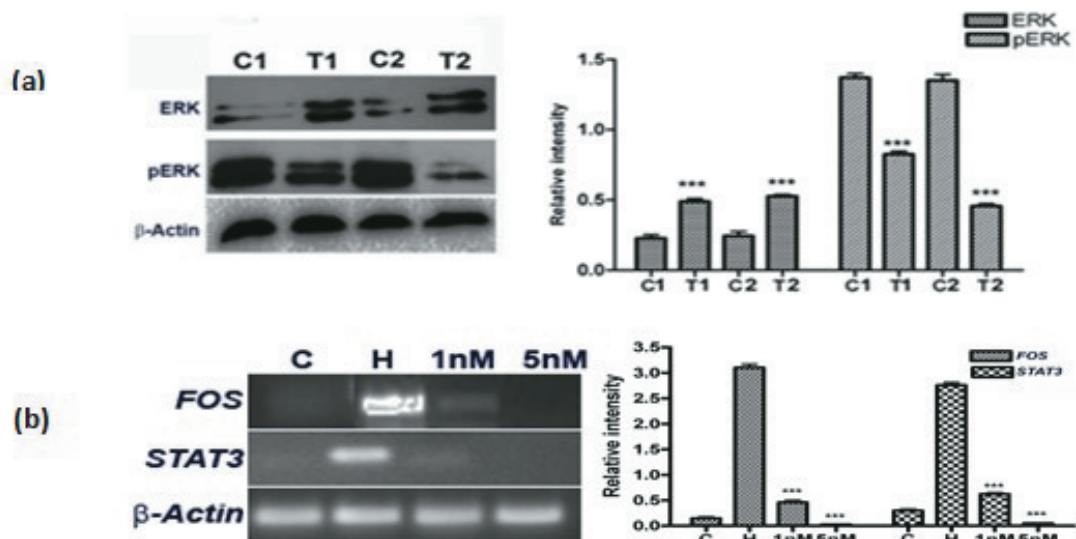


Fig. 1. PN attenuates the stromal cell MAPK pathway. (a) Western blot analysis data exhibit increased expression of ERK^{1/2} and attenuated expression of pERK^{1/2} in the PN-treated group on D5 and D6, as compared to the corresponding control pregnant rat uteri. (b) The expression of ERK^{1/2} target genes, FOS and STAT3, are significantly down-regulated by the treatment with PN during in vitro decidualization. C1, C2: control pregnant rats on D5 and D6, respectively; T1, T2: PN-treated pregnant rats on D5 and D6, respectively. C: Control; H: Hormone (MPA, E2 & db-cAMP)

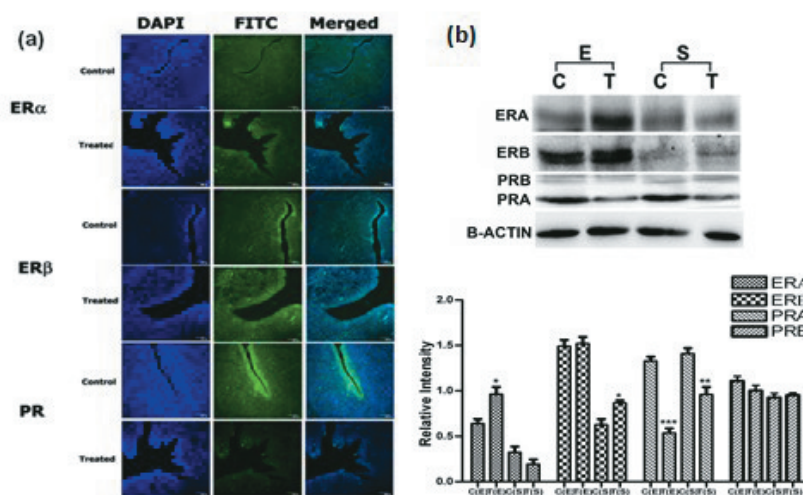


Fig. 2. Effect of PN on the uterine expression of ER and PR. The overlaid immunofluorescence images

(Fig. 2a) viewed under confocal microscope (x 200) represent D5 control and PN treated rat uterus analysed for the expression of ER, ERβ and PR. Western blot analysis

(Fig.2b) demonstrates increased epithelial expression of ERα and stromal expression of ERβ in the PN-treated D5 pregnant rat uterus. Attenuated PR expression is observed both in the epithelia as well as stroma C (E): control rat luminal epithelia, T (E): PN-treated rat luminal epithelia, C (S): control rat stromal cells, T(S): PN-treated rat stromal cell.

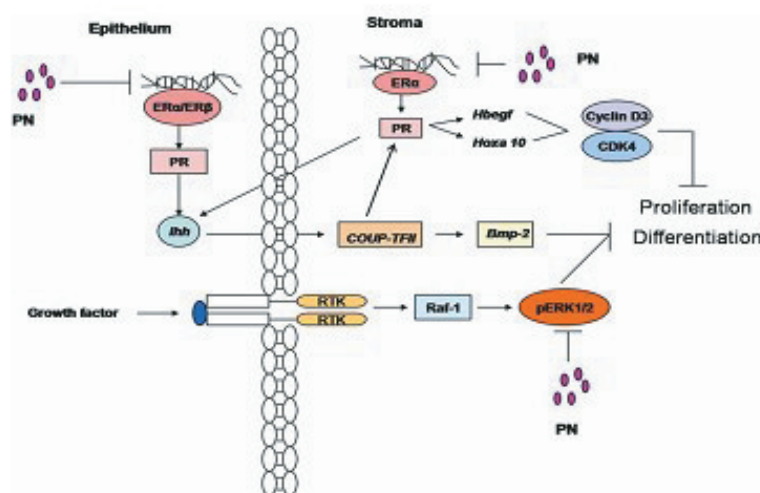


Fig. 3. Working model of PN in mediating anti-implantation effect. PN alters the epithelial and stromal cell expression of ER subtypes to attenuate endometrial PR expression. Withdrawal of PR activity, in turn, withholds the P4-mediated Ihh-Coup-Tf2-Bmp2 signaling and thereby provokes continued epithelial proliferation to block embryo attachment at one end, and suppresses the Bmp2 regulated stromal cell differentiation on the other. PN may additionally inhibit the growth factor-mediated activation of the MAPK pathway that promotes stromal cell proliferation, differentiation and migration.

PUBLICATIONS

Saraswat. G., Guha, R., Mondalm K., Saha P, Banerjee, S., Chakraborty, P., Konar, A., and Kabir. S. N. (2016) Molecular cues to the anti-implantation effect of nano-puerarin in rats. *Reproduction* **151**, 693-707

International: 3

INVITED TALKS

α-Dihydroxychalcone glycoside: An antioxidant with anti-inflammatory potential that acts dually via MAPK-NFκB and Nrf-2-Keap-1 pathways National Institute of Occupational Health, 19 February 2016. Ahmedabad.

Molecular cues to the anti-implantation effect of nano-puerarin in rats. University Colleges of Science and Technology, University of Calcutta. 20 December 2015. Kolkata.

Puerarin attenuates progesterone regulation of uterine COUP-TFII signaling Pathway and inhibits embryo implantation in rats. North East Hill University, Shillong, 21 November 2015, Meghalaya.

Roadmap to anti-implantation effect of nano-puerarin, a selective estrogen receptor modulator. University of Rajasthan, 12 September 2015. Jaipur

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Understanding the role of annexin A6 cardiac hypertrophy

Participants

SRF: Priyam Banerjee, Tanima Banerjee, Dipak Kar, Somaditya Mukherjee, Dibyanti Mukherjee, Sumanta Narayan Nandi, Apabrita Ayan Das

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Background

Pathological cardiac hypertrophy is a major risk factor associated with heart failure, a state concomitant with increased cell death. However, the mechanism governing progression of hypertrophy to apoptosis at the single-cell level remains elusive.

Aims and Objectives

To understand the role of annexin A6 (Anxa6), a Ca^{2+} dependent phospholipid binding protein in the transition of chronic hypertrophied cardiomyocytes to apoptosis.

Work Achieved

Treatment of the H9c2 cardiomyocytes with hypertrophic agonists up-regulates and re-localizes Anxa6 with increased cytosolic punctate appearance. Live cell imaging revealed that chronic exposure to hypertrophic agonists like phenylephrine (PE) compromises the mitochondrial membrane potential ($\Delta\Psi_m$) and morphological dynamics. Such chronic hypertrophic induction also activated the caspases 9, 3 and induced cleavage of the poly-(ADP-ribose) polymerase 1 (Parp1), which are the typical downstream events in the mitochondrial pathways of apoptosis. An increased rate of apoptosis was evident in the hypertrophied cardiomyocytes after 48-72 hours of treatment with the hypertrophic agonists. Anxa6 was progressively associated with the mitochondrial-fraction under chronic hypertrophic stimulation, and Anxa6 knockdown (KD) severely abrogated mitochondrial network and dynamics. Ectopically expressed Anxa6 protected the mitochondrial morphology and dynamics under PE treatment, but also increased the cellular susceptibility to apoptosis (**Fig 1**). Biochemical analysis showed that Anxa6 interacts with Parp1 and its 89 kDa cleaved product in a Ca^{2+} -dependent manner through the N-terminal residues (1-28). Furthermore, expression of Anxa6S13E, a mutant dominant negative with



respect to Parp1 binding, served as an enhancer of mitochondrial dynamics, even under chronic PE treatment. Chemical inhibition of Parp1 activity released the cellular vulnerability to apoptosis in Anxa6 expressing stable cell lines, thereby shifting the equilibrium away from cell death. Together, the present study depicts a dual regulatory function of Anxa6 that is crucial for balancing hypertrophy with apoptosis in cardiomyocytes.

Future Research Plans

In vivo evaluation of Annexin's role in cardiac hypertrophy

PUBLICATIONS

Banerjee, T. Kar, D. Radha Krishna, P. Prabhakar, S. Nomula, R. Mallula, V.S. Ravindranath, H. Sridhar, G. Adepu, R. Srikanth, G. Mabalirajan, U. Ghosh, B. Jaisankar, P. Johri, R. Chakraborty, D. Mishra, V. Chhabra, J. K. Shukla, M. Paul, B.N. Bandyopadhyay, S. Roy, S. Sharma, G.V. M. and Bandyopadhyay, A. (2015) A novel triazine-aryl-bis-indole derivative inhibits both phosphodiesterase IV and expression of cell adhesion molecules. *RSC Adv* **5**,70271-70281.

Banerjee, P.Chander, V.and Bandyopadhyay, A. (2015) Balancing functions of annexin A6 maintain equilibrium between hypertrophy and apoptosis in cardiomyocytes. *Cell Death Dis* **6**, e1873

PATENTS FILED / SEALED

Names: ARUN BANDYOPADHYAY, SIDDHARTHA ROY AND SANTU BANDYOPADHYAY

Patent Title: TRIAZINE-ARYL-BIS-INDOLES AND PROCESS FOR PREPARATION THEREOF

Country: USA, China, Europe

Patent No.: USA9085559, China102666529, Europe B2417129

Date filed / granted: USA 21/07/2015, 20/01.2016China Europe 23/03/2016

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BALARAM GHOSH, MABALIRAJAN ULAGANATHAN, SAKSHI BALWANI (CSIR-IGIB)

BHOLANATH PAUL, ASHOK KUMAR SAXENA (CSIR-IITR)

INVITED TALKS

Proteomic analysis of human plasma in Rheumatic heart disease. VIT, 3-6 December 2015. Vellore, India.

Annexin A6 maintains equilibrium between hypertrophy and apoptosis in cardiomyocytes; NEHU, 20 November 2015. Shillong, India.

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Understanding the molecular mechanism and pathophysiology of two metabolic disorders: ovarian cancer and insulin resistance

Participants

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Bose Institute, Kolkata

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University of Calcutta, Kolkata

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IACS, Kolkata

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Structural Biology and Bioinformatics Division

Dr. S. N. Kabir
Cell Biology and Physiology Division

Background

Due to present day life style and other reasons, metabolic disorders, including cancer is increasing significantly. In most of the cases inadequate therapy aggravate the problem manifold. Therefore, understanding mechanisms are necessary to combat such disorders. Early diagnosis issues and chemoresistance in cancer are other problems that need to be addressed. Hence, our approach was to explore the mechanism of initiation and progression of such diseases in suitable model. Further, we would like to identify the the possible drug target and early diagnostic markers.

Aims and Objectives

- To unveil the growth factor-mediated signalling events to induce EMT/Invasion of ovarian cancer.
- To decipher the signalling cross-talks during cancer progression and induction of stemness/chemoresistance in ovarian cancer
- Understanding the regulation and dysregulation of metabolism in cancer cell.
- To identify factors associated with and the associated mechanism in obesity-induced insulin resistance

Work Achieved

To unveil the growth factor-mediated signalling events to induce EMT/Invasion of ovarian cancer: Rapid aggressiveness, high metastatic potential and lack of early diagnosis dictate the increased mortality rate in ovarian cancer (OC) patients. Thus, identifying the molecular mechanisms underlying aggressiveness of OC is of great importance. We have earlier shown the function of different growth factor mediated signaling and their cross-talks in the progression of OC. Further, role of homeodomain transcription factor has been studied in this regard. Our group has identified the possible involvement of PITX2 homeodomain-



transcription factor in promoting invasiveness of OC cells through the regulation of TGF- β and activin-A signaling pathways (Basu et. al. Mol Cancer-2015, **Fig. 1**). Presently we investigate on growth factor-mediated differential splicing of specific growth-factor receptor genes that regulates EMT (Bhattacharya et. al. MS under preparation).

To decipher the signalling cross-talks during cancer progression and induction of stemness /chemoresistance in ovarian cancer: Positive and negative feedback loop that exists between different signaling cascades in cancer cells determines the fate of tumor progression. We are investigating the critical cross-regulation existing between the TGF- β and Wnt signalling activation, which were found to synergistically reduce the EMT in OC cells. We are also exploring the effect of growth-factors towards the critical regulation of stemness potential in OC (Mitra et. al. MS under preparation).

Understanding the regulation and dysregulation of metabolism in cancer cell: Metabolic cues and different cell-types present in the tumor microenvironment (TME) play a critical role in determining the invasive fate of cancer cells. Tumor cells undergo metabolic reprogramming in response to their surrounding microenvironment gaining survival advantage. Our group is currently focussing on the status of transcriptomic and bioenergetic reprogramming in cancer cells that specifies their invasive fate, in response to an oncometabolite highly enriched in the ascites and serum of OC patients (Ray et. al. under review). Our group has recently identified a plant-derived lectin could specifically induce apoptosis specifically in ovarian cancer cells (Roy Chowdhury et. al., MS communicated). We have currently identified the regulation of epigenetic modifiers towards metabolic changes associated with cancer progression (Ray et. al. MS under preparation).

To identify factors associated with and the associated mechanism in obesity-induced insulin

resistance: Enhanced oxidative stress associated with obesity often terminates into mitochondrial fission, restraining their respiratory efficiency. Reduction in the number of energy efficient mitochondrion generates metabolites like ceramides, which in consequence develops insulin resistance (IR). We explored the various causes/factors liable for obesity-induced mitochondrial dysfunctions widespread in insulin target tissues like adipose tissue and skeletal muscle. Our group has elucidated the role of differential expression of mitochondrial transporters (CPT1/2, Bhattacharjee et al, CPB-2015) in lieu of lipid-induced IR in skeletal muscles (**Fig. 2**). We have also been able to establish Thioredoxin Interacting Protein (TxNIP) to be critically associated with lipid-induced ROS generation and IR (Mandala et al, MS under review). Obesity is known risk factor for the people suffering from NAFLD and liver fibrosis and lack of early diagnosis aggravates this deadly disorder. We have identified retinol metabolism as one of the critical pathway significantly dysregulated during obesity (Das et al, MS under review). We identified genetic factors deregulating retinol metabolism leading to liver fibrosis which could serve as a future prognostic marker for hepatic steatosis.

Future Research Plans

In future, along with the ongoing mechanistic studies for the disease progression, we will focus on translational aspects as well.

Newly identified factors will be evaluated to make early diagnostic markers for OC and hepatic steatosis.

Further exploration of chemoresistance and stemness in OC will be performed and combination of different therapeutic alternatives will be evaluated to inhibit these events.

Oncometabolite-induced events in metabolic reprogramming in ovarian and colorectal cancer cells will be further evaluated.

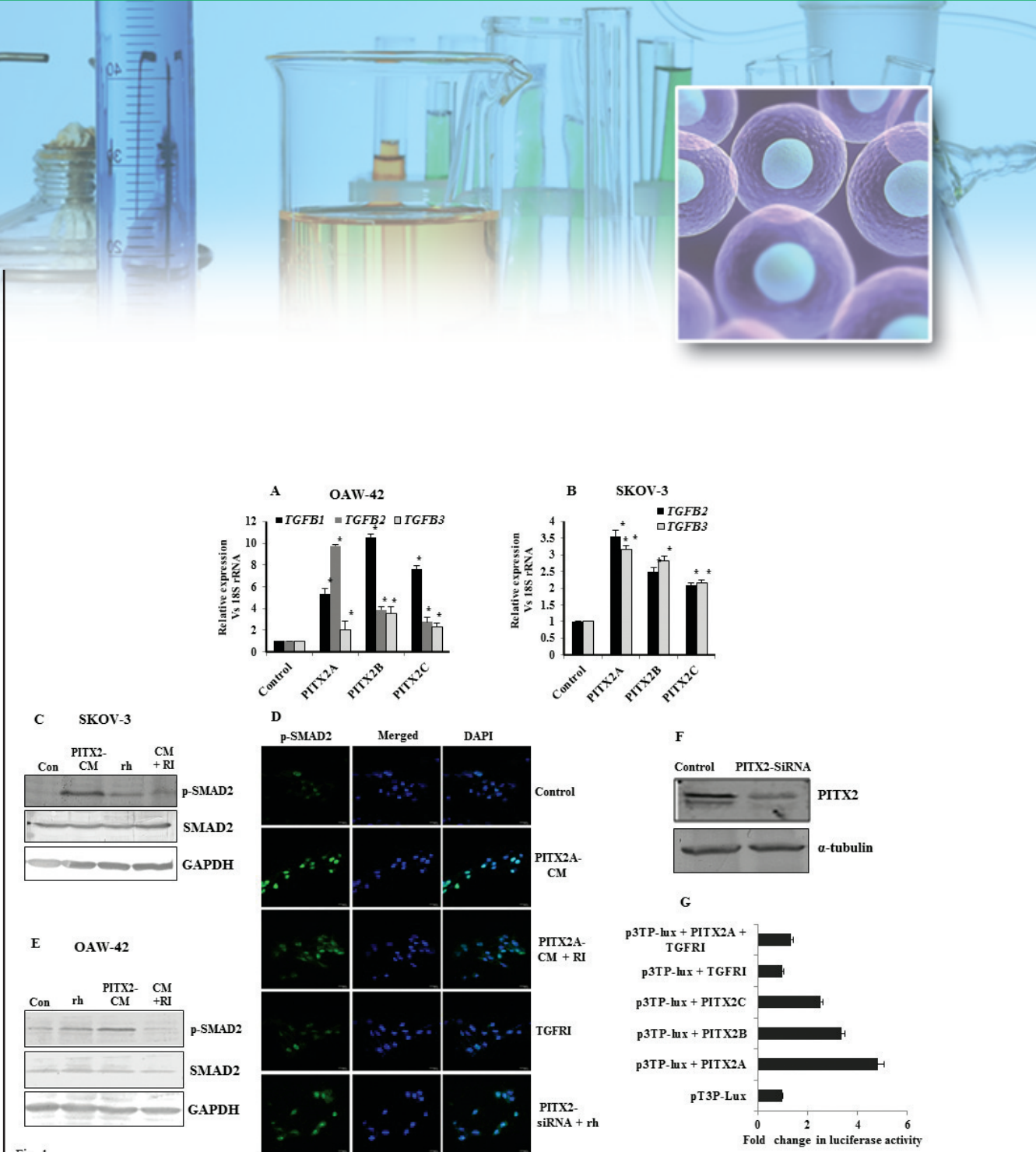


Fig. 1

Fig. 1: PITX2 induces TGF- β signalling pathway in ovarian cancer cells. (A-B) Q-PCR assay of TGF-B1/B2/B3 (for OAW-42 cells; A) and TGF-B2/B3 (for SKOV-3 cells; B) was done with specific primers with RNA isolated from PITX2-overexpressed respective cells. The comparative expression of respective genes is shown as relative 'fold' change (mean \pm S.E.M).

* represents $p < 0.05$. (C-D) The conditioned-medium (PITX2-CM) was collected after transient transfection with PITX2A. Freshly plated serum-starved SKOV-3 (C) and OAW-42 (D) cells were incubated for 2h with PITX2-CM alone or in combination with 20 ng/ml TGFRI (RI) followed by Western blot of the lysates with p-SMAD2 and SMAD2 antibodies. The lysate of the cell treated with rhTGF- β 1 (rh; for 30') was blotted with the respective antibodies. Here, GAPDH was used as loading

control. (E) Confocal imaging for p-SMAD2 was performed in SKOV-3 cells treated or transfected as mentioned, where the left panel shows the p-SMAD2 expression, DAPI-stained nuclei in the middle panel and the right panel shows their merged image. The images were taken at the same exposure time. Scale bar, 20 μ m. (F) Lysates were prepared from PITX2A-siRNA transfected OAW-42 cells for Western blot with PITX2-antibody. Here, α -tubulin was used as loading control. (G) OAW-42 cells were transfected with p3TP-Lux vector alone or along with expression constructs of PITX2 isoforms or pcDNA3 (empty vector) and treated with TGFRI for 16h for luciferase assay. The activities are shown as mean fold enhancement compared to the p3TP-construct without PITX2 expression after normalization with renilla luciferase activity.

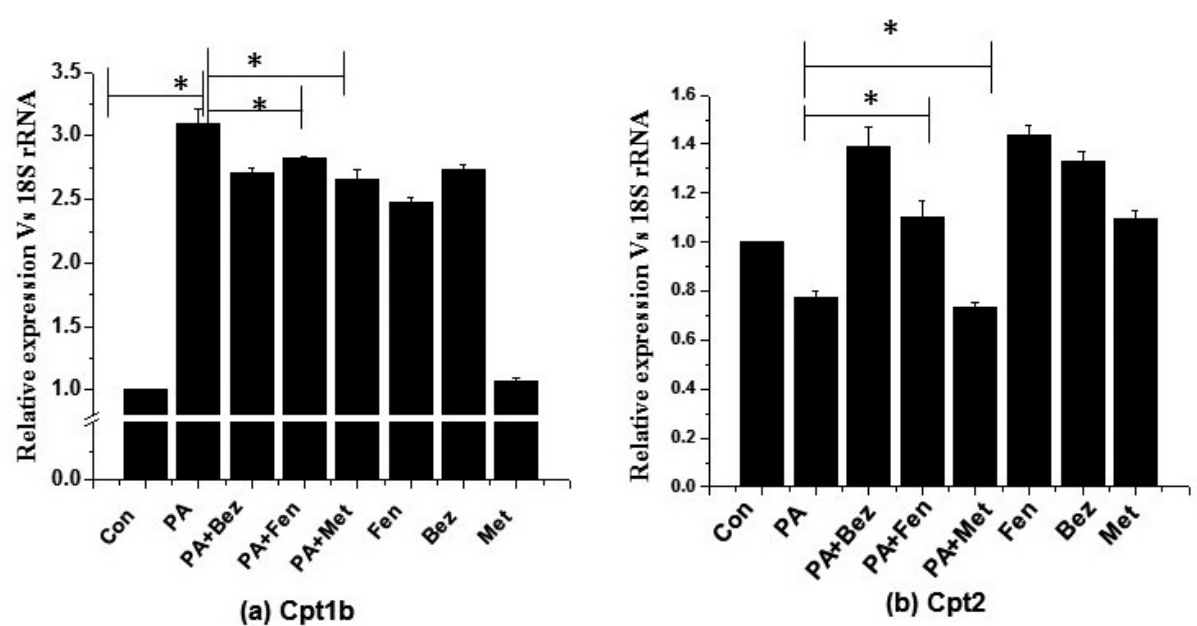


Fig. 2: Expression of CPT1b (a) and CPT2 (b) isoforms in myotubes in presence of different drugs. The myotubes were treated with PA and with/without drugs, like bezafibrate, fenofibrate and metformin (1mM). No drugs show significant inhibitory effect on PA-induced upregulation of CPT1b mRNA level. However, the CPT2 expression is induced upon fibrate and metformin treatment, which normalized the ratio of CPT isoforms in myotubes in presence of excess PA. Other drugs except metformin did not alter CPT2 expression. The statistical analysis is done as described in Methods. * represents ($p < 0.05$)



PUBLICATIONS

Basu, M., Bhattacharya, R., Ray, U., Mukhopadhyay, S., Chatterjee, U., and Roy, S. S. (2015) Invasion of ovarian cancer cells is induced by PITX2-mediated activation of TGF-beta and Activin-A. *Mol Cancer* **14**, 162

Naskar, A., Bera, S., Bhattacharya, R., Roy, S.S. and Jana S. (2015) Synthesis, characterization and cytotoxicity of polyethylene glycol coupled zinc oxide-chemically converted graphene nanocomposite on human OAW42 ovarian cancer cells. *Polymers for Advanced Technologies*, DOI: 10.1002/pat.3689

Bhattacharjee, S., Das, N., Mandala, A., Mukhopadhyay, S., and Roy, S. S. (2015) Fenofibrate Reverses Palmitate Induced Impairment in Glucose Uptake in Skeletal Muscle Cells by Preventing Cytosolic Ceramide Accumulation. *Cell Physiol Biochem* **37**, 1315-1328.

Roy Moulik, S., Pal, P., Majumder, S., Mallick, B., Gupta, S., Guha, P., Roy, S., and Mukherjee, D. (2016) Gonadotropin and sf-1 regulation of cyp19a1a gene and aromatase activity during oocyte development in the rohu, L. rohita. *Comp Biochem Physiol A Mol Integr Physiol* **196**, 1-10

AWARDS / HONOURS / MEMBERSHIPS

Memberships

Life Member, Indian Association of Cancer Research

Student Award

Rahul Bhattacharya

Best Poster Award, International conference on molecular signaling: recent trends in Biosciences, NEHU, Shillong, India, November 20-22, 2015.

Ashok Mandala

DP Burma Memorial Best Poster Award, Annual meeteing of Society of Biological Chemists India, held at Hyderabad, November 2015.

Ashok Mandala

Abstract title: Targeting thioredoxin interacting protein by novel dual PPAR α / γ agonist ameliorates lipid-induced insulin resistance. Oral and poster presentation, Federation of Asian and Oceanian Biochemists and Molecular Biologists (FAOBMB) travel fellowship to participate in Young Scientist Program(YSP), held in CCMB Hyderabad during 24-26 November 2015.

Shreya Roy Chowdhury

Abstract title: Lectin from *Sambucusnigra* induces apoptosis in ovarian cancer cells through mitochondrial dysfunction. Oral and poster presentation, Federation of Asian and Oceanian

Biochemists and Molecular Biologists (FAOBMB) travel fellowship to participate in Young scientist Program(YSP), held in CCMB Hyderabad during 24-26 November 2015.

CONFERENCES / WORKSHOPS

Number of abstracts

India: 6 International: 1

INVITED TALKS

Involvement of Homeodomain Transcription Factors in Progression of Cancer. National Symposium On Comparative Endocrinology & Reproductive Biology, Visva Bharati University, 1 -3 October 2015. Santiniketan, India,.

Free fatty acid induced insulin resistance and hepatic steatosis: possible role of mitochondrial transporters and defect in relinol metabolism. International conference on molecular signaling: recent trends in Biosciences, NEHU, 20 -22 November 2015. Shillong, India,.

Homeodomain' transcription factors and progression of cancer. 103rd Indian Science Congress, University of Mysore, 3-7 January 2016. Mysore, India.

Dr. Sandhya Rekha Dungdung



Cell-surface alteration of lectin and its receptor during epididymal maturation of caprine spermatozoa

Participants

SRF: Arpita Bhounik

RA: Dr. Sudipta Saha

Project Assistant: Prasanta Ghosh, Sandipan Mukherjee

Background

Maturing goat spermatozoa specifically at the distal-corpus epididymal stage show head-to-head autoagglutination when incubated *in vitro* in a modified Ringer's solution. The biochemical mechanism of autoagglutination event and its functional significance is not well understood. Sugar moieties on the sperm surface have been shown to undergo a variety of species-specific alterations during the epididymal sperm maturation as demonstrated with commercially available exogenous lectins. However, little is known about the levels of the endogenous lectin and their receptors on the outer surface of sperm undergoing maturation during epididymal transit.

Aims and Objectives

To delineate the biochemical basis of autoagglutination event and its physiological significance.

Work Achieved

A lectin-like molecule located on sperm surface specifically interacts with its receptor of the neighboring homologous cells to cause autoagglutination. Lectin is a Ca^{++} -dependent galactose-specific protein. Failure of the pre- and post-distal corpus sperm to show autoagglutination is due to lack of lectin-like molecule and its receptors, respectively. Maturing sperm at distal-corpus stage acquire lectin-like molecule followed by sharp disappearance of its receptor and this event is synchronously associated with the initiation of sperm forward motility that is essential for fertilization *in vivo*. Lectin and its receptor isolated from sperm plasma membrane showed high efficacy for blocking autoagglutination phenomenon. Lectin and its receptors undergo marked manipulation during the epididymal maturation process. The lectin like molecule, which is undetectable in sperm in the early part of the maturation, appears sharply on the sperm surface at the distal-corpus stage of sperm maturity. It is



of interest to note that the appearance of the lectin like molecule on the sperm surface has a temporal correlation with the maturation-dependent initiation of flagellar motility in spermatozoa. On the other hand, the lectin receptor as demonstrated with exogenous lectins: RCA₁ and RCA₂, is abundant in sperm in the initial phase of their epididymal maturation and it decreases markedly as the cells acquire maturity. This view has been confirmed and extended by studying with the isolated sperm lectin. The immature sperm receptor level is rather high up to the distal-corpus stage and then it decreases sharply at the terminal phase of sperm transit (distal-corpus to cauda) when the cells acquire flagellar motility. The results demonstrate that both the galactose-specific lectin and its receptors are localized on the head part of distal-corpus sperm. The observed sperm autoagglutination event can thus be attributed to the interaction of lectin of a cell with the receptors of the neighboring cells and vice versa. Failure of pre- and post-distal corpus sperm to show any appreciable autoagglutination property is due to lack of lectin and its receptors, respectively on the sperm head surface. The present study demonstrates for the first time, the epididymal maturational profile of a sperm external surface lectin like molecule (galactose-specific) and its endogenous receptors on the same cell population. The terminal stage of sperm maturation i. e. induction of flagellar motility is associated with a sharp disappearance/inactivation of the lectin receptor and appearance of the lectin (**Fig. 1**). It appears from our results that the lectin like molecule acquired by the mature sperm may induce sperm motility whereas the receptor may suppresses the motility-mediating potential of the lectin.

Future Research Plans

Purification and functional characterization of lectin and its receptor from sperm plasma membrane

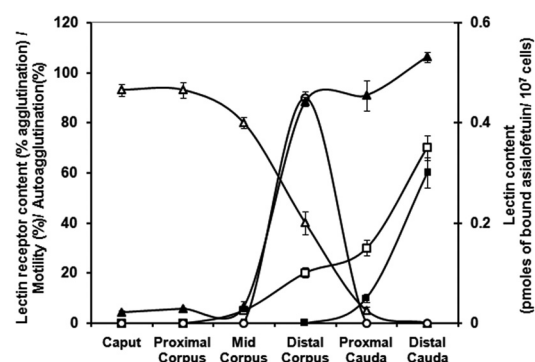


Fig. 1: Correlation of sperm levels of lectin (▲) and its receptor (△) with autoagglutination phenomena (□) and induction of total motility (■) and forward motility (■) in the maturing goat epididymal spermatozoa. The sperm level of the lectin (▲), in maturing spermatozoa were estimated by incubating the cells with radiolabelled asialofetuin D-galactose-specific lectin receptor levels (△) of the maturing sperm have been expressed as percentage of sperm agglutination caused by the isolated sperm surface lectin. Maturing sperm total motility (□) and forward motility (■) were estimated by a microscopic method.

PUBLICATIONS

Book Chapters / Invited Reviews

Gopal Chander Majumder, Sudipta Saha, Kaushik Das, Arpita Bhoomik, Debdas Bhattacharyya and sandhya Rekha Dungdung (2015) Role of Sperm Surface Molecules in Motility Regulation. Review in Book: Mammalian Endocrinology and Male Reproductive Biology, CRC Press, Taylor & Francis Asia Pacific, New Delhi, India, (Ed. Prof. Shiokumar Singh), ISBN 978-1-4987-2735-8, pp. 197-244.

Sandhya Rekha Dungdung, Arpita Bhoomik, Sudipta Saha, Prasanta Ghosh, Kaushik Das, Sandipan Mukherjee (2016) Sperm Motility Regulatory Proteins: A Tool to Enhance Sperm Quality. Review in Book: Insights from Animal Reproduction, InTech, Rijeka, Croatia (Ed. Dr. Rita Payan). ISBN: 978-953-51-4629-2, pp 161-177.

CONFERENCES / WORKSHOPS

Number of abstract India: 2

INVITED TALKS

Sperm motility-associated proteins in male and female reproductive fluids. 103rd Session of Indian Science Congress, Mysuru University, 3 -7 January 2016. Mysuru, India

Dr. Tushar Chakraborty

Tushar@iicb.res.in



Biology of chronic arsenic toxicity

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Debendranath Guha Mazumder

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Background

Arsenic contaminated groundwater in West Bengal is being used for drinking and irrigation for a long time. The chronic exposure to this poison was detected in 70s from pathological symptoms and ailments. The symptoms are many, and includes malignancies. The underlying molecular basis of arsenicism however remains still elusive.

Aims and Objectives

The present work tries to understand the molecular changes of chronic arsenic toxicity in and around chromosomes. The focus is on possible epigenetic changes via DNA methylation. This will help us to assess the long term impact of arsenic exposure and risks. This will help us to assess threat to the future generation and devise appropriate strategies.

Work Achieved

Association of Cytochrome P450 and GST MITI polymorphism and arsenical skin lesions in a population exposed to arsenic through food chain in West Bengal, has been mapped. We found strong correlation between Arsenic Induced Skin lesions and Genetic Polymorphism at specific DNA methylation loci.

Future Research Plans

Further characterization of the pathological impacts of Arsenic exposure on enzymes responsible for activating most environmental pre-carcinogens, and enzymes capable of detoxifying the electrophilic carcinogens will be undertaken.

INVITED TALKS

Environment at Crossroads: The Planetary Limits. Annual Meeting of SINP Alumni Association SINP, Bidhan Nagar. 1 March 2016, Kolkata

World History of Agricultural Revolutions. Centre for Pollination Studies and Indo-Norway Collaborative Project in Agro Ecology, Calcutta University, Ballyganj Science College, 12 February 2016. Kolkata, India

Agromicrobiome and Agricultural Sustainability. National Symposium entitled "Microvision" sponsored by DST at the Orissa University of Agricultural Technology, Bhubaneswar, 25 December 2015, Orissa, India

Dr. Subhas Ch. Biswas



The regulation of PUMA by JNK/c-Jun pathway in Alzheimer's disease

Participants

JRF: Subhalakshmi Guha, Pallabi Bhattacharyya, Akash Saha, Anoy Das

SRF: Rumana Akhter, Priyanka Sanphui, Pampa Saha, Suraiya Saleem

Project Assistant: Hrishita Das

Collaborator(s)

Name of collaborator outside CSIR-IICB

Lloyd A Greene

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Organic and Medicinal Chemistry Division

Dr. Surajit Ghosh

Organic and Medicinal Chemistry Division

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Organic and Medicinal Chemistry Division

Background

Severe neuronal loss in selective areas of brain underlies the pathology of Alzheimer's disease (AD). A substantial body of research in last three decades suggesting that, A β is toxic to neurons and it causes neuron death. But unfortunately the underlying mechanism of A β mediated neuron death is elusive. In this context, activation of the c-Jun N-terminal kinase (JNK) pathway and induction of the AP-1 transcription factor c-Jun has previously been reported in AD. However, downstream targets of JNK/c-Jun in A β -induced neuron death are yet to be identified.

Aims and Objectives

To identify the downstream target(s) of JNK/c-Jun in A β induced neuron death.

To check the specific contribution of these target proteins in neuron death evoked by A β .

Work Achieved

We found that two important pro-apoptotic proteins, Bim (Bcl-2 interacting mediator of cell death) and Puma (p53 up-regulated modulator of apoptosis) are upregulated and are the downstream targets of c-Jun in A β -treated neurons. JNK/c-Jun pathway has been found to be activated in cultures of cortical neurons following treatment with oligomeric A β and in AD transgenic mice. We show that inhibition of this pathway by selective inhibitor blocks induction of Puma evoked by A β . We also observed the functional co-operativity between JNK and p53 pathways in regulating Puma expression in neurons treated with A β . Moreover we identified a novel AP1-binding site on rat puma gene which is necessary for direct binding of c-Jun with Puma promoter. Finally, we prove that Bim and Puma are essential for A β mediated neuron death by knocking down these two genes through siRNA mediated gene delivery. We also found, knocking down of c-Jun by siRNA provides significant protection from A β toxicity and that

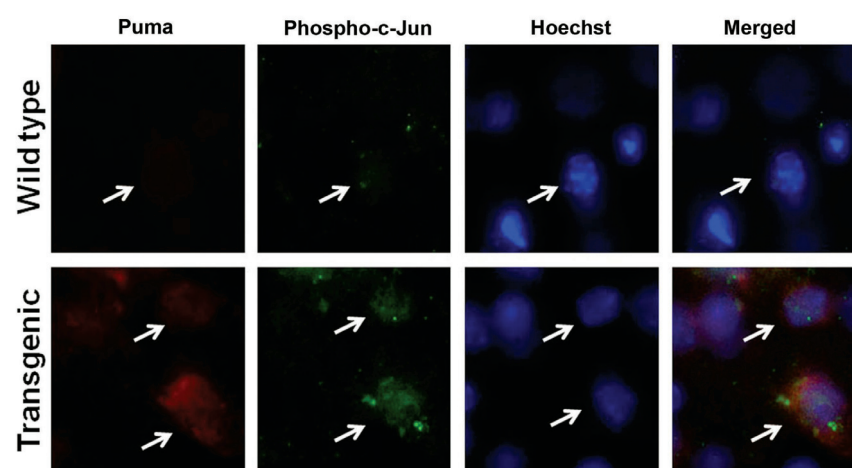


Fig. 1: Phospho-c-Jun is elevated and co-stained with Puma in AD transgenic mice brain. The brain sections of A β PPswe-PS1de9 transgenic mice were co-immunostained with phospho-c-Jun and PUMA antibodies following the protocol described in experimental procedure. Hoechst was used to stain nuclei. Representative images from four sections from three transgenic animals and two wild type animals with similar results are shown here. Images were taken for each case using inverted fluorescence microscope at x63 objective and camera set to the same exposure. Arrows indicate cells co stained for phospho-c-Jun and PUMA.

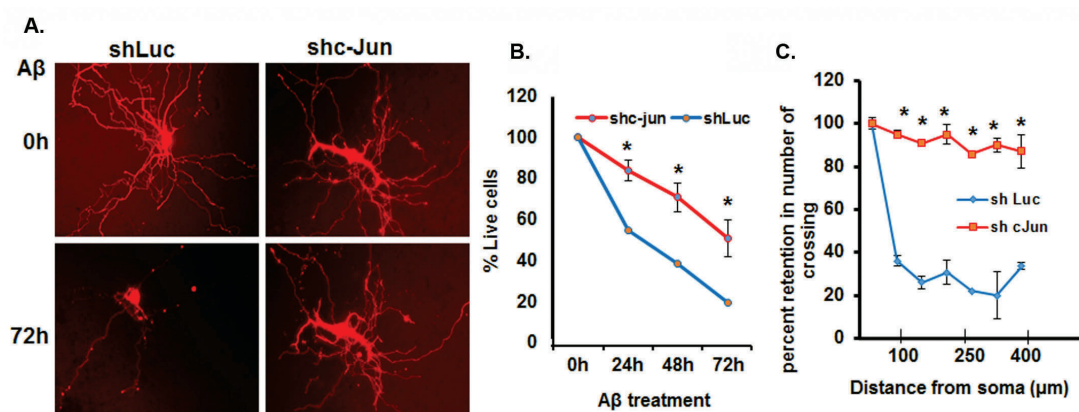


Fig. 2: Downregulation of c-Jun by shRNA protects neurons from death evoked by A β . **A.** Primary cultured rat hippocampal neurons (21 DIV) were transfected with shc-Jun or control shLuc and maintained for 48 h and then subjected to A β (1.5 μ M) for 72 h. Representative images of shc-Jun and shLuc transfected hippocampal neurons are shown. Representative images of shc-Jun and shLuc transfected neurons are shown. Images were taken under X20 objective. **B.** Numbers of surviving transfected (red) cells were counted under fluorescence microscope just before A β treatment and after 24 h, 48 h and 72 h of the same treatment and percentage of viable cells are represented graphically. Data are from three independent experiments, each with comparable results, and are shown as mean \pm S.E.M performed in triplicates. The asterisks denote statistically significant differences from control (shLuc): * p <0.05. **C.** c-Jun knockdown prevents neuronal degeneration. Sholl analysis of single imaged hippocampal neurons by using ImageJ was done as described under experimental methods. Data represent mean \pm S.E.M of six different neurons from three independent cultures for each class. Asterisks denote statistically significant differences from shLuc (control); p < 0.03.

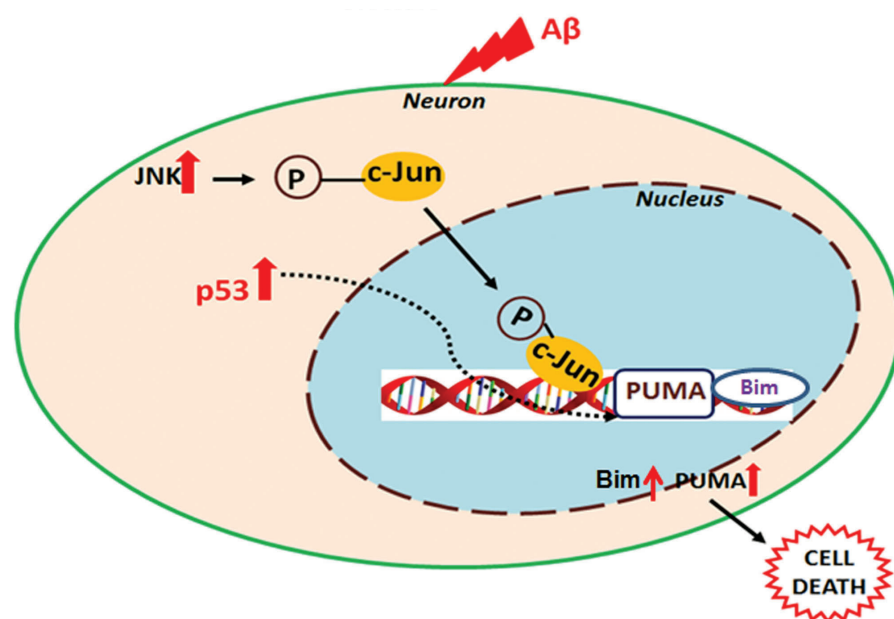


Fig. 3: This study highlights the vital role of JNK/c-Jun pathway in mediating neuronal cell death in AD and identifies the pro-apoptotic genes, Bim and Puma as transcriptional targets of c-Jun in A β -treated neurons. We propose that Akt/FoxO3a, JNK/c-Jun and p53 pathways are activated independently, converge and trigger expression of pro-apoptotic BH3-only genes Bim and Puma that act cooperatively to induce death of neurons in response to A β .

induction of Bim and Puma is inhibited in A β treated neurons. Taken together, our results suggest that both Bim and Puma are target of c-Jun and elucidate the intricate regulation of Puma expression by JNK/c-Jun and p53 pathways in neurons upon A β toxicity.

Future Research Plans

Identification of novel targets by studying new hypothesis that explains disease pathogenesis better. Among several death modalities, autophagy and apoptosis play important roles in the death of neurons. The general mechanism which governs these two phenomena mutually is still not understood in AD. We propose to identify common upstream molecule(s) that induce both apoptosis and autophagy in neuron.

Identification of glial factors that mediate neuron death and survival. We plan to characterize pro- and anti-inflammatory molecules secreted by activated astrocytes and to determine their specific role on neuronal death and survival in appropriate models of AD, with a view to develop drugs against these targets.

Pre-clinical validation of identified lead molecules against AD. We have already designed and synthesized several novel lead molecules based on established pathways and targets which have shown significant efficacy in cell and animal models of AD.

Development of diagnostics and therapeutics for Alzheimer's disease. Human samples (CSF and plasma) shall be collected based on the



neuropsychology and other initial evaluations done on potential early stage of AD patients. Analysis of the presence of biomarkers such as beta-amyloid, Tau, pro-inflammatory cytokines and other disease related secretory molecules will be undertaken.

PUBLICATIONS

Akhter, R., Sanphui, P., Das, H., Saha, P., and Biswas, S. C. (2015) The regulation of p53 up-regulated modulator of apoptosis by JNK/c-Jun pathway in beta-amyloid-induced neuron death. *J Neurochem* **134**, 1091-1103

Saha, P., and Biswas, S. C. (2015) Amyloid-beta induced astrogliosis and astrocyte death: Implication of FoxO3a-Bim-caspase3 death signaling. *Mol Cell Neurosci* **68**, 203-211

Biswas, A., Kurkute, P., Saleem, S., Jana, B., Mohapatra, S., Mondal, P., Adak, A., Ghosh, S., Saha, A., Bhunia, D., and Biswas, S. C. (2015) Novel hexapeptide interacts with tubulin and microtubules, inhibits Aβ fibrillation, and shows significant neuroprotection. *ACS Chem Neurosci* **6**, 1309-1316

PATENTS FILED / SEALED

Name Surname: SURAJIT GHOSH

Patent Title: A HEXAPEPTIDE INTERACTS WITH TUBULIN/MICROTUBULE AND EXHIBITS SIGNIFICANT NEUROPROTECTION AGAINST Aβ TOXICITY THEREOF

Country: United States

Application No: 15/062,773

Patent No.: Patent Pending

Date filed / granted: Filed on 07/Mar/2016

Co-inventors and their Institutes: ATANU BISWAS (CSIR-IICB), BATAKRISHNA JANA (CSIR-IICB), SASWAT MOHAPATRA (CSIR-IICB), SUBHAS CHANDRA BISWAS (CSIR-IICB), SURAIYA SALEEM (CSIR-IICB), PRASENJIT MONDAL (CSIR-IICB), ANINDYASUNDAR ADAK (CSIR-IICB), SUBHAJIT GHOSH (CSIR-IICB), ABHIJIT SAHA (CSIR-IICB), DEBMALYA BHUNIA (CSIR-IICB)

Patent filed by: CSIR-IICB

AWARDS / HONOURS / MEMBERSHIPS

Students

Ms. Pampa Saha

Award

2nd prize for best oral presentation for presenting a paper in NeuroUpdate 2015, 28th November 2015, Kolkata, India

CONFERENCES / WORKSHOPS

Number of abstract

India: 2

CONFERENCES / EVENTS ORGANIZED BY CSIR-IICB

NeuroUpdate Kolkata 2015, Kolkata, India, 28 November 2015

INVITED TALKS

Alzheimer's disease: molecular players in neuron death;

NeuroUpdate Kolkata 2015, Kolkata, India, November, 2015,

Alzheimer's disease: molecular players in neuron death and potential targets for therapy, Lead paper, Bhubaneswar, India, March, 2016

Dr. Rupasri Ain

rupasri@iicb.res.in



Regulations of trophoblast stem cells differentiation and placental angiogenesis at the maternal-fetal interface

Participants

JRF: Trishita Basak, Debdyuti Nandi

SRF: Sarbani Saha, Shreeta Chakraborty

Project Assistant

Safirul Islam

Background

The placenta is an extra-embryonic tissue that provides the physiological interface between mother and fetus and is critically involved in controlling the environment in which the embryo/fetus develops. Placental morphogenesis includes a) differentiation of trophoblast stem cells into multilineage pathway, b) epithelial mesenchymal transition of trophoblast cells imparting invasive phenotype, c) extensive angiogenesis. Disruptions in placental development can lead to early pregnancy loss, intrauterine growth retardation (IUGR), and tumorigenesis. These represent serious health problems whose etiologies are not sufficiently understood.

Placental development is the result of co-ordination between the driving forces of morphogenesis, cell proliferation, differentiation and cell-cell interaction at the maternal-fetal interface to accommodate the needs of the developing embryo. The goal of our research is to further our understanding of cellular interaction and molecular regulation of placental development and trophoblast cell differentiation and function.

Aims and Objectives

Decipher the molecule(s) involved in the regulation of placental angiogenesis and their mechanism of action, miRNA mediated regulation of trophoblast stem cell differentiation.

Work Achieved

Nitric Oxide Synthase Trafficking Inducer (NOSTRIN): a novel modulator of angiogenesis at the maternal-fetal interface. Endothelial nitric oxide synthase (eNOS) and its bioactive product



nitric oxide (NO) are known to be a mediator of many endothelial cell functions including angiogenesis and vascular permeability. Genetic disruption or pharmacological inhibition of eNOS attenuated angiogenesis during tissue repair resulting in delayed wound closure, which was reversed by addition of NO donors. These observations emphasize the ability of eNOS-derived NO to promote angiogenesis. We investigated the function of NOSTRIN, known as an eNOS sequestering protein, in placental bed. We demonstrated that NOSTRIN mRNA levels gradually increased from early to late gestation in decidua/placenta of both mice and rat. NOSTRIN mRNA was detected by *in situ* hybridization in both endothelial cells and trophoblast cells of the developing placenta. Furthermore, NOSTRIN mRNA and protein expression was found to be differentiation dependent in trophoblast cells *ex vivo*. On the contrary, eNOS expression declined drastically upon differentiation of trophoblast stem cells. The reciprocal expression of NOSTRIN and eNOS led us speculate that NOSTRIN might have some yet unexplored eNOS independent cellular function. We demonstrated that NOSTRIN affects the functional-transcriptome of endothelial cells leading to down regulation of several imperative genes, related to invasion and angiogenesis. NOSTRIN also affects the expression of secreted cytokines involved in inflammatory responses. Ectopic over-expression of NOSTRIN functionally restricts endothelial cell proliferation, invasion, adhesion and VEGF-induced capillary tube formation. Furthermore, NOSTRIN directly interacts with TRAF6 leading to suppression of NF κ B activity and inhibition of Akt phosphorylation. Interestingly,

TNF- α induced NF κ B pathway activation is overturned by NOSTRIN. These results have widespread biological implications as aberrant NOSTRIN expression leading to deactivation of NF κ B pathway and consequently triggering anti-angiogenic cascade might inhibit tumorigenesis and cancer progression.

Furthermore, in a dexamethasone-induced IUGR rat model, NOSTRIN levels increased remarkably in vasculature rich metrial gland at the maternal-fetal interface. This profound elevation of NOSTRIN was associated with curtailment of NF κ B-Akt signaling axis and down regulation of an assortment of pro-angiogenic genes. These results indicate novel role of NOSTRIN in regulating angiogenesis at the maternal-fetal interface and also in regulating IUGR.

MicroRNA regulation of Insulin like growth factor-II during mouse placental development: Insulin-like growth factor 2 (IGF2) plays a vital role in fetal and placental development throughout gestation. Placental expression of IGF2 decreases substantially in intra-uterine growth restriction (IUGR) and Igf2 null mice develop small placentas. We examined the role of microRNAs in regulating Igf2 gene expression during mouse placental development. Using bioinformatic analysis, we have identified microRNAs that have conserved binding sites in the 3'-UTR of Igf2. Using luciferase reporter assay, we demonstrated that miR141-3p and miR-200a-3p mimics substantially down regulated relative luciferase activity by binding to 3'-UTR of Igf2, which was reversed by using miR141-3p and miR-200a-3p inhibitors. Furthermore, in a similar assay, use of Igf2 3'-UTR that lacked the binding site for the microRNAs did not have any effect on



luciferase activity. Interestingly, the expression of miR141-3p and miR-200a-3p were inversely and temporally correlated to the expression of IGF2 during mouse placental development. Overexpression of miR141-3p and miR-200a-3p in mouse trophoblast stem cells suppressed endogenous expression of IGF2. Consequently, IGF2 silencing by miR141-3p and miR-200a-3p diminished Akt activation in mouse trophoblast stem cells. Our study provides evidence for regulation of Igf2 by microRNAs and further elucidates the role of miR141-3p and miR-200a-3p in the mouse placental development.

Future Research Plans

Elucidate the transcriptional regulation of NOSTRIN in endothelial and trophoblast cells. Illustrate the consequences of CRISPR-Cas9 mediated deletion of NOSTRIN gene in differentiating trophoblast cells in terms of affecting trophoblast cell function. Identify miRNAs and their regulatory gene network that governs trophoblast stem cell self-renewal and impart their invasive phenotype upon differentiation.

PUBLICATIONS

Saha, S., Choudhury, J., and Ain, R. (2015) MicroRNA-141-3p and miR-200a-3p regulate insulin-like growth factor 2 during mouse placental development. *Mol. Cell. Endocrinol* **414**, 186-193

Book Chapters / Invited Reviews

Shreeta Chakraborty and Rupasri Ain (2016) "Endothelial Cell Biology: Assessment of Endothelial Cell Function" in Trends in Experimental Biology, Excel India Publishers, New Delhi, India (Ed. Dr. L Kma), Volume-II. L. pp. 1-27.

EXTRAMURAL FUNDING

Studies on trophoblast and natural killer cell interaction at the maternal-fetal interface. 2013-2016 (Department of Science and Technology, India)

Transgenic Over-Expression of NOSTRIN in Mice and Pregnancy-Induced Hypertension. 2014-2016 (Department of Biotechnology, India)

Transgenic Over-Expression of NOSIP in Mice and Pregnancy-Induced Hypertension. 2014-2017 (Indian Council of Medical Research, India)

MiRNAs in trophoblast stem cell differentiation. 2016-2019 (Department of Science and Technology, India)

Dr. Partha Chakrabarti



Unraveling the molecular basis of fatty liver disease

Participants

JRF: Sougata Niyogi

SRF: Dipsikha Biswas Mainak Ghosh, Titli Nargis, Moumita Adak

DST-INSPIRE Faculty: Md Wasim Khan

T O: Dipika Ray

Collaborator(s)

Name of collaborator outside CSIR-IICB

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Dr. Om Tantia

ILS hospital, Kolkata

Name of collaborator within CSIR-IICB

Dr. Saikat Chakrabarti

Structural Biology and Bioinformatics Division.

Dr. Dipyaman Ganguly

Cancer Biology and Inflammatory Disorder Division

Dr. Sanjay Dutta

Organic and Medicinal Chemistry Division

Background

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease and is strongly associated with obesity and type 2 diabetes. NAFLD is a term used to describe a spectrum of conditions characterized mainly by the histological finding of macrovesicular hepatic steatosis and now considered to be the hepatic component of the metabolic syndrome. The hallmark feature of NAFLD pathogenesis, both histologically and metabolically, is the accumulation of TAG in the liver which is caused by defects in both lipid storage and mobilization. A significant number of NAFLD patient progresses to a pathognomonic stage called non-alcoholic steatohepatitis (NASH) characterized by inflammation and fibrosis. NASH can further progress to non-reversible stage of liver cirrhosis and cancer.

There is no cure for chronic liver diseases of metabolism. Understanding the molecular pathogenesis of NAFLD and NASH is key to identify therapeutic targets and development of drugs.

Aims and Objectives

Defining the role of lipolysis in the pathogenesis of NAFLD with a focus on rate-limiting lipolytic enzyme Adipose triglyceride lipase (ATGL).

Understanding the contribution of anti-inflammatory hepatokine PEDF on hepatocyte and Kupffer cells during NASH progression.

Deciphering the role of inflammasome activation in NAFLD and NASH.

Work Achieved

We have identified hepatic ATGL as a novel target of E3 ubiquitin ligase COP1 and their interaction controls hepatic TAG turnover. We also find that depletion of COP1 in liver abrogated hepatic steatosis thereby suggesting that COP1 could be a novel target for ameliorating lipid accumulation in NAFLD.

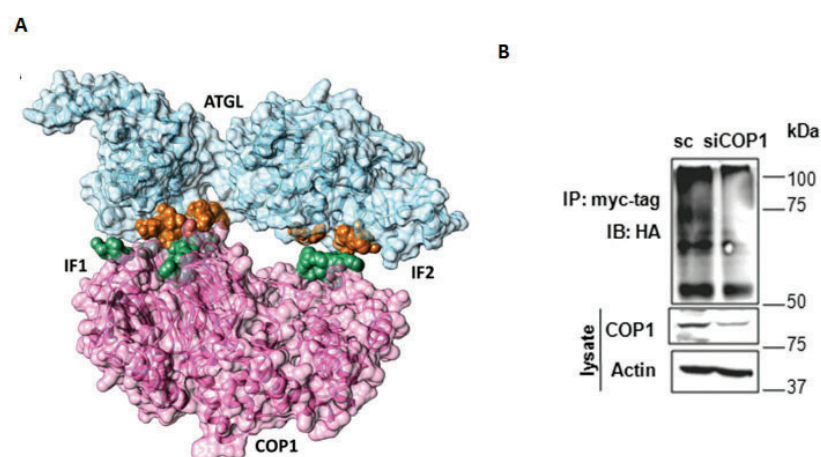


Fig. 1: COP1 directly binds to ATGL and targets it for proteasomal degradation. **(A)** Three dimensional structure of ATGL protein predicted by *ab-initio* and comparative modeling. The residues, which interact with ATGL are highlighted in green and presented in sphere orientation. Docked complex of ATGL (blue) and COP1 (pink). Interface residues are shown as spheres in orange (ATGL) and green (COP1) colors, respectively. **(B)** Ubiquitination status of ATGL in COP1 depleted hepatocytes.

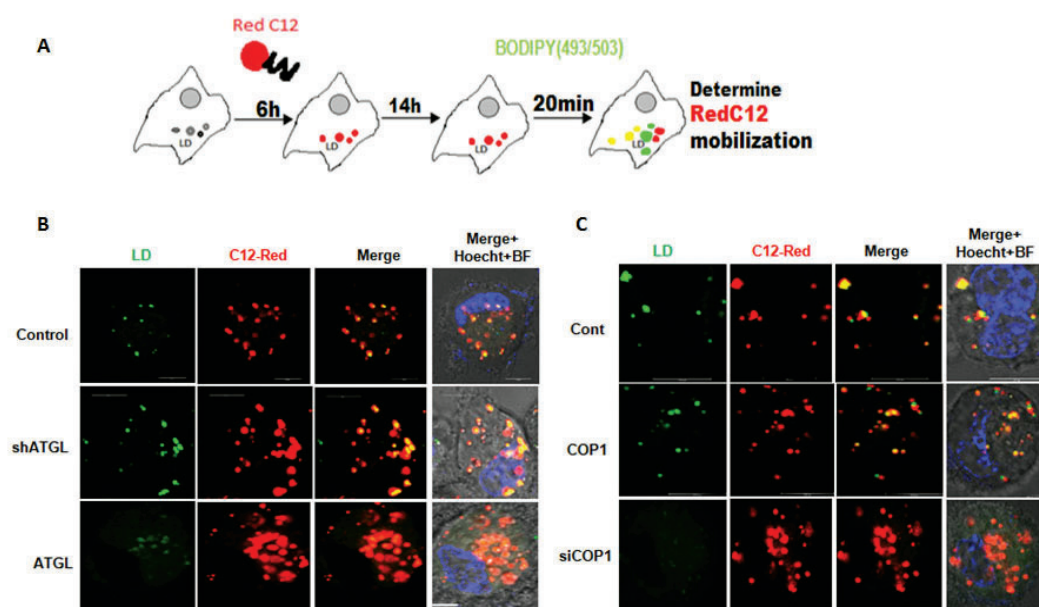


Fig. 2: COP1 recapitulates fatty acid mobilization of ATGL. **(A)** Schematic presentation of fluorescent FA pulse-chase assay. Cells were labeled with BODIPY 558/568 C₁₂ (Red C₁₂), a saturated FA analog followed by treatment with hydrophobic BODIPY 493/503 (green) for LD staining and visualizing fluorescence with confocal microscopy. **(B)** Confocal microscopy showing LDs and Red C12 of control, ATGL knock down (shATGL) or ATGL overexpressing (ATGL) HepG2 cells following the assay described earlier in Fig. 2A. Scale bar: 10 μm. **(C)** Confocal microscopy showing LDs and Red C12 following the assay as described in (A) for indicated experimental conditions. BF, bright field; Scale bar, 10 μm.

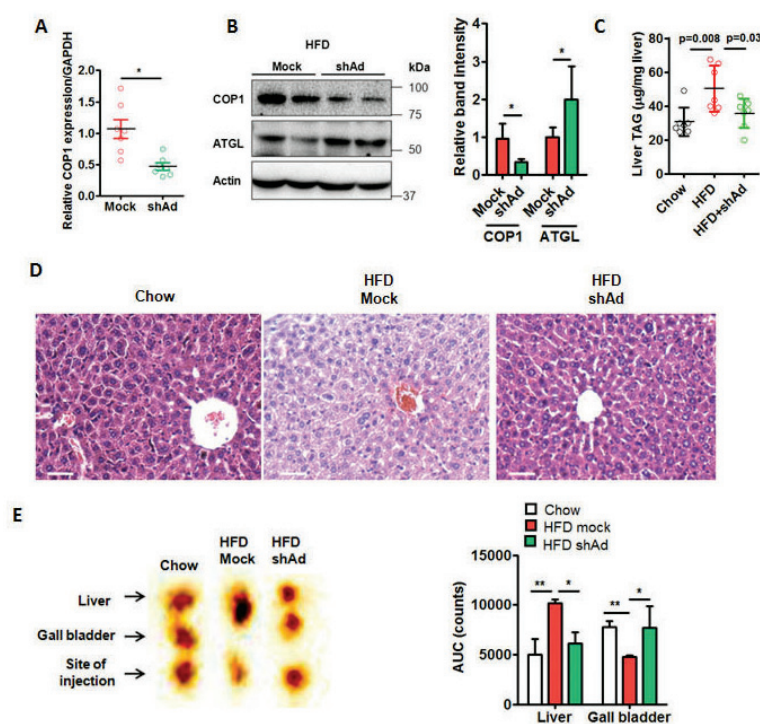


Fig. 3: COP1 is a critical regulator of TAG accumulation in fatty liver disease. (A-B) high fat diet fed mice were injected with adenovirus carrying shRNA against murine COP1 (shAd, green) or with vehicle (Mock, red). Relative mRNA expression (A) and protein levels (B) of COP1 and ATGL in livers of indicated mice. Relative quantification of the band intensity normalized with actin (n=6). Data are expressed as mean±SD relative to Mock. (C) Liver TAG levels of chow fed control (black), HFD (red) and shAd (green) mice. (D) The H&E staining of liver sections from indicated mice. (E) Liver activity measured by analyzing ^{99m}Te-Mebrofenin signal 30 min after injection (n=4). quantification of ^{99m}Te-Mebrofenin distribution in liver and gall bladder by calculating the area under the curve (AUC) at different time points for 30 min through 180 time frames. Data are expressed as mean±SD relative to chow. (J). Data information: *p<0.05, **p<0.01 compared with chow or Mock.

We find that differential composition of cytokines in the inflammatory milieu of NASH controls PEDF expression in hepatocyte. PEDF levels conversely suppress inflammation in NASH.

PEDF regulates ATGL protein levels both in hepatocytes and in Kupffer cells and thus fine tunes lipid turnover in liver microenvironment.

Future Research Plans

Validation of in vitro results in pre-clinical animal models of NASH; feeding methionine & choline deficient diet and feeding atherogenic diet.

Further dissection of signaling pathways and cellular events in NASH pathogenesis.

Developing a research program involving NAFLD and NASH patients towards identification of diagnostic/prognostic markers.

PUBLICATIONS

Khan, M.W., Biswas, D., Ghosh, M., Mandloi, S., Chakrabarti, S., and Chakrabarti, P. (2015) mTORC2 controls cancer cell survival by modulating gluconeogenesis. *Cell Death Discovery* 1, 15016

Khan, M.W., and Chakrabarti, P. (2015) Gluconeogenesis combats cancer: opening new doors in cancer biology. *Cell Death Dis* 6, e1872

Singh, M., Shin, Y.K., Yang, X., Zehr, B., Chakrabarti, P., and Kandror, K.V. (2015) *J Biol Chem* 290, 17331-8

Chakrabarti, P., and Kandror, K.V. (2015) The Role of mTOR in Lipid Homeostasis and Diabetes Progression. *Curr Opin Endocrinol Diabetes Obes* 22, 340-46

AWARDS / HONOURS / MEMBERSHIPS

Student

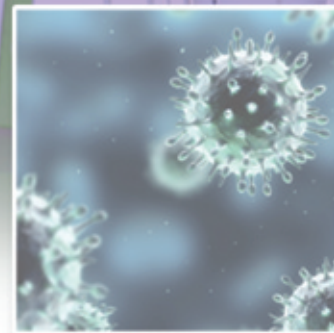
Dipsikha Biswas

Award

DBT travel fellowship for attending international conference (Herren Hausen symposium, Nature Medicine conference, Germany)

SeaHorse Travel Award for Keystone Symposium (Diabetes: new insights into molecular mechanisms and therapeutic strategies, Japan)

Infectious Diseases and Immunology Division



Dr. Syamal Roy (Head up to January 2016), Dr. Nahid Ali (Head from February 2016), Dr. Rukhsana Chowdhury, Dr. Rupak K. Bhadra, Dr. Uday Badopadhyay, Dr. Debjani Mandal, Dr. Mita Chatterjee Debnath and Dr. Subhajit Biswas

The major objective of Infectious Diseases and Immunology Division is to understand the molecular pathology of leishmaniasis, cholera, malaria, hepatitis B virus infections and gastropathy as well as evaluation of radioisotopes for biological applications. Work on leishmaniasis is comprised of

- (i) development of a simple, non-invasive and effective diagnostic approach,
- (ii) comprehensive assessment of liposome-encapsulated drugs as therapeutic agent as well as designing antileishmanial treatment strategies by altering lipid composition of host cell membrane,
- (iii) studies on the immunobiology of leishmaniasis towards identifying potential vaccine candidates and
- (iv) functional analysis of antigen presentation and antigen processing in *Leishmania* infected antigen presenting cells.

Work on cholera is comprised of

- (i) investigations on genetic regulation of biofilm formation and antibiotic resistance in *Vibrio cholerae*,
- (ii) understanding the roles of *Helicobacter pylori* gene HP0102 in pathogenicity and (iii) assessment of the role of gastric microbiome in determining clinical outcome of *H. pylori* infection.

Malaria and gastropathy work is comprised of

- (i) study on the role of *Plasmodium falciparum* mitochondria for parasite growth and survival and liver mitochondrial dysfunction and associated

apoptosis during host-malaria interaction,

- (ii) study on the gastric mucosal apoptosis during *H. pylori*-mediated and non-mediated gastropathy and

- (iii) identification and designing of anti-inflammatory molecule targeting macrophage migration inhibitory factor (MIF) and study of their structure-activity relationship.

Work on hepatitis B virus infections includes

- (i) epidemiological study of occult hepatitis B infection (OBI) and
- (ii) identification and characterization of different S protein mutations important for OBI genesis.

Dr. Syamal Roy



Immunobiology of Leishmaniasis

Participants

JRF: Satarupa Ganguli

SRF: Sandip Mukherjee

RA : Koushik Roy

T/O: Kshudiram Naskar

Collaborator(s)

Name of collaborator outside CSIR-IICB

Institute of Tropical Medicine, Antwerp, Belgium

Name of collaborator within CSIR-IICB

Dr. Malini Sen

Cancer Biology and Inflammatory Disorder Division

Background

The diseases visceral Leishmaniasis or kala azar is widening its base in the Indian sub-continent and elsewhere. The disease is characterized by the immune suppression- the cause of which is not very clear. The causative agent of visceral leishmaniasis, *Leishmania donovani* replicates within the macrophages and dendritic cells of the mammalian host. The dendritic cells and macrophages are known as the antigen presenting cells(APCs). The infected APCs are unable to function as properly which may contribute to the decreases expansion of antileishmanial host protective T-cells population. The main stay of treatment was Antimonials until recently. Due to dwindling efficacy, the drug is no longer in use for the treatment of kala azar. Thus understanding the mechanism of resistance to Antimonials is an important issue as resistance to this drug is still present in the recent field isolates Thus there is a genuine need for newer drugs and effective vaccine to combat this dreaded disease.

Aims and Objectives

To understand mechanism of Immune suppression in Leishmaniasis

To understand the mechanism of resistance to antimonials

Work Achieved

The anti-leishmanial T-cell immunity is the key to the elimination of intracellular parasites. The parasites have multitude of mechanisms to evade the host immune system and also to the drug pressure of antimonials, the commonly used drug for treatment of leishmaniasis in the recent past. One of the mechanisms of immune evasion that intracellular parasites employ is to take up membrane cholesterol resulting in increase the lateral mobility of membrane proteins. Decrease in membrane cholesterol favored conformational change in transmembrane MHC-II protein in the



infected host cells which allowed faster dissociation of cognate peptide from the peptide-MHC complex leading to defective expansion of anti-leishmanial T-cells. Thus by manipulating lipid metabolism of infected host, parasites may evade host immune system. Such defects can be corrected by the liposomal delivery of cholesterol. Resistance to antimonials is the key deterrent in the use of such a drug in the Indian sub-continent. Whole-genome sequence data has the potential to show significant population structure, and also allows one to identify changes in genome structure. Whole genome sequences from 204 clinical isolates to track the evolution and epidemiology of *L. donovani* was carried out. A genetically distinct population frequently resistant to antimonials has a two base-pair insertion in the aquaglyceroporin gene *LdAQP1* that prevents the transport of trivalent antimonials. We find evidence of genetic exchange between ISC populations, and show that the mutation in *LdAQP1* has spread by recombination. Our results reveal the complexity of *L. donovani* evolution in the Indian sub-continent in response to drug treatment.

Future Research Plans

To design an effective DNA vaccine for visceral leishmaniasis

PUBLICATIONS

Mukherjee, B., Paul, J., Mukherjee, S., Mukhopadhyay, R., Das, S., Naskar, K., Sundar, S., Dujardin, J. C., Saha, B., and Roy, S. (2015) Antimony-Resistant *Leishmania donovani* Exploits miR-466i To Deactivate Host MyD88 for Regulating IL-10/IL-12 Levels during Early Hours of Infection. *J Immunol* **195**, 2731-2742

Roy, K., Mandloi, S., Chakrabarti, S., and Roy, S. (2016) Cholesterol Corrects Altered Conformation of MHC-II Protein in *Leishmania donovani* Infected Macrophages: Implication in Therapy. *PLoS Negl Trop Dis* **10**, e0004710

Imamura, H., Downing, T., Van den Broeck, F., Sanders, M. J., Rijal, S., Sundar, S., Mannaert, A., Vanaerschot, M., Berg, M., De Muylder, G., Dumetz, F., Cuypers, B., Maes, I., Domagalska, M., Decuyper, S., Rai, K., Uranw, S., Bhattarai, N. R., Khanal, B., Prajapati, V. K., Sharma, S., Stark, O., Schonian, G., De Koning, H. P., Settimo, L., Vanhollebeke, B., Roy, S., Ostyn, B., Boelaert, M., Maes, L., Berriman, M., Dujardin, J. C., and Cotton, J. A. (2016) Evolutionary genomics of epidemic visceral leishmaniasis in the Indian subcontinent. *eLife*; **5**: e 12613

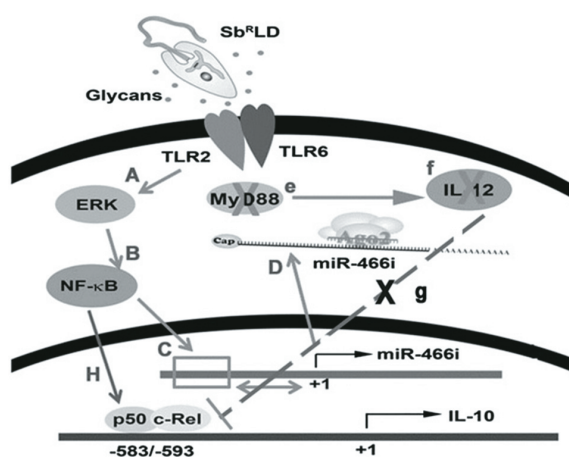


Fig : Schematic representation of molecular mechanism of MyD88 deactivation during infection with antimony resistant *Leishmania donovani* (Sb^RLD). Interaction of Sb^RLD with host cell TLR2/TLR6 led to activation of ERK as indicated by (A) in the diagram. (B) represents p50/c-Rel activation and translocation in the nucleus resulting in binding with 5 kb upstream of miR-466i promoter as indicated by (C). This binding led to activation of miR-466i as represented by (D) and resulted in deactivation of MyD88 by binding with its 39-UTR, represented as (e). Deactivation of MyD88 resulted in reduced IL-12 level represented as (f). Reduced IL-12 level led to removal of suppression over IL-10 promoter (g), which resulted in binding of p50/c-Rel to the IL-10 promoter leading to its activation as represented by (H). Uppercase letters represent activation, whereas lowercase letters represent deactivation or suppression.

Dr. Nahid Ali

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Induction of IL-10 and TGF β from CD4⁺CD25⁺FoxP3⁺ T cells correlates with parasite load in indian Kala-azar patients infected with *Leishmania donovani*

Participants

JRF: Md Kamran, Sonali Das

SRF: Pradyot Bhattacharya, Abdus Sabur, Nicky Didwania, Rudra Chhajjer, Sarfaraz Ahmad Ejazi, Md Shadab, Manjarika De

Project Assistant: Anirban Bhattacharyya

Collaborator(s)

Name of collaborator outside CSIR-IICB

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Patna, Bihar

Dr. Mehebubar Rahaman, Dr. Rama Prosad Goswami and
Dr. Bibhuti Saha School of Tropical Medicine, Kolkata, West
Bengal

Background

Visceral leishmaniasis (VL) is distinguished by a complex interplay of immune response and parasite multiplication inside host cells. However, the direct association between different immunological correlates and parasite numbers remains largely unknown.

Aims and Objectives

Assessment of correlation of parasite load with different clinical parameters as well as immunological components (cellular subsets and cytokines) associated with disease severity/alleviation.

Exploration of a link between cellular subsets and cytokines responsible for parasite persistence thereby establishing secretory sources of these cytokines.

Work Achieved

We examined the plasma levels of different disease promoting/protective as well as Th17 cytokines and found IL-10, TGF β and IL-17 to be significantly correlated with parasite load in VL patients ($r=0.52$, 0.53 and 0.51 for IL-10, TGF β and IL-17, respectively). We then extended our investigation to a more antigen-specific response and found leishmanial antigen stimulated levels of both IL-10 and TGF β to be significantly associated with parasite load ($r=0.71$ and 0.72 for IL-10 and TGF β respectively). In addition to cytokines we also looked for different cellular subtypes that could contribute to cytokine secretion and parasite persistence. Our observations manifested an association between different Treg cell markers and disease progression, as absolute numbers of CD4⁺CD25⁺ ($r=0.55$), CD4⁺CD25^{hi} ($r=0.61$) as well as percentages of CD4⁺CD25⁺FoxP3⁺ T cells ($r=0.68$) all correlated with parasite load. Encouraged by these results we investigated a link between these immunological components and interestingly found both CD4⁺CD25⁺ and CD4⁺CD25⁺FoxP3⁺



Treg cells to secrete significantly ($p < 0.05$) higher amounts of not only IL-10 but also TGF β in comparison to corresponding CD25⁻ T cells. Our findings shed some light on source(s) of TGF β and suggest an association between these disease

promoting cytokines and Treg cells with parasite load during active disease. Moreover, the direct evidence of CD4⁺CD25⁺FoxP3⁺ Treg cells as a source of IL-10 and TGF β during active VL could open new avenues for immunotherapy towards cure of this potentially fatal disease.

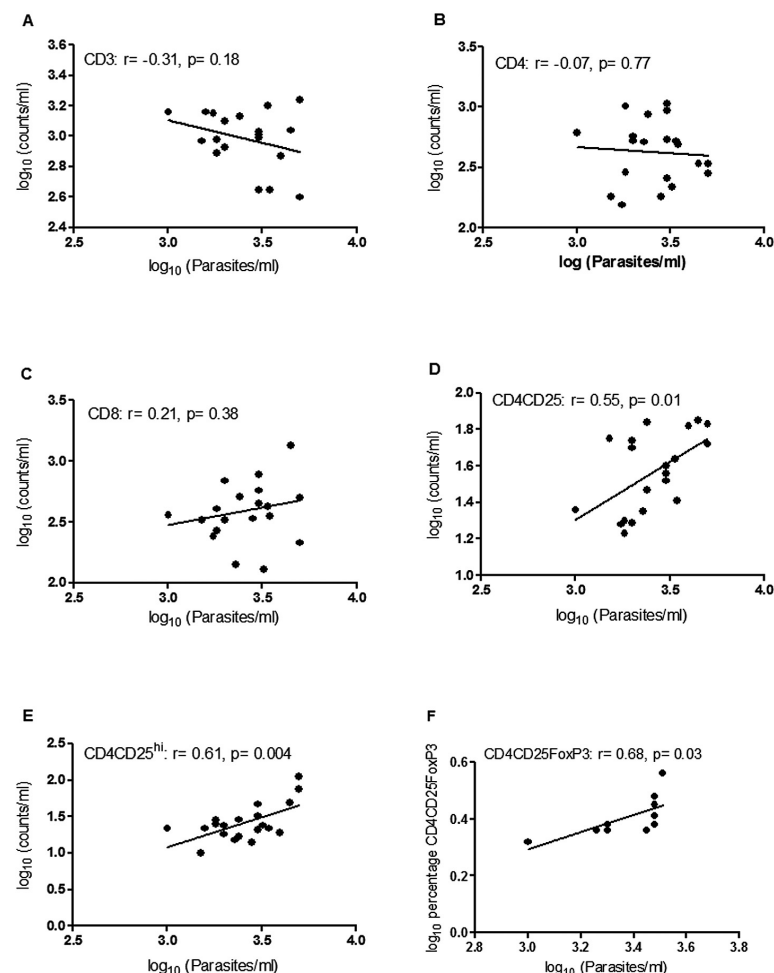


Fig. 1: Correlation of different T cell subtypes and CD4CD25FoxP3 with parasite load in VL patients. Absolute numbers of CD3 (panel A), CD4 (panel B), CD8 (panel C), CD4CD25 (panel D), and CD4CD25^{hi} (panel E) were determined by flow cytometry in whole blood samples of VL patients ($n = 20$). Percentages of CD4CD25FoxP3-positive cells (panel F) were calculated by flow cytometry in PBMCs of VL patients ($n = 10$). Parasite loads (Parasites/ml) were determined by real-time PCR. Correlation was calculated using Spearman/Pearson correlation test. Diagonal lines represent linear regression.

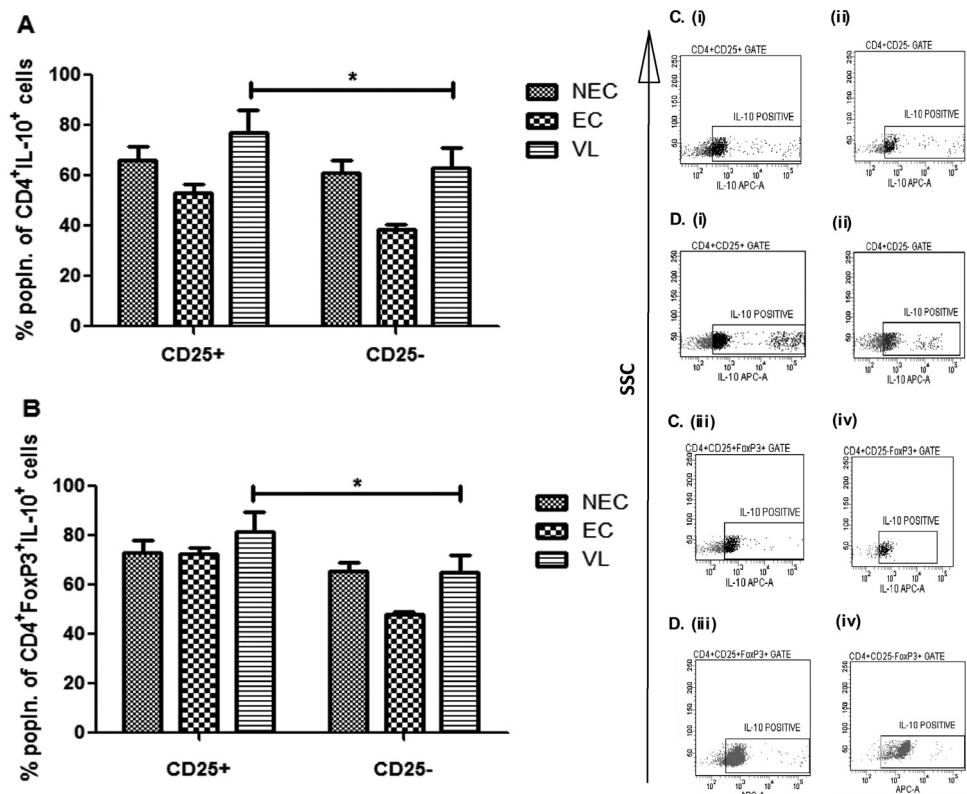


Fig. 2: Identification of cellular sources of IL-10 in PBMCs of VL patients ($n=10$), ECs ($n=5$) and NECs ($n=5$). Total PBMCs were freshly cultured in the presence of PMA (50 ng/ μ l), ionomycin (1 μ g/ μ l) for 2 hrs and for additional 1 hr in presence of brefeldin A (10 μ g/ μ l) before staining. (A) Percentages of CD25⁺ and CD25⁻ cells among CD4⁺IL-10⁺ cells. (B) Percentages of CD25⁺ and CD25⁻ cells among CD4⁺FoxP3⁺IL-10⁺ cells. Data are represented as mean \pm SE. P values were calculated using Wilcoxon matched pairs signed rank test for paired samples; $P<0.05$ was considered significant. (C), (i)-(iv) Data showing one representative healthy control. (D), (i)-(iv) Data showing one representative active VL patient.

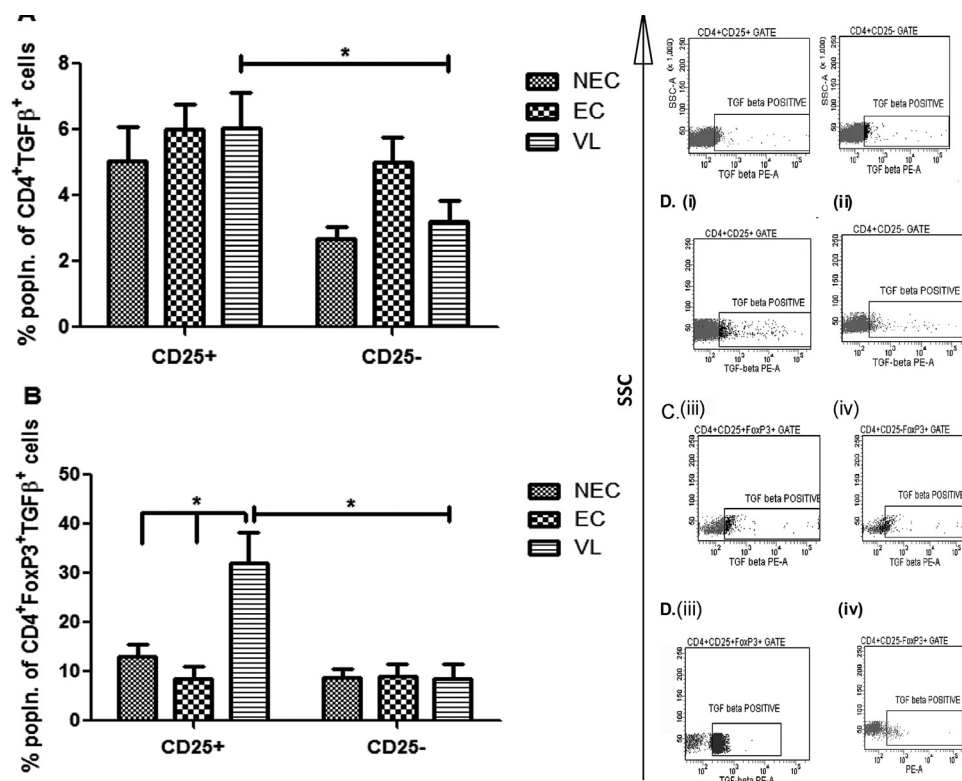


Fig. 3: Identification of cellular sources of TGFβ in PBMCs of VL patients (n=10), ECs (n=5) and NECs (n=5). Total PBMCs were freshly cultured in the presence of PMA (50 ng/μl), ionomycin (1 μg/μl) for 2 hrs and for additional 1 hr in presence of brefeldin A (10μg/μl) before staining. (A) Percentages of CD25⁺ and CD25⁻ cells among CD4⁺ TGFβ⁺ cells. (B) Percentages of CD25⁺ and CD25⁻ cells among CD4⁺FoxP3⁺ TGFβ⁺ cells. Data are represented as mean ± SE. P values were calculated using Wilcoxon matched pairs signed rank test for paired samples; P<0.05 was considered significant. (C), (i)-(iv) Data showing one representative healthy control. (D), (i)-(iv) Data showing one representative active VL patient.

Future Research Plans

Encouraged by our observations we now aim to investigate the role of CD8⁺CD25⁺FoxP3⁺ Treg cells in producing IL-10 and TGFβ during infection and predict the more potent source of these cytokines among CD4 and CD8 Tregs

A broader interest, in this aspect, includes exploration of the role of IL-27 and IL-23 in inducing IL-10 and TGFβ along with IL-35, IL-13 and other Th17 cytokines from CD4 and CD8 T cell subsets to get a holistic view of VL pathogenesis

PUBLICATIONS

- Dar, A. A., Enjamuri, N., Shadab, M., Ali, N., and Khan, A. T. (2015) Synthesis of unsymmetricalsulfidesand their oxidation to sulfones to discover potent antileishmanial agents. *ACS Comb Sci* **17**, 671-681
- Bhattacharya, P., Ghosh, S., Ejazi, S. A., Rahaman, M., Pandey, K., Das, V. N. R., Das, P., Goswami, R. P., Saha, B., and Ali, N. (2016) Induction of IL-10 and TGFβ from CD4⁺CD25⁺FoxP3⁺ T cells correlates with parasite load in Indian kala-azar patients infected with *Leishmania donovani*. *PLoS Negl Trop Dis* **10**, 1-20
- Choudhury, S.T., Das, N., Ghosh, S., Ghosh, D., Chakraborty, S., and Ali, N. (2016) Vesicular (liposomal and nanoparticulated)



delivery of curcumin: a comparative study on carbon tetrachloride mediated oxidative hepatocellular damage in rat model. *Int J Nanomedicine* **11**, 1-15

Dar, A. A., Shadab, M., Khan, S., Ali, N., and Khan, A.T. (2015) One-pot synthesis and evaluation of antileishmanial activities of functionalized s-alkyl/ aryl benzothiazole-2-carbothioate scaffold. *J Org Chem* **81**, 3149-3160

PATENTS FILED / SEALED

Name Surname: NAHID ALI AND SARFRAZ AHMED EJAZI

Patent Title: A KIT USEFUL FOR MEASURING A NON-RECOMBINANT MEMBRANE ANTIGEN (LAG) IN THE URINE SAMPLE.

Country: India

Patent No.: PCT/IN2015/000268

Date filed / granted: Filing date: 29/06/2015

Co-inventors and their Institutes

Patent filed by DBT / CSIR-IICB / another organization: CSIR-IICB

AWARDS / HONOURS / MEMBERSHIPS

National Women Bioscientist Award (Senior Category -2014), DBT

J.C. Bose Fellowship (2015), DST

Top 10 Innovators Award for dipstick technology (2015), DST-Lockheed Martin India Innovation, Indo-US Science and Technology Forum, Stanford Graduate School of Business, IC² Institute, University of Texas at Austin and TiE Silicon Valley, USA.

Memberships

Chairperson of Academic Affairs of CSIR-IICB.

Member Secretary and Convenor of Human Ethical Committees of CSIR-IICB.

Member of the Library Committee of CSIR-Indian Institute of Chemical Biology.

Member of the Collegium and Empowered Committee for assessing the performance of Scientists at CSIR-IICB.

Convener of the B. K. Bachhawat Memorial Lecture Committee of CSIR-IICB.

Co-ordinator for Assessment of Grade IV Scientist in the area of 'Biosciences and Biotech and Chemical Sciences at CSIR-IICB.

Departmental Core Member in the Assessment Committee at CSIR-New Delhi.

Member of the Consultative Mechanism and Local Grievance Committee of CSIR-IICB.

Member of Patent Advisory Committee and Technology Translation Committee at CSIR-IICB.

Internal member of the Selection Committee for engagement of Research Fellows, and Project Assistants of CSIR-IICB.

Member of the Selection Committee for recruitment of Assistant Grade III for CSIR-CGCRI.

Member of the 73rd CSIR Foundation Day Celebration Committee at CSIR-IICB.

External Member of the Selecting Committee to select PhD students to be registered under AcSIR, at CSIR-CGCRI.

Member of Selection Committee for interviewing short listed Scientists for recruitment at CSIR- CGCRI.

Served as a Judge for selecting of the Best Science Teacher Award sponsored by National Academy of Sciences India (Kolkata Chapter) for the year 2015.

External expert for JRF selection for a West Bengal DBT funded project of Dr. Anirban Siddhanta at Dept. Of Biotech St. Xavier's College, Kolkata 2 May 2015.

INVITED TALKS

An easy test for diagnosis of kala-azar. DST Lockheed Martin, India Innovation Growth Programme (IIGP), 5 May 2015. New Delhi, India.

Easy diagnostic test for visceral leishmaniasis and post kala-azar dermal leishmaniasis. CSIR Technology Awards-2015, CSIR-HQ, Rafi Marg, 1 September, 2015. New Delhi, India.

Target antigens against Leishmania and cationic liposomes: a perfect mix. Immunocon-2015, 42nd Annual Conference of India Immunology Society, ICMR- Rajendra Memorial Research Institute of Medical Sciences, 9 -11 October 2015. Patna, India.

Elucidating the mechanism of disease progression for designing clinical intervention against Visceral Leishmaniasis. Research Council meeting. 14 -15 October 2015. IICB, Kolkata. India

Host interactome analysis: Understanding the role of host molecules in parasite infection. Research Council meeting at IICB, 14 -15 October 2015. Kolkata, India.

Designing vaccines against visceral leishmaniasis: importance of liposomes. World Vaccines Congress-2015, 2 -4th November 2015. Hyderabad, India.

Novel diagnostic approaches for kala-azar and the multiple facets of cationic liposomes in leishmaniasis and cancer. Special Research Council meeting at IICB, 16 January 2016. Kolkata, India.

Dr. Rukhsana Chowdhury

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Host contact dependent virulence regulation in gastrointestinal pathogens

Participants

SRF: Saurabh Bhattacharya, Chirantana Sengupta

RA: Maitreyee Mandal

Project Associate: Oindrilla Mukherjee, Ronita De

Collaborator(s)

Name of collaborator outside CSIR-IICB

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R.G.Kar Medical College, Kolkata

Name of collaborator within CSIR-IICB

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Structural Biology and Bioinformatics Division

Dr. Snehasikta Swarnakar

Cancer Biology and Inflammatory Disorder Division

Background

Adherence of non invasive pathogens to host cells is of primary importance in host-pathogen interaction leading to disease. The effect of adherence to host cells on expression of several important processes in the gastrointestinal pathogens *Vibrio cholerae* and *Helicobacter pylori* has been investigated.

Aims and Objectives

Virulence regulation by gastric cell contact-induced genes in *H. pylori*

Mechanism of *V. cholerae* biofilm formation on intestinal cells

Role of gastric microbiome in determining clinical outcome of *H. pylori* infection

Role of oral microbiome in determining clinical outcome of tobacco chewing

Work Achieved

Multiple roles of H. pylori gene HP0102 in pathogenicity: Adherence of *H. pylori* to the gastric epithelial cell line AGS strongly upregulated expression of a gene HP0102 in the adhered bacteria in all *H. pylori* strains examined, including several Indian clinical isolates. The gene is highly conserved and ubiquitously present in all 69 sequenced *H. pylori* genomes at the same genomic locus as well as in 15 Indian clinical isolates. The gene is associated with two distinct phenotypes related to pathogenicity. In gastric epithelial cell-adhered *H. pylori*, it has a role in upregulation of the major virulence gene *cagA* and consequent induction of elongation and scattering of the



infected AGS cells. Furthermore, HP0102 has a role in chemotaxis and a Δ HP0102 mutant exhibited low acid escape response that might account for the poor colonization efficiency of the mutant.

Adherence to intestinal cells promotes biofilm formation and antibiotic resistance in Vibrio cholerae: *Vibrio cholerae* is known to form biofilms for persistence in the environment. We have demonstrated that even during infection, biofilm genes are upregulated and microscopic observation indicated that biofilm formation is initiated almost immediately after adherence of *V. cholerae* to intestinal cells and also during infection in animal models. Of possible clinical relevance was the observation that *V. cholerae* in the INT 407 associated biofilms was significantly more resistant to antibiotics than unadhered planktonic cells.

Role of gastric microbiome in determining clinical outcome of H. pylori infection: Metagenomic sequencing of 16SrRNA gene from gastric endoscopy samples collected from individuals with or without antral erosion was performed. Bioinformatic analysis is in progress.

Role of oral microbiome in determining clinical outcome of tobacco chewing: Metagenomic sequencing of 16SrRNA gene from saliva samples collected from individuals with or without tobacco chewing habits and precancerous or cancerous lesions was performed. Bioinformatic analysis is in progress.

Future Research Plans

Determination of the association of gastric microbiota with clinical outcome of *H. pylori* infection

Determination of the association of oral microbiota with clinical outcome of tobacco chewing habit

PUBLICATIONS

Baidya, A. K., Bhattacharya, S., and Chowdhury, R. (2015) Role of the Flagellar Hook-Length Control Protein FliK and sigma28 in *cagA* Expression in Gastric Cell-Adhered *Helicobacter pylori*. *J Infect Dis* **211**, 1779-1789

CONFERENCES / WORKSHOPS

Number of abstract International: 1

Dr. Rupak K. Bhadra

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Molecular dissection of the regulatory mechanisms under nutritional and other stresses in *Vibrio cholerae*

Participants

JRF: Quoelee Biswas

SRF: Pallabi Basu, Dipayan Rakhsit

RA: Dr. Mousumi Saha

Project Assistant: Shib Prasad Sharma

Technician: Pratap Chandra Koyal

Background

Bacterial pathogens constantly face numerous environmental stresses both under *in vitro* and *in vivo* conditions. Our group is working on the regulation of nutritional stresses using the human cholera pathogen *Vibrio cholerae* as a model. Nutritional stress in bacteria evokes stringent response (SR), which is a global regulatory mechanism controlling various gene regulatory circuits working towards the survival mode of the organism. SR is efficiently managed by the generation of two intracellular small signaling molecules, pppGpp and ppGpp, together called (p)ppGpp. We have functionally characterized most of the genes, namely, *relA*, *spoT*, *cgtA*, *relV*, *dksA* and *gppA* of *V. cholerae*, which are involved intricately in managing the SR of this pathogen under amino acid, glucose or fatty acid starvation. The *relV* gene was discovered in this lab and it codes for the (p)ppGpp synthetase enzyme RelV. Homology modeling and bioinformatics analysis of RelV is shown in **Fig. 1**. (p)ppGpp binds with the RNA polymerase (RNAP) enzyme and regulates transcription of several genes either positively or negatively so that cells can enter into survival mode as long as the stress is there. However, (p)ppGpp needs a 17.5-kDa small protein, called DksA, as a co-factor to exert its control over expression of genes. Interestingly, like (p)ppGpp, DksA also binds with the secondary channel of RNAP and thus, it is an unusual transcription factor. We have shown earlier that *V. cholerae* DksA somehow modulates the virulence gene expression in *V. cholerae*. At present our group is involved in deciphering the molecular mechanisms behind this observation and for this site-directed and other mutational approaches are being taken. This approach may help in dissecting the role of DksA of *V. cholerae* in the regulation of virulence and stringent response.

Aims and Objectives

Mutational analysis of the stringent response regulator protein DksA of *V. cholerae*

Role of DksA and pppGpp/ppGpp in fine regulation of virulence gene expression in *V. cholerae*



Work Achieved

Site directed and deletion analysis of the DksA of *V. cholerae* identified several important amino acids of the protein and critical role played by the C-terminal region of DksA. Analysis of expression of key virulence associated genes indicated that both DksA and pppGpp/ppGpp may play intricate role in fine regulation of expression of virulence factors. Further work is in progress.

Future Research Plans

Further experiments are needed to establish firmly the exact role of the stringent response regulators in controlling virulence as well as their role in survival in environmental conditions. We are involved in functional characterization of the *gppA* gene, which codes for a hydrolase and it is needed to convert pppGpp to ppGpp. Mutants are created and functional assays are in progress.

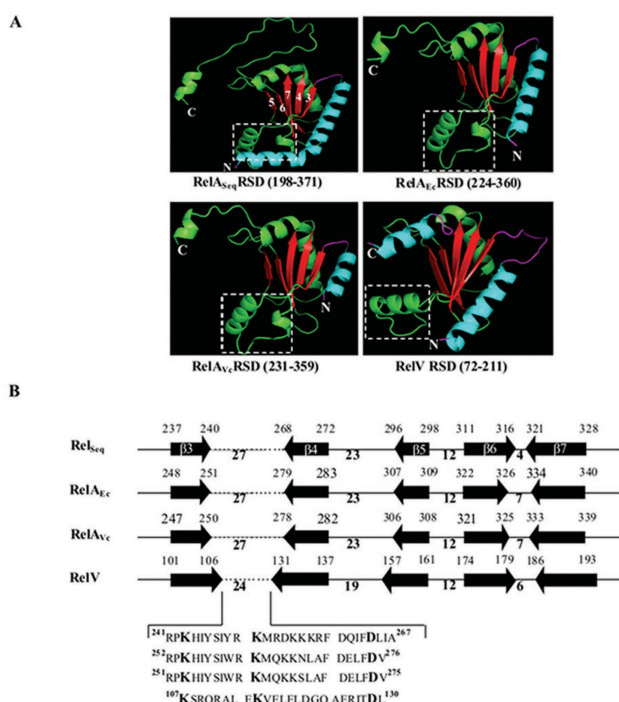


Fig. 1: Structural homology modelling and bioinformatics analysis of RelV.

(A) Comparative homology modelling of RelA-SpoT domain (RSD) region of RelV, Rel protein of *Streptococcus equisimilis* (Rel_{seq}), RelA of *Escherichia coli* (RelA_{ec}) and *Vibrio cholerae* (RelA_{vc}). The RSD region along with its flanking sequences of each of these enzymes was obtained using KEGG database (www.genome.jp/kegg/) and numbers in the parentheses indicate the number of amino acid residues in each fragment. Each of these amino acid sequences was used for homology modelling through PyMOL (www.pymol.org) using the crystal structure of RelSeq as a reference. The structure of each protein

is homologous with expected β -pleated sheets (red arrows). Directions of arrows indicate their parallel or antiparallel orientation and numbers on arrows of Rel_{seq} indicate β -sheet numbers, which are arranged similarly in RelA_{ec}, RelA_{vc} and RelV proteins as shown. The α -helices within the RSD region are shown in green. The α -helices and β turns outside of the bioinformatically predicted boundary of RSD are shown in cyan and purple, respectively. N and C indicate N- and C-terminal of proteins, respectively. White dashed line box depicts the "catalytic loop" region of each protein, the sequence of which is given in panel 'B'.

(B) Schematic diagram (not drawn to scale) showing only the details of β -pleated sheet regions of RSD. Black arrows indicate β -sheet and the numbers within it as described in panel 'A'. Direction of each arrow indicates their orientation as shown in panel 'A'. Name of each protein has been given in the left margin and they are as described in panel 'A'. Numbers above each arrow indicate their starting and ending amino acid residue position on each β -sheet. Amino acid residues comprising each inter β -sheet are given below the dotted or continuous black line. Dotted line indicates the catalytic loop region shown in panel 'A' and amino acid sequence of each loop of the proteins is shown below following the same order of proteins as mentioned above. Conserved amino acid residues in the loop region are shown in big font size and bold face.

Book Chapter

Shreya Dasgupta, Bhabatosh Das, Pallabi Basu and Rupak K Bhadra (2016) Molecular basis of stringent response in *Vibrio cholerae*. In Stress and Environmental Control of Gene Expression in Bacteria. Wiley-Blackwell Publishers. (Ed. Dr. Frans J. de Bruijn), pp. 507-516.

CONFERENCES / WORKSHOPS

Number of abstract India: 1 International: 2

CONFERENCES / EVENTS ORGANIZED BY CSIR-IICB

17th All India Congress of Cytology and Genetics and the Symposium on "Exploring Genomes: The New Frontier.

22nd -24th December 2015. CSIR-IICB, Kolkata.

Dr. Uday Bandyopadhyay

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Ellagic acid, a dietary polyphenol inhibits tautomerase activity of human macrophage migration inhibitory factor and its pro-inflammatory responses in human peripheral blood mononuclear cells

Participants

JRF: Shubhra J. Saha, Shiladitya Nag, Subhashis Deasharma

SRF: Souvik Sarkar, Somnath Mazumder, Asim A. Siddiqui, Chinmoy Banerjee, Rudranil De

Collaborator(s)

Name of collaborator outside CSIR-IICB

Susanta Adhikari

Department of Chemistry

Calcutta University, West Bengal, India

Background

Nonsteroidal antiinflammatory drugs (NSAIDs) are very common to treat pain and inflammation. NSAID targets cyclooxygenase (COX) and the development of gastric mucosal injury is the main side effect of NSAID therapy. Therefore, identification of new class of antiinflammatory molecule that will not target COX but other proinflammatory target like Macrophage migration inhibitory factor (MIF) is of global demand.

Aims and Objectives

Identification and designing of antiinflammatory molecule targeting Macrophage migration inhibitory factor (MIF).

Structure-activity relationship studies of the identified MIF inhibitor.

Work Achieved

Ellagic acid (EA), a phenolic lactone, inhibited tautomerase activity of human macrophage migration inhibitory factor (MIF) noncompetitively ($K_i = 1.97 \pm 0.7 \mu\text{M}$). The binding of EA to MIF was determined by following the quenching of tryptophan fluorescence. We synthesized several EA derivatives, and their structure-activity relationship studies indicated that the planar conjugated lactone moiety of EA was essential for MIF inhibition. MIF induces nuclear translocation of NF- κ B and chemotaxis of peripheral blood mononuclear cells (PBMCs) to promote inflammation. We were interested in evaluating the effect of EA on nuclear translocation of NF- κ B and chemotactic activity in human PBMCs in the presence of MIF. The results showed that EA inhibited MIF-induced NF- κ B nuclear translocation in PBMCs, as evident from confocal immunofluorescence microscopic data. EA also inhibited MIF-mediated chemotaxis of PBMCs. Thus, we report MIF-inhibitory activity of EA and inhibition of MIF-mediated proinflammatory responses in PBMCs by EA.



Future Research Plans

Synthesis and evaluation of gallic acid-based potent MIF inhibitor as a novel antiinflammatory molecule.

PUBLICATIONS

Sarkar, S., Siddiqui, A. A., Mazumder, S., De, R., Saha, S. J., Banerjee, C., Iqbal, M.S., Adhikari, S., Alam, A., Roy, S. and Bandyopadhyay, U. (2015) Ellagic acid, a dietary polyphenol, inhibits tautomerase activity of human macrophage migration inhibitory factor and Its pro-inflammatory responses in human peripheral blood mononuclear cells. *J. Agric Food Chem.* **63**, 4988-4998

Mahata, B., Banerjee, A., Kundu, M., Bandyopadhyay, U. and Biswas, K. (2015) TALEN mediated targeted editing of GM2/GD2-synthase gene modulates anchorage independent growth by reducing anoikis resistance in mouse tumor cells. *Sci Rep.* **12**, 5: 9048

Iqbal, M. S., Siddiqui, A. A., Alam, A., Goyal, M., Banerjee, C., Sarkar, S., Mazumder, S., De, R., Nag, S., Saha, S. J. and Bandyopadhyay, U. (2016) Expression, purification and characterization of Plasmodium falciparum vacuolar protein sorting 29. *Protein Expr Purif* **120**, 7-15

PATENTS FILED / SEALED

Name Surname: UDAY BANDYOPADHYAY

Patent Title: TRYPTAMINE DERIVATIVES, THEIR PREPARATION AND THEIR USE IN GASTROPATHY

Country: European Patent

Patent No: 2616439

Grant date: 16/12/2015

Co-inventors: Pal Chinmay, Bindu Samik, Adhikari Susanta Sekhar.

Patent filed by: CSIR-IICB

Patent Title: TRYPTAMINE DERIVATIVES, THEIR PREPARATION AND THEIR USE IN GASTROPATHY

Country: Japan

Patent No: 5868980

Grant date: 15/01/2016

Co-inventors: PAL CHINMAY, BINDU SAMIK, ADHIKARI SUSANTA SEKHAR.

Patent filed by: CSIR-IICB

INVITED TALKS

Mitochondria: A subcellular target to prevent non-steroidal anti-inflammatory drug (NSAID)-induced gastric ulcer. Colloquium on Biology.

Indian Association for the Cultivation of Science, on 17 March 2016, Kolkata.

The management and utilization of free heme by malaria parasite for survival and induction of liver dysfunction in host. Satyendralal Das Memorial Lecture:

National Institute of Cholera and Enteric Diseases (NICED) on 29 February 2016. Kolkata.

Gastric ulcer: cause and correction. IAS orientation:

CSIR-Indian Institute of Chemical Biology on 22 January 2016. Kolkata, India

Induction of oxidative stress in Plasmodium falciparum: A potential approach to develop novel antimalarial. Ronald Ross Memorial Oration:

Vidysagar University, Department of Physiology on 23 September 2015. Midnapore, India

Dr. Mita Chatterjee Debnath

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Synthesis, characterization and biological evaluation of $^{99m}\text{Tc}(\text{CO})_3$ -labeled pharmacophores for radiodiagnostic applications

Participants

JRF: Kazi Julekha

SRF: Rinku Baishya, Dipak kumar Nayak, Soumya Ganguly, Raghuvir Gaonkar

Woman Sct: Dr. Kakali De

Project Assistant: Ramkrishna Sen

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Sankha Chattopadhyay

(VECC, Saltlake, Kolkata)

Dr. Satbir Singh Sachdeva

BRIT, Mumbai

Background

Technetium-99m is a transition metal and the most widely used SPECT radionuclide in nuclear medicine that aids in the diagnosis of various medical conditions. The *fac*- $^{99m}\text{Tc}(\text{CO})_3(\text{H}_2\text{O})_3]^+$ core is compact, kinetically inert, bears three readily exchangeable aqua ligands allows labeling of low molecular weight bioactive pharmacophores with full retention of biological activity and specificity.

This laboratory has made significant effort towards the development of $^{99m}\text{Tc}(\text{CO})_3$ -labeled bioactive pharmacophores to be used as diagnostic radiopharmaceuticals for tumor targeting and infection diagnosis.

Aims and Objectives

The aim is to develop novel $^{99m}\text{Tc}(\text{CO})_3$ -based pharmacophores for use in infection diagnosis by scintigraphic imaging, $^{99m}\text{Tc}(\text{CO})_3$ -labeled peptides coupled to bioactive pharmacophores to be used as diagnostic radiopharmaceuticals for tumor targeting. We also tried to understand the coordination behavior of nitrofuryl thiosemicarbazones against the tricarbonyl rhenium(I) precursor.

Work Achieved

In the pursuit of novel pharmacophores for use in infection diagnosis by scintigraphic imaging, we reported the labeling of nitrofuryl thiosemicarbazones and a wide variety of fluoroquinolones with the *fac*- $^{99m}\text{Tc}(\text{CO})_3(\text{H}_2\text{O})_3]^+$ precursor. $^{99m}\text{Tc}(\text{CO})_3$ chelates of methyl, ethyl and phenyl nitrofuryl thiosemicarbazone of varying lipophilicity were prepared and investigated to understand the influence of the physicochemical behavior of the complexes on biological activities in the present study.

A series of thiosemicarbazone complexes were therefore prepared from $\text{Re}(\text{CO})_5\text{Br}$, which proved to be an excellent starting material for the synthesis of tricarbonyl rhenium(I) complexes. Both

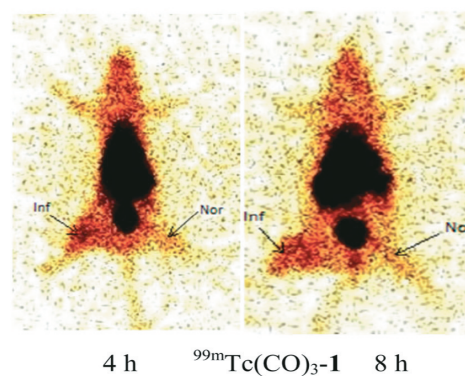


monomeric $[\text{ReBr}(\text{CO})_3\text{-LH}]$ and dimeric $\{[\text{Re}(\text{CO})_3\text{-L}]_2\}$ complexes were produced and characterized by X-ray crystallographic and spectroscopic studies. Electrochemical studies were carried out in order to determine the reduction potential of the nitro aromatic group. Initial evaluations of the $^{99\text{m}}\text{Tc}(\text{CO})_3$ -complexes in *S. aureus* infected rat model were also performed. The potentiality of the $^{99\text{m}}\text{Tc}(\text{CO})_3$ labeled peptide based pharmacophores as tumor targeting agent was evaluated by biodistribution and scintigraphic experiments in tumor bearing mice

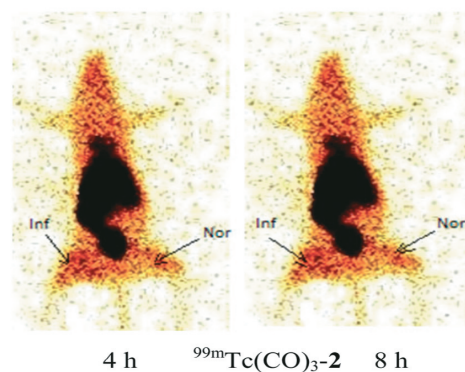
Future Research Plans

This strategy for tumor targeting may also create the opportunity to develop peptide receptor targeted radiotherapy after radiolabeling the pharmacophore with rhenium-188, the β -emitting radionuclide. Bioactive peptide based nanoparticulated drug delivery system for potential application in cancer therapy could also be developed and target ability of the formulation will be verified by $^{99\text{m}}\text{Tc}$ -labeling.

(I)



(II)



(III)

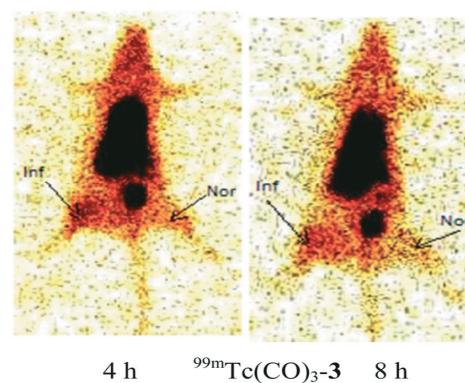
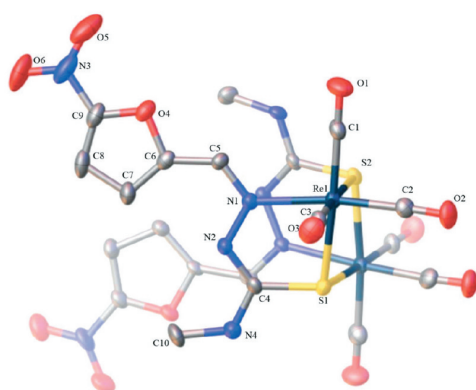
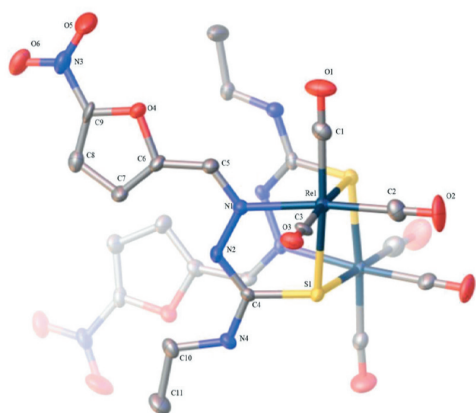


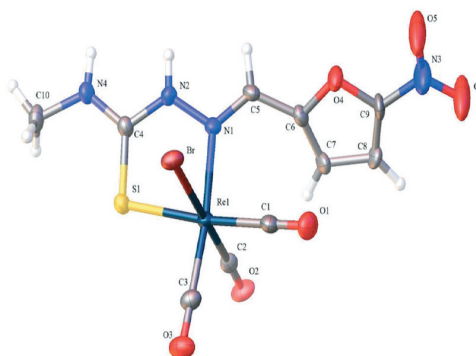
Fig. 1: Scintigraphic images of $^{99\text{m}}\text{Tc}(\text{CO})_3$ -thiosemicarbazone in *S. aureus* Infected rats at 4 h and 8 h post-injection(i. v.): (I) $^{99\text{m}}\text{Tc}(\text{CO})_3\text{-1}$, (II) $^{99\text{m}}\text{Tc}(\text{CO})_3\text{-2}$, (III) $^{99\text{m}}\text{Tc}(\text{CO})_3\text{-3}$.



(a) $[\text{Re}(\text{CO})_3\text{-1}]_2$



(b) $[\text{Re}(\text{CO})_3\text{-2}]_2$



(c) trans-(E)- $\text{ReBr}(\text{CO})_3\text{-1a}$

PUBLICATIONS

Nayak, D.K., Baishya, R., Natarajan, R., Sen, T., and Debnath, M. C. (2015) Tricarbonyl $^{99\text{m}}\text{Tc}(\text{I})$ and $\text{Re}(\text{I})$ -thiosemicarbazone complexes: synthesis, characterization and biological evaluation for targeting bacterial infection. *Dalton Trans* **44**, 16136-16148

Gaonkar, R. H., Ganguly, S., Baishya, R., Dewanjee, S., Sinha, S., Gupta, A., and Debnath, M. C. (2016) Exploring the Potential of $(^{99\text{m}}\text{Tc}(\text{CO})_3\text{-Labeled Triazolyl Peptides for Tumor Diagnosis. Cancer Biother Radiopharm}$ **31**, 110-117

EXTRAMURAL FUNDING

Evaluation of the therapeutic efficacy of liposomal and nanoparticulated flavonoids in combating oxidative hepatocellular degeneration. July 2013 to March 2017 (DAE, BRNS-Mumbai, India)

In vitro and in vivo evaluation of $^{99\text{m}}\text{Tc}(\text{CO})_3\text{-labelled RGD conjugated bioreductive pharmacophore and nucleoside analogue for potential use as tumor targeted SPECT radiopharmaceuticals}$ September 2015 to August 2018. SERB, DST-India

CONFERENCES / WORKSHOPS

Number of abstract India: 2

CONFERENCES / EVENTS ORGANIZED BY CSIR-IICB

Organised a Training Programme on Laboratory Safety: Biosafety, Chemical Safety Radiation Safety and Fire Safety on 1 February 2016, J. C. Roy Auditorium, CSIR-Indian Institute of Chemical Biology.

Fig. 2: Molecular structure of $\text{Re}(\text{CO})_3\text{-thiosemicarbazone}$ complexes, showing 30% probability displacement ellipsoids: (a) $[\text{Re}(\text{CO})_3\text{-1}]_2$, (b) $[\text{Re}(\text{CO})_3\text{-2}]_2$, (c) trans-(E)- $\text{ReBr}(\text{CO})_3\text{-1a}$

Dr. Subhajit Biswas

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Epidemiology and molecular characterization of hepatitis B virus (HBV) infections especially occult HBV infections (OBIs) in India

Participants

JRF: Sayantani Bhowmik

Background

OBI is defined as low level of HBV DNA in the liver or blood plasma with **undetectable** HBV surface antigen (HBsAg, the antigenic part of HBV structural proteins) outside the sero-conversion window period. OBIs have been mostly reported from asymptomatic carriers. Therefore, the risk of blood transfusion from OBI donors needs to be properly evaluated especially in context of developing countries like India as the incidence of OBI is on the rise and donors' blood is commonly screened only for HBsAg. Significant research is warranted to determine the molecular aetiology and develop detail understanding of the pathogenesis of OBI in the context of the Indian sub-continent.

Aims and Objectives

To study the epidemiology of OBI.

To identify and characterize prevalent S protein mutations responsible for "immune escape" or excretion defect thereby contributing to OBI genesis.

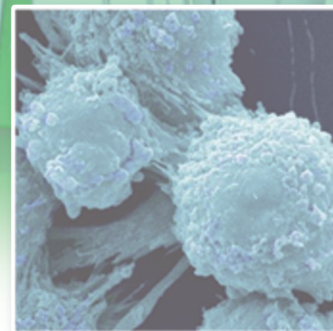
Work Achieved

Baseline research has been initiated and is in full progress.

Future Research Plans

Develop strategy of rapid identification/molecular characterization and management of OBI cases.

Cancer Biology & Inflammatory Disorders Division



Dr. Chitra Mandal, Dr. Santu Bandyopadhyay (Head till August 2015), Dr. Samit Chattopadhyay, Dr. Susanta Roychowdhury, Dr. Padma Das, Dr. Snehasikta Swarnakar (Head from September 2015 onwards), Dr. Mrinal K. Ghosh, Dr. Malini Sen, Dr. Dipyaman Ganguly, Dr. Amitava Sengupta, Dr. Shila Elizabeth Besra and Dr. Krishna Das Saha

Cancer Biology & Inflammatory Disorders (CBID) division is a vibrant research group comprising of great combination of expert scientists contributing remarkably in the cutting-edge research in both basic and applied work on cancer biology, inflammation biology and overlapping areas. Some of cancer research work received huge appreciation from scientific community as featured in journals of Nature Publishing group. Cancer cell has a unique character involving abnormal growth with the potential to invade remote parts of the body that is inherent in its very origin. Beyond the unique biology of cancer cells, the relationship of cancer and chronic inflammation has gained immense importance in past decade or so. Cellular signalling pathways get extensively rewired with dysregulation of important cellular growth regulators during inflammation. Moreover, cancer immunosurveillance (the interaction between cancer and the host immune system) and cancer immunotherapy are emerging issues engaging lot of research effort worldwide. IICB scientists of CBID divisions are taking into consideration all these different aspect of the relevant areas and conducting their coordinated research programs in a target based approach. The division aims at taking a very futuristic approach to address basic mechanism of initiation and progression of

cancer and chronic inflammation. The overall goal is to eventually provide proper therapies to patients with cellular malignancies.

CBID scientists are engaged in studying cancer cells from different tissue origins at molecular and cellular levels by different approaches, e.g. transcriptomic, genomics, metabolomics, proteomic, glycoproteomic and bioinformatic. The other focuses includes new therapeutics using natural products and target based synthetic peptides against cancer as well as novel targeted delivery approach for anti-cancer molecules. Biology of cancer initiating stem cells, both in solid tumors and in hematologic malignancies are being investigated by multiple CBID laboratories. In addition, contribution in the field of epigenetic regulation, transcription, chromatin biology with potential translational applications in cancer, AIDS and inflammatory diseases are noteworthy. Laboratories in the divisions are working in the following specialised areas:

- Genetic association and patho physiological role of matrix metalloproteases in gastric, ovarian and oral cancers are being investigated. Identifying novel target for new generation of anticancer therapy sourced from natural product or rationally designed small molecule is being undertaken. Exploring prognostic and diagnostic biomarker for specific clinical context in cancer and inflammatory disorders is being carried on. Underpinning the key pathogenic node in chronic inflammatory disorder to develop target based therapy and investigating signalling dynamics underlying endothelial mesenchymal transition during endometriosis has also been focused.



- Efforts are ongoing to investigate functional role of a novel protein SMAR1 in regulating the activity of tumour suppressor protein during cancer cell survival and growth. In terms of elucidating specific pathways involved in cancer metastasis, the role of MAR binding proteins in regulating alternative splicing of cellular receptor is being explored. Moreover, the implications of small compounds to treat Inflammatory Bowel Diseases (IBD) through balancing between Th17 and Treg ; and understanding the chromatin dynamics of T helper cell differentiation in inflammatory diseases are few other important research areas.
- Identification of probable target proteins and signalling dynamics are being carried out to understand cancer biology and pathogenesis, with the hope to discover the new generation chemotherapeutics. Efforts are also being made in understanding crosstalk among Wnt/ β -catenin, EGFR, ER and NF- κ B signalling in cancer, regulation of RNA helicases, Ubiquitinases and deubiquitinases in oncogenesis. Furthermore, research are being undertaken to study the role of casein kinase II (CK2) in modulation of cancer cell signaling.
- Role of specific signaling pathways (e.g. Wnt signaling) and particular immune cells (dendritic cells) and cytokines (e.g. type I interferons) in chronic inflammation is being investigated which can provide unique insight in specific clinical contexts of inflammatory disorders as well as in the overlapping areas with cancer biology.
- Deciphering cancer immunosurveillance mechanisms and immune architecture of tumor microenvironment are being pursued to gain insights into the key regulatory pathways to explore key immunotherapeutic targets. Development of autoimmunity-inspired immunomodulatory therapy against solid cancer and importance of dendritic cells in the clinical context of autoimmunity are major challenges too.
- Investigation is being carried out to understand cell-autonomous and non-cell-autonomous molecular determinants that regulate hematopoietic stem cells (HSC) self-renewal, differentiation and interaction with hematopoietic microenvironment. Scientists are actively engaged on identifying molecular epigenetic regulators involved in leukemic hematopoiesis and the role of bone marrow mesenchymal stromal microenvironment in leukemic hematopoiesis.
- An integrated approach for identifying lead molecules (novel molecules from natural sources or rationally designed synthetic molecules with target-specific activities) having anti-cancer and anti-inflammatory properties, is also actively pursued. Research are being highlighted to improve therapeutic and pharmacological properties of lead compound via nanoformulation and their potentiality are being examined in vitro and in vivo cancer model.
- Logistic and knowledge-based collaborations are ongoing with different clinical institutions in the city and beyond, for joint venture in translational research endeavours.

Dr. Chitra Mandal

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Glycobiological approach in understanding pathogenic infections and cancer: development of therapeutics from medicinal plant

Participants

JRF: Shalini Nath, Susmita Mondal, Kaustuv Mukherjee, Joyshree Karmakar

SRF: Saptarshi Roy, Arup Bag, Devawati Dutta, Eswara Murali Satyavarapu, Samarpan Maiti

RA: Dr. Manjusha Chakrobarty

T / O: Asish Mullick

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Avinash Sonawane

Associate Professor, KIIT University, Bhubaneswar, India

Dr. Chhabinath Mandal

Course Coordinator, NIPER, Kolkata

Name of collaborator within CSIR-IICB

Dr. Biswadip Banerji & Dr. Chinmay Chowdhury

Organic and Medicinal Chemistry Division

Dr. Nahid Ali

Infectious Diseases & Immunology Division

Dr. Saikat Chakrabarti

Structural Biology and Bioinformatics Division

Background

Although proteins, lipids, nucleic acids are the main constituents of a cell, sugar chains or glycans, which are ubiquitously found on cell surfaces, were mostly ignored due to the difficulty in analyzing and studying them. Alongside, there is a demand for low cost therapeutics.

Aims and Objectives

The main aim of our laboratory is to understand the mystery of glycosylation of biomolecules with special emphasis on the role of sialoglycoconjugates in three different models and its potential applications in disease management, its specificity and recognition in immune responses mainly in the field of cancer biology/tumor immunology and host-pathogen interactions dealing with visceral leishmaniasis (VL) and *Pseudomonas aeruginosa* (PA). We have analyzed cancer, VL and PA-associated biomolecules by exploring the diversity of sialylation with a common set of questions through proteomic, bioinformatic and glycobiological aspects.

Additionally, another important aim of our laboratory is to deliver low cost affordable healthcare to all using India's vast resources of medicinal plants.

Work Achieved

We have established a novel sialic acids-mediated pathway utilized by *Leishmania* for successful infection (MS under revision).

We are analyzing the impact of PA-associated sialylation in its interaction with macrophages and dendritic cells (DBT project granted).

We have observed alteration of glycosylation machineries responsible for enhanced survival pathways in pancreatic cancer.

We have established an herbal molecule (CM-5) from an edible plant. It induced apoptosis both *in vitro* and *in vivo* in different types of cancer including glioma (GBM), pancreatic, ovarian and



cervical cancer along with cancer stem like cells with varieties of oncogenic mutations. We found that our compound is inhibiting mitochondrial complex III and thus increased cellular reactive oxygen species which in turn lead to inhibition of mTORC1/2 in GBM. (Grant approved, DST).

We have developed an herbal molecule as anti-leishmanial agent in VL infection (US patent filed, ICMR Grant technically approved).

Future Research Plans

Preparation of CM-5 and/or CM-5 enriched fraction for commercialization

In depth studies of how altered glycosylation is helping cancer cells to escape from apoptosis in pancreatic cancer

System biology approach to understand the cross talking with cellular signaling for target identification in GBM.

The role of glycosylation in host-pathogen interaction (VL and PA)

PUBLICATIONS

Mandal A, Das S, Roy S, Ghosh AK, Sardar AH, Verma S, Saini S, Singh R, Abhishek K, Kumar A, Mandal Chitra, Das P. (2016) Deprivation of L-Arginine Induces Oxidative Stress Mediated Apoptosis in *Leishmania donovani* Promastigotes: Contribution of the Polyamine Pathway. *PLoS Negl Trop Dis*. **10**, 1371-1395

Das MR, Bag AK, Saha S, Ghosh A, Dey SK, Das P, Mandal Chitra, Ray S, Chakrabarti S, Ray M, Jana SS. (2016) Molecular association of glucose-6-phosphate isomerase and pyruvate kinase M2 with glyceraldehyde-3-phosphate dehydrogenase in cancer cells. *BMC Cancer* **16**, 152-163

Aparajita Pal, Dipa Talukdar, Anirban Roy, Subhankar Ray, Asish Mallick, Chitra Mandal, Manju Ray (2015) Nanofabrication of methylglyoxal with chitosan biopolymer: a potential tool for enhancement of its anticancer effect" *Int J Nanomed* **10**, 3499-3518

PATENTS FILED

Name Surname SAPTARSHI ROY, ESWARA MURALI SATYAVARAPU, MD. SHADAB, SUSANTA KAR, NAHID ALI, CHITRA MANDAL.

Patent Title: ANTI-LEISHMANIAL ACTIVITY OF A NATURAL CARBAZOL ALKALOID MOLECULE MAHANINE: ENHANCED

EFFICACY AND DRUG DELIVERY THROUGH LIPOSOMAL FORMULATION.

Country: US Patent Filed (Ref. No. 0232NF2015).

Date filed / granted September 2015.

Patent filed by CSIR-IICB & CSIR-CDRI.

AWARDS / HONOURS / MEMBERSHIPS

Awarded Distinguished Biotechnology Research Professor (2016) by DBT

Five Years Extension of Sir J.C. Bose Fellowship (2016-2020) by DST

Sir J. C. Bose Annual Memorial Award (2016) by Indian Science Monitor

Dr. Jan Chandra Ghosh Memorial lecture Award (2015) by The Science Association of Bengal

Memberships

Nominated as an expert on behalf of the INSA to be a member of the International Organizing Committee, (IOC) to organize an International Symposium on "Global Health Issues in Asia" scheduled on 19-21 October 2015 in Daejeon, Korea

Invited to be a member of the Glycobiology editorial board during 2016-2010 (A prestigious International journal in the field)

Member of the Sectional Committee for Medicine to serve Indian Academy of Sciences since 2016 onwards

Serving as a "Core Member" of the committee in the area of Life Sciences of the of the SERB (DST) 2016 onwards

Serving as a "Co-opted Member" of the committee on Health Sciences of SERB (DST) 2016 onwards

EXTRAMURAL FUNDING

Evaluation of antileukemic and immunogenicity properties of engineered Escherichia coli asparaginase-II for the treatment of acute lymphatic leukemia in preclinical model, January 2016-2019, DST, India

Targeting HSP-90 as cancer therapy: Design and synthesis of mahanine-derived Second-Generation lead molecules. March 2016-February 2019, DST, India

Role of sialylated glycan on Pseudomonas aeruginosa in interaction with innate immune cells: A glyco-proteomics approach. Recommended for funding, DBT, India

Anti-leishmanial activity of a novel carbazol alkaloid mahanine: its mechanism of action and drug delivery through liposomal formulation. Technically approved, ICMR India

CONFERENCES / WORKSHOPS

Number of abstracts	India:	5
	International:	2

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Tumor Suppressor SMAR1 mediates global gene regulation performing multiple functions

Participants

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Dr. Siddhartha Roy

Background

Nuclear matrix and its associated proteins provides structural framework to the nucleus tethering several proteins that are important for many processes like transcription, splicing, DNA repair etc. SMAR1, a nuclear matrix binding protein belongs to a family of MAR binding proteins (MARBP). Earlier studies from our lab have shown that SMAR1 is a chromatin modifier that recruits HDAC1 to the promoter and brings about modulation of the activity of promoters like that of Cyclin D1, Bax, Puma etc. that are involved in maintaining cellular fate. Recently, functions of SMAR1 as a stress response protein is well elucidated wherein SMAR1 is reported to modulate the acetylation status of DNA damage repair protein Ku70 by interacting with HDAC6 (Chaudhary et. al., *Cell Death and Disease*, 2014). Additionally, SMAR1 is reported to negatively regulate the alternative splicing by modulating the acetylation status of Sam68 by recruiting HDAC6 (Nakka et. al. 2015, PNAS). Recently, we also showed that the switch between effector T cells and regulatory T cells is governed by SMAR1. T cell polarization is controlled by SMAR1 as SMAR1 allows the T cells to commit to Th2 lineage and suppresses the Th1 and Th17 lineage commitment (Chemmannur et al., *Mucosal Immunology*, 2015). FoxP3, a major factor in Treg cell differentiation is controlled by SMAR1 and this maintains the fine balance between Treg and Th17 phenotype (Mirlekar et.al. *Mucosal Immunology*, 2015). The ChIP-seq analysis predicted a plethora of SMAR1 gene targets, to which SMAR1 can bind in the presence and absence of p53. A significant number of genes, however, favor the binding of SMAR1 irrespective of p53 status. (Mathai et. al., under revision in *Scientific Reports*).



Aims and Objectives

Role of SMAR1 in Wnt signaling pathway

Metabolic regulation of epigenetic changes in tumor suppressor gene SMAR1

Proteomic profiling of SMAR1 regulated genes and their implication in tumorigenesis, antigen processing and presentation.

Work Achieved

Role of SMAR1 in Wnt signaling pathway: In cancer cells there is aberrant activation of signaling pathways that help maintaining their cancerous phenotype and their proliferation potential. One such signaling cascade is Wnt signaling. Few tumor suppressors that negatively regulate Wnt signaling have been reported so far in mammals. TCF4/LEF1 can act both as an activator or repressor depending on their binding to β -catenin. Studies have reported that when HDACs bind to LEF1 there is repression of the gene thus regulating the down-stream targets. Active Wntsignalling / β -catenin pathway results in breast, colon, prostate and liver cancers. Tumor suppressors like GSK 3 β , Adenomatous Polyposis Coli (APC), Axin, etc. check β -catenin ubiquitin degradations mediated by β -Trcp1. Factors like Wnt ligands, DKK, CDC20, APC/C, mutation in β -catenin degradations sites stabilize β -catenin expressions resulting in poor prognosis. For the first time SMAR1 (Scaffold Matrix Attachment Binding Protein 1), a tumor suppressor has been shown to regulate β -catenin negatively through transcriptional repression. Reduced expression of SMAR1 through ubiquitin degradation in colon cancers upon active Wnt 3a signalling is the precursor for enhanced β -catenin stability.

Our studies have revealed that SMAR1 is a negative regulator of β -catenin and may prevent the Wnt

signaling activation. We found that SMAR1 negatively regulate β -catenin and thus prevent activation of Wnt signaling. Our findings also show that a Wnt 3a activation result in the down-regulation of SMAR1 and over-expression of SMAR1 was found to revert the effect. CDC20 has been reported to be stabilized upon Wnt 3a activation and is also responsible for SMAR1 degradation. CDC20 recruits E3 ligase to SMAR1 and results in SMAR1 degradations leading to its instability. During active Wnt signaling CDC20 gets stabilized and results in SMAR1 degradations. We found that blocking the ubiquitin sites in SMAR1 using peptides (AT-01C) prevented its degradation that attenuated β -catenin expression. This segment of peptide is derived from MPT63, a secretory protein of *Mycobacterium tuberculosis*. Isothermal titration calorimetry and Autodock experiments suggested that AT-01C interacts with SMAR1. Hence, prevention of SMAR1 degradation using small molecule compounds or peptides can serve as a potential therapeutics in cancer. Since SMAR1 suppresses β -catenin, we checked LEF1/TCF4 promoter binding of β -catenin.

We are reporting for the first time that SMAR1, a tumor suppressor protein regulates β -catenin at the transcriptional level. Most of the reports have shown to regulate β -catenin either by degradation or by preventing its binding to TCF4/LEF1. Inhibition of Wnt signaling pathway is an important event in controlling some of the cancers where Wnt/ β -catenin is very active.

Metabolic regulation of epigenetic changes in tumor suppressor SMAR1: Rapidly proliferating cells show significant increase in glycolysis known as the “Warburg effect”. The role of SMAR1 as a stress response protein in repair of DNA damage was already reported from our lab. A rapidly



proliferating cancer cell has to circumvent many stresses in order to survive and continue proliferation one of which is the metabolic stress. A cancer cell has high energy requirements because of their highly proliferative nature thus it was interesting to check the effect of glucose deprivation on levels of SMAR1.

Epigenetic regulation of a gene is primarily obtained by methylation of the DNA stretch and also the methylation and acetylation of histones. Methylation of cytosine residue is mainly observed where a methyl group gets attached to cytosine. This is brought about by the DNMTs; mainly Dnmt1 which is a maintenance methyl transferase, Dnmt3a and Dnmt3b which are the de-novo DNMTs. Upon methylation several methyl binding proteins like MeCP2, Sin3a etc. come and bind to the methylated cytosine moieties on the DNA. Methylation of the promoter region causes two major events; firstly it recruits HDACs which de-acetylates the histone. This causes the second change i.e, change in the chromatin conformation which makes the DNA inaccessible to the RNA polymerase machinery. SAM, the only methyl group donor, is generated primarily through the folate pathway in normal cells but in case of malignant cells where glycolysis is increased multifold, SAM is also generated through the one-carbon metabolism pathway as an offshoot to the glycolysis pathway.

We showed that the levels of SMAR1 can be altered by changing the nutrient supply to the cell i.e, by changing the cellular metabolism which in turn causes the change in the methylation status of the *SMAR1* promoter. We found that MeCP2 interacts with both HDAC1 and HDAC2 in untreated cells. We also observed that in untreated cells there is

methylation of H3K9 and H3K27 and these methylation marks are lost upon glucose deprivation. Apart from these findings we also observed an overall decrease in the levels of HDAC1 and HDAC2 upon glucose deprivation. We can speculate that since the overall levels of the HDACs go down and since there is a loss of methylation, together it causes the transcriptional activation of the tumor suppressor gene *SMAR1*. To validate this further we treated the cells with Trichostatin A which is a general HDAC inhibitor and this treatment allowed transcription of *SMAR1* gene.

Proteomic profiling of SMAR1 regulated genes and their implication in tumorigenesis and antigen processing and presentation: SMAR1 triggers cell cycle arrest and apoptosis through transcriptional regulation of specific target genes. SMAR1-dependent regulation of the up-regulated protein calnexin was further studied. To delineate the mechanism of how SMAR1 regulates calnexin gene expression, a bioinformatics analysis of calnexin promoter was performed. Interestingly SMAR1 and GATA2 binding sites were observed proximal to each other in calnexin promoter. Chromatin immunoprecipitation confirms the binding of SMAR1 and GATA2 on calnexin promoter. SMAR1 forms triple complex with GATA2 and HDAC1. Recruitment of HDAC1 results in deacetylation of GATA2, under deacetylated condition GATA2 acts as repressor resulting in downregulation of calnexin gene. This study mechanistically highlights the coordinated regulation of calnexin gene by SMAR1 and GATA2. SMAR1 controls the expression of these proteins suggesting direct role of SMAR1 in ER homeostasis.

We also found SMAR1 as one of the ER responsive protein. Further we are checking the role of SMAR1



in MCF7 resistance against tunicamycin and antigen processing and presentation. Preliminary findings indicates mycobacterium antigen ESAT6 downregulates SMAR1 and at the mean time overexpression of Calnexin suggesting its role in antigen processing and presentation. Thus, this study reveals protein targets of SMAR1 and highlights the role of SMAR1 during various biological responses.

Future Research Plans

Maintenance of cellular homeostasis through transcriptional regulation of SMAR1: Its role in zebrafishembryonic development

Regulation of catalytic subunit of telomerase by SMAR1

Role of SMAR1 in regulation alternative splicing of metabolic genes PKM1 and PKM2

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Ali, F., A. A. H., Taye, N., Mogare, D. G., Chattopadhyay, S., and Das, A. (2016) Specific receptor for hydrazine: mapping the in situ release of hydrazine in live cells and in an in vitro enzymatic assay. *Chem Commun (Camb)* **52**, 6166-6169

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AWARDS / HONOURS / MEMBERSHIPS

Fellow of 'The World Academy of Sciences (TWAS) 2015 for the advancement of science in developing countries

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Role of mutant p53 target gene *EFNB2* in human cancer: a chemical biology approach to overcome drug resistance

Participants

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Structural Biology and Bioinformatics Division

Background

The tumor suppressor gene *TP53* is somatically mutated in almost 50% of the human cancers. The majority of *TP53* mutations observed in human cancers abrogate the sequence-specific DNA-binding activity toward the wild-type p53 responsive element. It is increasingly evident that many mutant p53 forms not only lose their tumor suppressive function but also gain new oncogenic properties that are independent of wild-type p53. This notion has been termed as the *gain-of-function (GOF) hypothesis*. Through Bioinformatic analysis and ChIP-seq analysis we have identified several GOF mutant p53 target genes. One such putative target gene is *EFNB2*. We studied the mechanism of transcriptional regulation of *EFNB2* gene by various GOF mutant p53 proteins. Also, investigated whether such regulation affects the chemoresistance property of cancer cells and, if so, the mechanism of regulation of chemoresistance.

Aims and Objectives

How does Mutant p53 control the expression of *EFNB2* in response to drug?

Why does knockdown of Ephrin-B2 rescues chemosensitivity of the tumor cells?

Design effective RNAi and peptide mimetic molecules against Ephrin-B2 to augment chemosensitivity of mutant p53 bearing tumors.

Work Achieved

Chemo-resistance represents a major obstacle in the successful treatment of human cancer. Human tumours harboring missense mutations in the *TP53* gene are positively correlated with increased incidence of chemo-resistance. We performed a bio-informatic and genomic analysis to identify potential gene(s) that may contribute to the



chemoresistance property of mutant p53 bearing cancer cells. The Trans-membrane protein ephrin-B2 encoded by *EFNB2* gene that interacts with Eph family of receptor Tyrosine Kinases was found to be one important candidate. The Eph/Ephrin interactions are important in various cellular processes including development, nervous system patterning (axon guidance), angiogenesis, and cancer. The ephrin-B2 has been found to be over-expressed in many human primary tumor tissues. We provide evidence that GOF mutant p53 transcriptionally activates *EFNB2* expression in the chemo-resistant cancer cells in response to DNA damaging chemotherapeutic drugs. We further show that the mutant p53 in association with NF-Y complex transcriptionally upregulates *EFNB2* expression. We also showed that p300 mediated acetylation of mutant p53 protein facilitated the recruitment of GOF mutant p53 on the *EFNB2* promoter. Moreover, we show that sensitivity of mutant p53 cell lines to many DNA damaging drugs can be restored by knockdown of *EFNB2* expression. We established that GOF mutant p53 mediated upregulation of ephrinB2 induces ABCG2 expression, promotes tumorigenesis through the Src-ERK pathway, and drives EMT via the Src-FAK pathway. Thus, targeting ephrin-B2, has the potential to eradicate drug-resistant cells when applied in conjunction with other effective treatments

Future Research Plans

We are developing following agents that may inhibit ephrin B2: (a) liposome encapsulated *EFNB2* RNAi molecule; (b) peptidomimetics targeting *EFNB2* and (c) small molecule targeting *EFNB2*-EPH interaction. We are also validating the expression of Ephrin B2 as predictive biomarker for the chemo-resistance of mutant p53 harbouring cancer.

PUBLICATIONS

- Alam, S. K., Yadav, V. K. Bajaj, S. Datta, A. Dutta, S. K. Bhattacharyya, M. Bhattacharya, S. Debnath, S. Roy, S. Boardman, L. A. Smyrk, T. C. Molina, J. R. Chakrabarti, S. Chowdhury, S. Mukhopadhyay, D. and Roychoudhury, S. (2016) DNA damage-induced ephrin-B2 reverse signaling promotes chemoresistance and drives EMT in colorectal carcinoma harboring mutant p53. *Cell Death Differentiation* **23**,707-722
- Ghuwalewala, S. Ghatak, D. Das, P. Dey, S. Sarkar, S. Alam, N. Panda, C. K. and Roychoudhury, S. (2016) CD44(high)CD24(low) molecular signature determines the Cancer Stem Cell and EMT phenotype in Oral Squamous Cell Carcinoma. *Stem Cell Res* **16**, 405-417
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Evaluation of molecular mechanism towards apoptotic and autophagic effects of betulinic acid analogue and its nanocapsulated delivery

Participants

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Collaborator(s)

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Background

Naturally occurring substances play an important role in drug discovery and development. In fact, a majority of anticancer and anti-infectious agents are of natural origin. Despite the obvious benefits of chemo treatment, which is an effective drug treatment designed to kill cancer cells in individuals, there are several adverse side effects to this form of treatment that should be considered in every cancer treatment strategy as they tend to have various therapeutic effects and patients may ultimately die due to multiple organ failure. This sets out the need to explore alternative therapeutic agents. Today, numerous natural compounds extracted from plants source are reported to possess growth inhibitory effects on various tumor cells. Therefore, it has been found that some medicinal plants are potential sources for chemical compounds having useful biological activity of great diversity and the bioactive compounds obtained from them are normally non-toxic or less toxic to humans. As compared to synthetic compounds, natural compounds have more structural diversity and novelty and many natural chemicals are able to interact with proteins, and other biological molecules. Also it is more complex in structure than synthetic molecules. This complexity allows for more selective binding to targets.

Aims and Objectives

Assessment of in vitro Anti-proliferative activity of Betulinic Acid analogues and Identification of the most potent compound.

Analysis of the apoptotic mode of cell death.

Evaluation of autophagy pathway.

Preparation and characterization of nanoencapsulated lead compound and their study of Anti-proliferative activity.

Work Achieved

Betulinic acid, a member of pentacyclic triterpenes has shown important biological activities and most



interestingly anticancer property. To overcome its poor aqueous solubility and low bioavailability, structural modifications of its functional groups are made to generate novel lead(s) having better efficacy and less toxicity than the parent compound. Anticancer activity of the modified compounds was evaluated against different cancer cells and normal human PBMC by MTT assay. Analogue **2c** was found as the most potent inhibitor of HT-29 cell line with IC_{50} value $14.9 \mu M$. Anticancer activity of **2c** was also measured against another Human colon adenocarcinoma cell line, HCT-15 and interestingly IC_{50} value was found $21.6 \mu M$. As **2c** deciphering lowest IC_{50} against HT-29, its role as an inducer of apoptosis was investigated in HT-29 cell line only, by various key regulatory experiments of apoptotic pathway. Elevated level of ROS generation, activation of caspase 3 and caspase 9, DNA fragmentation, higher expression of Bax and Bad, lower expression of Bcl-2 and Bcl-xl, and increased level of Bax/Bcl-xl ratio indicate **2c** as an promising inducer of apoptosis that specifically follows the mitochondria dependent pathway. Furthermore, bio-physical studies indicate that compound **2c** acts as a minor groove binder to the DNA. Autophagy, another mode of PCD, was investigated as apoptosis is always not to be considered as the only mechanism underlying cell's death. Recent studies have also shown that a regulation exists between the UPS and autophagy, the two cellular catabolic systems. So, proteasomal degradation pathway was next studied to investigate whole catabolic pathway after e of **2c** on HT-29 cells. The lead compound, Betulinic acid analogue **2c** was found to induce autophagy through increased percentage of autophagosome formation and that was evaluated by using Cyto-ID Green probes, alteration in the expression level of autophagic proteins by western blot analysis, upregulation of mRNA expression level of Beclin 1 and LC3B, the marker proteins engaged in autophagy initiation and autophagy flux progression respectively and time dependent enhancement of autophagic vacuoles formation

by fluorescence staining with AVO and MDC in HT-29 cells. On treatment with **2c** the conversion of LC3A to LC3B was increased appreciably while p62 expression level was decreased indicating an increased autophagic flux formation. The expression level of Beclin-1, Atg 5, Atg 7, LC3B and p62 was reconfirmed through Confocal Laser Scanning Microscopy in **2c** treated HT-29 cells. Formation of autophagolysosome was confirmed by colocalization of various autophagic components. Concordantly, proteasomal degradation pathway was found to be downregulated. Finally, study of crosstalk in between autophagy and apoptosis revealed their independent occurrence upon **2c** exploration. To enhance the therapeutic efficacy and drug availability to the required zone, lead molecule Betulinic acid analogue, **2c** was encapsulated with PLGA by a modified emulsion-diffusion-evaporation method and it revealed a better efficacy than that of the compound to its free form with IC_{50} $7.33 \mu M$ against HT-29 cell line. Nanocapsulated **2c** was found to induce apoptosis in HT-29 cells more efficiently than that of free drug (**2c**). So, all these observations indicating that **2c** may prove itself to be a potent therapeutic agent against colon carcinoma.

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Dr. Snehasikta Swarnakar



Involvement of matrix metalloproteinases in ethanol-induced gastric ulcer: effect of black tea

Participants

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Sr. Technician: Anirban Manna

Collaborator(s)

Name of collaborator within CSIR-IICT

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Background

The diverse etiological factors are involved in gastric ulcer and its healing is a complex mechanism. Gastric ulceration develops majorly due to an imbalance between aggressive and cytoprotective factors in stomach involving acid-pepsin secretion, excessive ROS formation, and, cellular regeneration, microvascular dysfunction, prostaglandins, epidermic growth factors secretion etc. In addition, gastric ulceration is associated with dysregulation of ECM remodeling of gastric tissues, where matrix metalloproteinases (MMPs) play a pivotal role. Not only as a stimulant, but tea (*Camelia sinensis*) has also beneficial role in human health for its antioxidant, flavanol, flavonoid and polyphenol contents. We focused on the biochemical mechanism of ethanol-induced gastric ulcer and its prevention by black tea extract in relevance to regulation of MMP-9 and other pro-inflammatory cytokines.

Aims and Objectives

To investigate the role of MMP-9 mediated molecular pathways in gastric inflammation and potential of black tea extract to reduce it.

Also, to understand the interaction between the lead molecule of black tea extract with MMP-9 as well as MMP-2.

Work Achieved

The major finding of our study is that black tea extract shows significant potential in preventing gastric injury induced by ethanol by downregulating the activity as well as expression of MMP-9 and the restoring the balance of MMP-9:TIMP-1 ratio. Data fortified the fact that activity of mitochondrial enzymes and mitochondrial membrane potential are regulated by tea extract pretreatment. Further long term clinical trials are in progress to evaluate above findings.

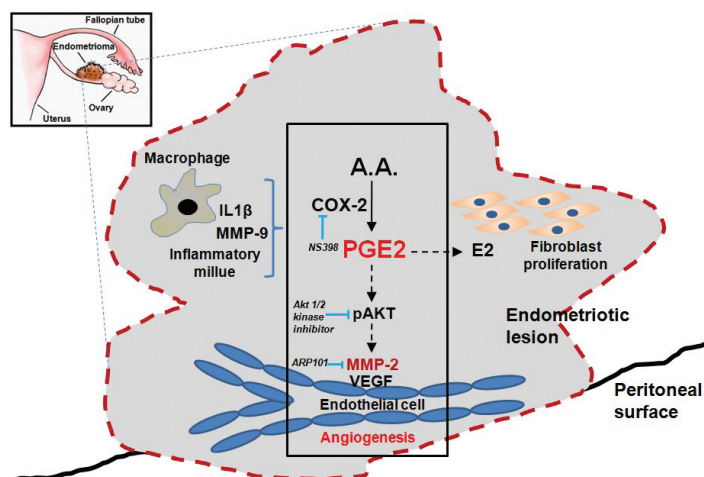


Fig: Prostaglandin E2 regulates MMP-2 to promote and angiogenesis in endometriosis. Inhibition of the COX-2 or PAKT or MMP2 regresses angiogenesis and subsequent endometriosis progression.

Treatment groups	Lipid peroxidation (μmol conjugated diene / mg protein)	Myeloperoxidase activity (units/mg protein)	Total thiol(-SH) Group (MM/mg protein)
Control	1.3 ± 0.03	0.9 ± 0.07	185 ± 0.04
Ethanol induced ulcer (A)	10.35 ± 0.09	6.9 ± 0.65 (0%)	120 ± 0.05
Tea extract (1ml) + (A)	1.5 ± 0.05	3.52 ± 0.4	137 ± 0.03
Treatment Groups	Succinate Dehydrogenase (μm DCIP reduced/ mg protein)	NADH oxidase (nmole oxidase/min/mg protein)	ROS (DCF fluorescence intensity)
Control	3.55 ± 3.6	1.06 ± 5.4	105 ± 5.5
Ethanol induced ulcer (A)	0.90 ± 2.5	3.79 ± 1.4	320 ± 8.15
Tea extract(1ml) + (A)	2.14 ± 1.08	1.68 ± 1.57	176 ± 7.08

Fig. 2a: Pretreatment with tea extract inhibited inflammatory reactions, and oxidative stress generated during ulceration. Black tea was effective in protecting the lipid peroxidation in microsomal fractions of gastric tissues than ulcerated ones. The anti-inflammatory property of black tea was judged by their potency to inhibit myeloperoxidase activity. Pretreatment with black tea extract significantly increased the intracellular glutathione level during prevention of gastric ulcer (Table A). BTE also showed significant effect on mitochondrial respiratory enzymes and ROS production (Table B).

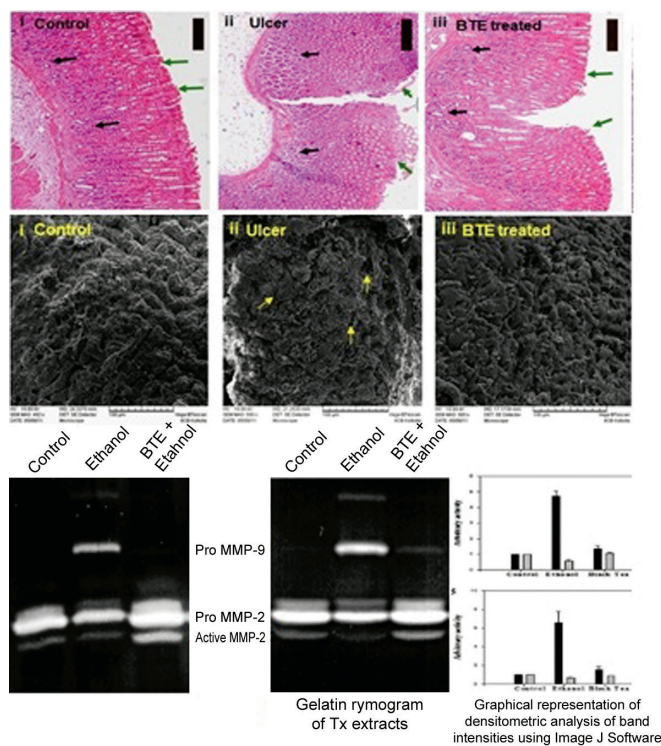
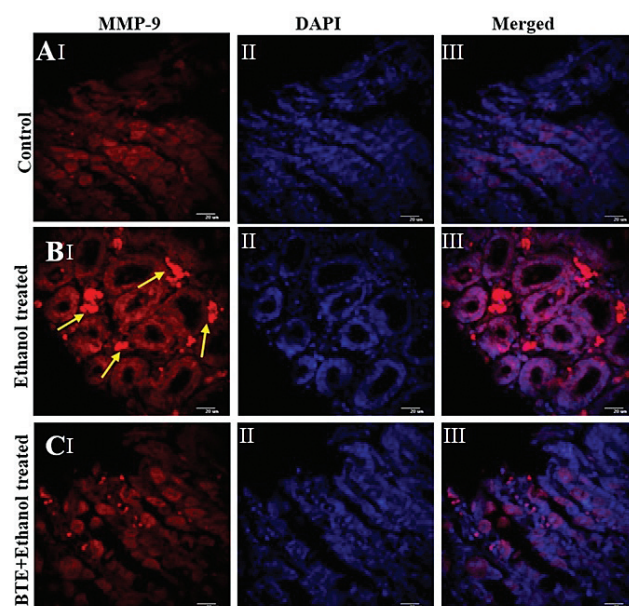


Fig. 1b: Gelatin zymography: Gelatin zymograms for PBS and T_x extracts of gastric tissues of different groups of rats showed that tea extract prevented ethanol-induced gastric ulcer through attenuation of proMMP-9 activity.

Fig. 3: Overexpression of MMP-9 was prominently observed in the extracellular epithelial region in ethanol-treated tissues. MMP-9 and DAPI fluorescence co-localization was seen in higher magnification in ethanol treated tissues, while pretreatment with black tea extract showed reduced MMP-9 expression.





Future Research Plans

The lead molecules of tea extract, catechin and theaflavin may be useful in preventing gastric inflammation, but it is more bioavailable when they are in nanocapsulated form. So, our future goal is to make a nanoformulated catechin and theaflavin. Also, design of analogs of catechin would be valuable for structure-activity relationship for protective effect in cellular injury.

PUBLICATIONS

Verma, S., Kesh, K., Dey, S., Bhattacharyya, S. and Swarnakar, S. (2015) An Overview of Matrix Metalloproteinase-9 Polymorphism and Gastric Cancer Risk. *Asian Pacific J Can Prev* **16**, 7393-7400 -

Bhattacharya, P., Swarnakar, S., Mukhopadhyay, A. and Ghosh, S. (2016) Exposure of composite tannery effluent in snail, *Pila globosa*: A comparative assessment of impacts of the untreated and membrane process treated effluents. *Ecotoxicol Environ* **126**, 45-55

Banerjee, P., Dey, TK., Sarkar, S., Swarnakar, S., Mukhopadhyay, A. and Ghosh, S. (2016) Treatment of cosmetic effluent in different configurations of ceramic UF membrane based bioreactor: Toxicity evaluation of the untreated and treated wastewater using catfish (*Heteropneustes fossilis*). *Chemosphere* **146**, 133-144

Datta, D.Talapatra, SN. and Swarnakar S. (2016) An overview of lectins from fresh water and marine microinvertebrate. *World Sci News* **46**, 77-87

CONFERENCES / WORKSHOPS

Number of abstract India: 6

INVITED TALKS

Science in everyday life. Surjasen High School, Jahangirpur, 13 April, 2015 Nadia, WB.

Prevention of gastric ulceration by Black Tea: an insight into Extracellular matrix remodeling of gastric tissues. Tea board of India, May 2015. Kolkata.

Cellular responses: Role of nanobrain and sound resonance. NIMS, June 2015, Japan.

Additive effect of tobacco over promoter polymorphism of MMP-7 in gastric cancer risk IDARS Symposium Sydney, Australia. August 2015

Elucidating the angiogenesis role of MMP-2 in endometriosis. International conference in Angiogenesis: Technology and therapeutics, Sastra University. September 2015, Gujrat

Action of proteases during progression of endometriosis. International congress on endometriosis. November 2015.

Functional stability of MMP-2 as sensor for stress-induced ulcer. International conference on translational research in ionizing radiation, free radicals, antioxidants and functional food, SFRR. January 2016, India.

Science in human health and diseases. Dhubulia Shyamaprasad Shikshayatan. March 2016, Nadia, WB.

Dr. Mrinal Kanti Ghosh

mrinal.res@gmail.com



The DEAD box protein p68: a crucial regulator of AKT/FOXO3a signaling axis in oncogenesis

Participants

JRF: Veenita Khare

SRF: Moumita Sarkar, Nilanjana Das

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Uttara Chatterjee

Park Clinic, Kolkata

Dr. Suresh Bajoria

RTIICS, NH, Kolkata

Background

Increased abundance of proto-oncogene AKT and reduced expression of tumor suppressor Forkhead box O3 (FOXO3a), the downstream target of AKT, is frequent in carcinogenesis. Mechanistic insights of AKT gene regulation are limited. DEAD box RNA helicase p68 is overexpressed in various cancers and acts as a transcriptional co-activator of several transcription factors, including β -catenin. This report highlights a novel mechanism of oncogenesis attributed to p68 by upregulation of AKT and its ensuing effect on tumor suppressor FOXO3a in colon cancer.

Aims and Objectives

To gain mechanistic insights into AKT gene regulation.

To investigate the involvement of p68 in AKT gene regulation.

To analyse the subsequent effect of p68 mediated AKT gene regulation on its bonafide target FOXO3a.

To assess the implication of p68/AKT/FOXO3a signaling axis in oncogenesis.

Work Achieved

Our study illustrates a novel regulatory mechanism of AKT/FOXO3a signaling axis by DEAD box protein p68, highlighting it as a potential candidate for therapeutic interventions. We propose that p68 occupies the AKT promoter with β -catenin and NF- κ B and increases its transcription. The increase of active AKT results in enhanced phosphorylation of FOXO3a, leading to its nuclear exclusion and eventual degradation by the proteasomal system. Consequently, there is downregulation of FOXO3a target genes critically, implicated in tumorigenesis. p27Kip1, one of the key tumor suppressor that functions as a cell cycle checker, is downregulated. Also, the repressive effect of FOXO3a, ascribed to tumor promoters Cyclin D1 and vascular endothelial growth factor, is abrogated. These string of events triggered by p68 lead to heightened cellular proliferation and survival, culminating in tumorigenesis.

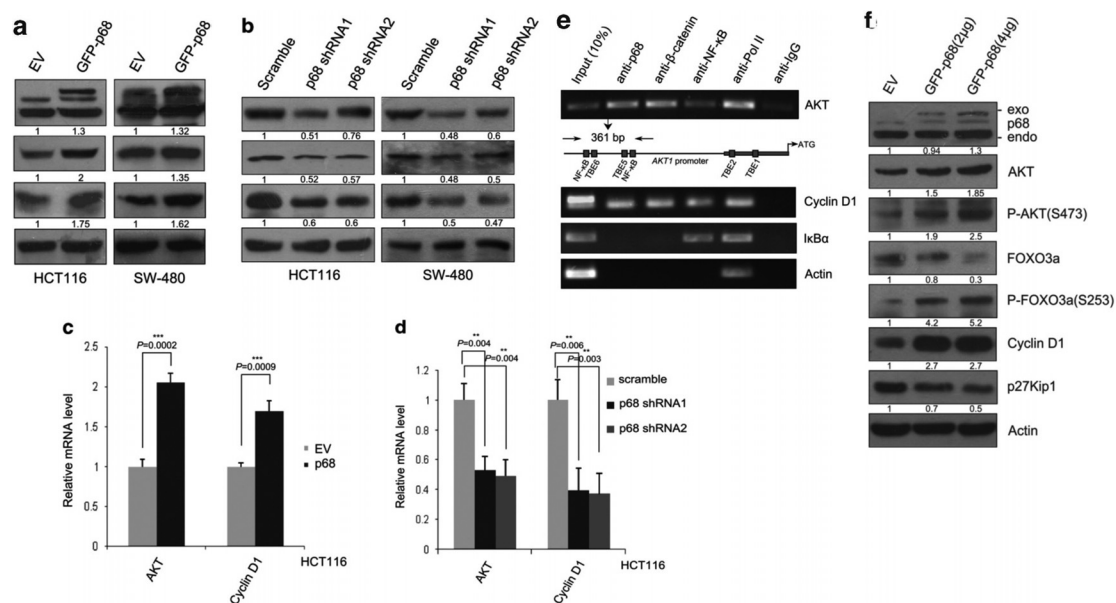


Fig. 1: AKT gene expression regulation, reduction of FOXO3a level in an AKT-dependent manner and cooperation with β -catenin and NF- κ B in regulating AKT promoter activity by p68 in colon cancer cells.

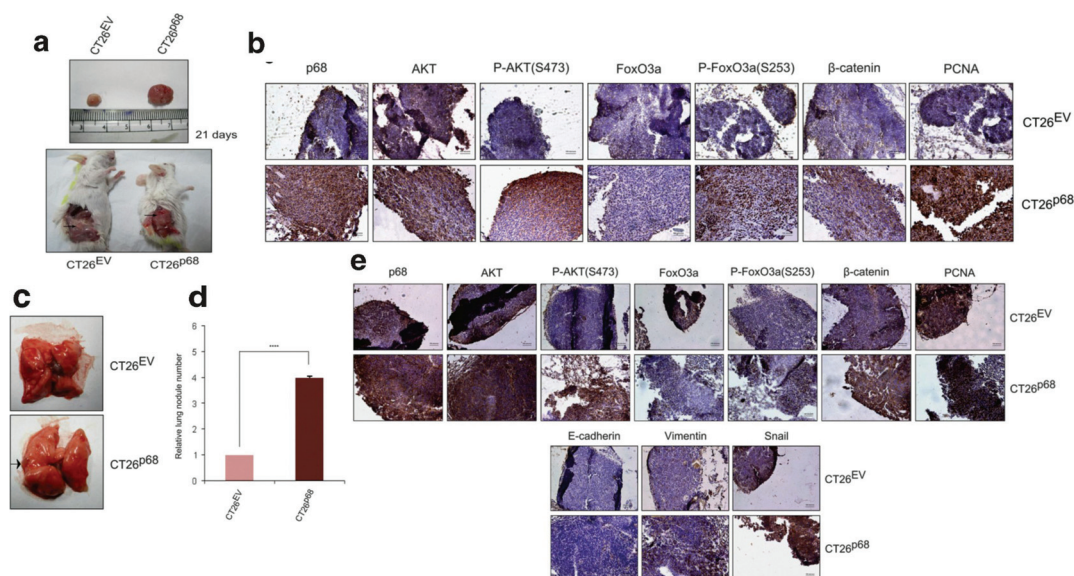


Fig. 2: Overexpression of p68 leads to enhanced primary tumor growth and also augments lung metastasis through upregulation of AKT and consequent reduction of FoxO3a.

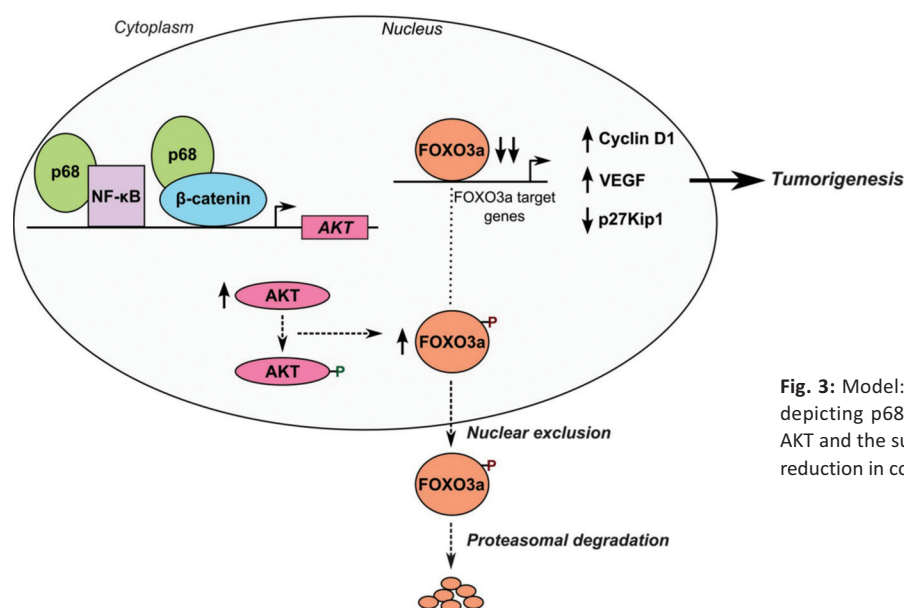


Fig. 3: Model: schematic representation, depicting p68-mediated upregulation of AKT and the subsequent effect of FOXO3a reduction in colon carcinogenesis.

Future Research Plans

Understanding the DEAD box protein p68 as a therapeutic target to combat oncogenesis.

Further investigating p68-mediated regulation of AKT2 and AKT3 promoter regions and their role in tumorigenesis.

PUBLICATIONS

Das, N., Datta, N., Chatterjee, U., and Ghosh, M. K. (2016) Estrogen receptor alpha transcriptionally activates casein kinase 2 alpha: A pivotal regulator of promyelocytic leukaemia protein (PML) and AKT in oncogenesis. *Cell Signal* **28**, 675-687

Book Chapters / Invited Reviews

Review articles

Paul, I., and Ghosh, M. K. (2016). Chaperones and Glioma Immunotherapy. *J. Cancer Sci Ther* **8**, 069-070

Sarkar, M., and Ghosh, M. K. (2016) DEAD box RNA helicases: crucial regulators of gene expression and oncogenesis. *Front Biosci (Landmark Ed)* **21**, 225-250

AWARDS / HONOURS / MEMBERSHIPS

2015: Fellow National Academy of Sciences, India (FNASc)

2015: Fellow West Bengal Academy of Science & Technology (FAScT)

Memberships

Life-Member: Indian Society of Translational Research (ISTR), INDIA.

Life-Member: Chemical Biology Society (CBS), INDIA.

EXTRAMURAL FUNDING

Development of Nanoparticle-based Directed Delivery Systems for Peptide Therapeutics. 2015 - 2018. (DST Nano Mission, India)

Co- Investigator: Development of Synthetic Transcription Factors against pluripotency to Target Cancer Stem Cells. (DST, India)

CONFERENCES / WORKSHOPS

Number of abstracts India: 1

INVITED TALKS

Signaling Crosstalk and Gene Regulation in Cancer to Identify Novel Drug Targets: Frontiers in Translational and Regenerative Biology. CRNN, 31 January 2016. Kolkata.

Role and Regulation of RNA Helicase p68 in Cancer: 17 Asian Association of Environmental Mutagen Societies (AAEMS), IICB, 22-24 December 2015. Kolkata.

Signaling Crosstalk and Gene Regulation in Cancer to Identify Novel Target(s) for Therapy: NCCS, 19-21 November 2015, Pune.

Mechanistic understanding of signaling crosstalks in cancer: Therapeutic strategy for intervention to ablate tumorigenesis: Research Council, CSIR-IICB, 18 September 2015. Kolkata.

Dr. Malini Sen

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Mechanism of metabolic regulation by Wnt-induced secreted protein 3 (WISP3)

Participants

SRF: Milan Patra, Srinivasarao Repudi

JRF: Deepesh K. Padhan

Collaborator

Name of collaborator outside CSIR-IICB

Dr. Sushil K. Mahata

University of California, San Diego, USA

Background

Despite established links of Wnt Induced Signaling Protein -3 (WISP3) or CCN6 with Progressive Pseudo Rheumatoid Dysplasia, functional characterization of WISP3 remains incomplete. In light of the documented negative correlation between accumulation of reactive oxygen species (ROS) and WISP3 expression, we deciphered if WISP3 regulates ROS accumulation through its influence on mitochondrial function. We found that WISP3 localizes to mitochondria, and depletion of WISP3 in the chondrocyte cell line C-28/I2 by siRNA results in altered mitochondrial electron transport and respiration. Enhanced Electron Transport Chain (ETC) activity of WISP3 depleted cells is reflected by increased mitochondrial ROS in association with augmented mitochondrial ATP synthesis, mitochondrial membrane potential and calcium. Additionally, WISP3 depleted cells display ROS dependent PGC1- α induction that correlates with increased mitochondrial mass / volume density together with altered mitochondrial morphology. Interestingly, transcription factor Nrf2 represses WISP3 expression. Taken together, our results suggest that WISP3 acts as a molecular brake appropriately balanced by Nrf2 in regulating mitochondrial function.

Aims and Objectives

Deciphering the influence of WISP3 on mitochondrial function

Correlating metabolic regulation by WISP3 with its effect on mitochondrial biogenesis (PGC1- α expression and function), mitochondrial electron transport and mitochondrial ROS accumulation as primary indicators of cellular metabolic activity.

Work Achieved

We have found that WISP3 plays a significant role in controlling mitochondrial ROS, mass and calcium accumulation. WISP3 acts as a molecular brake in regulating mitochondrial electron transport and metabolism.

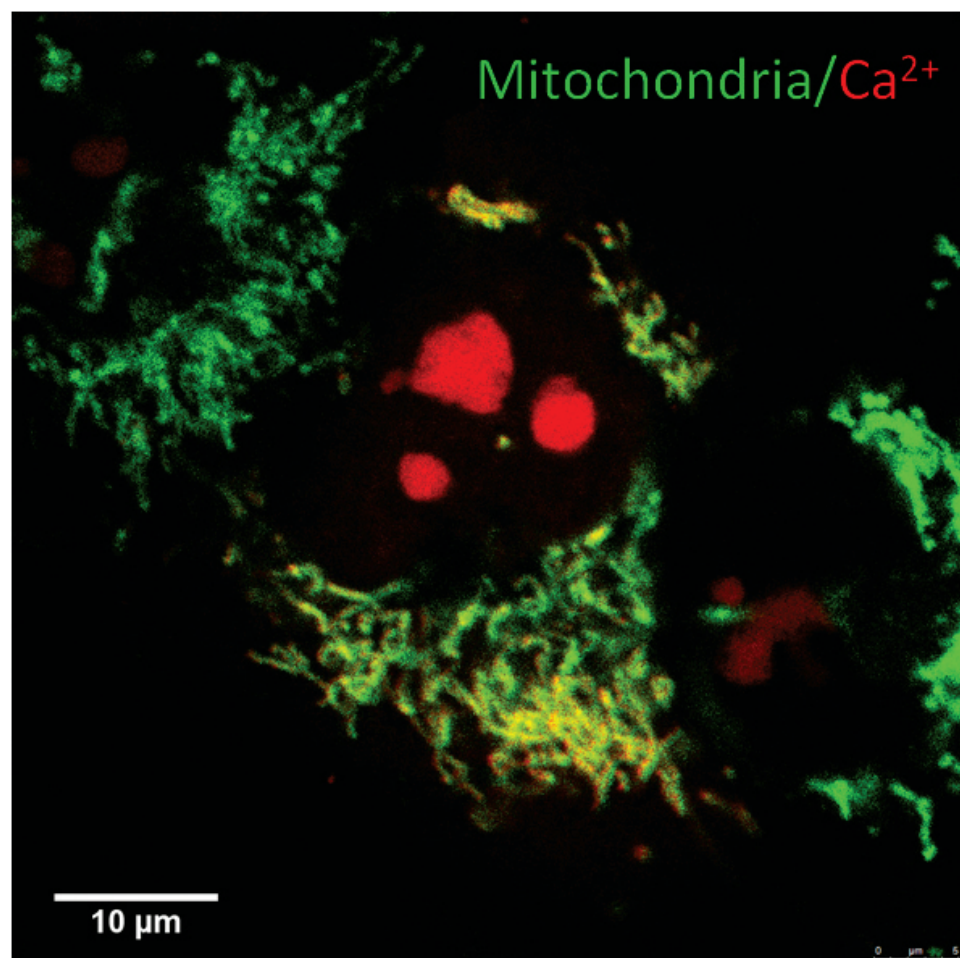


Fig. 1: Confocal microscopy depicts mitochondrial Ca^{2+} uptake estimated by co-localization (yellow) of Ca^{2+} (Rhod2: red) with mitochondria (Mitotracker green FM: green) in a WISP3 depleted chondrocyte line.

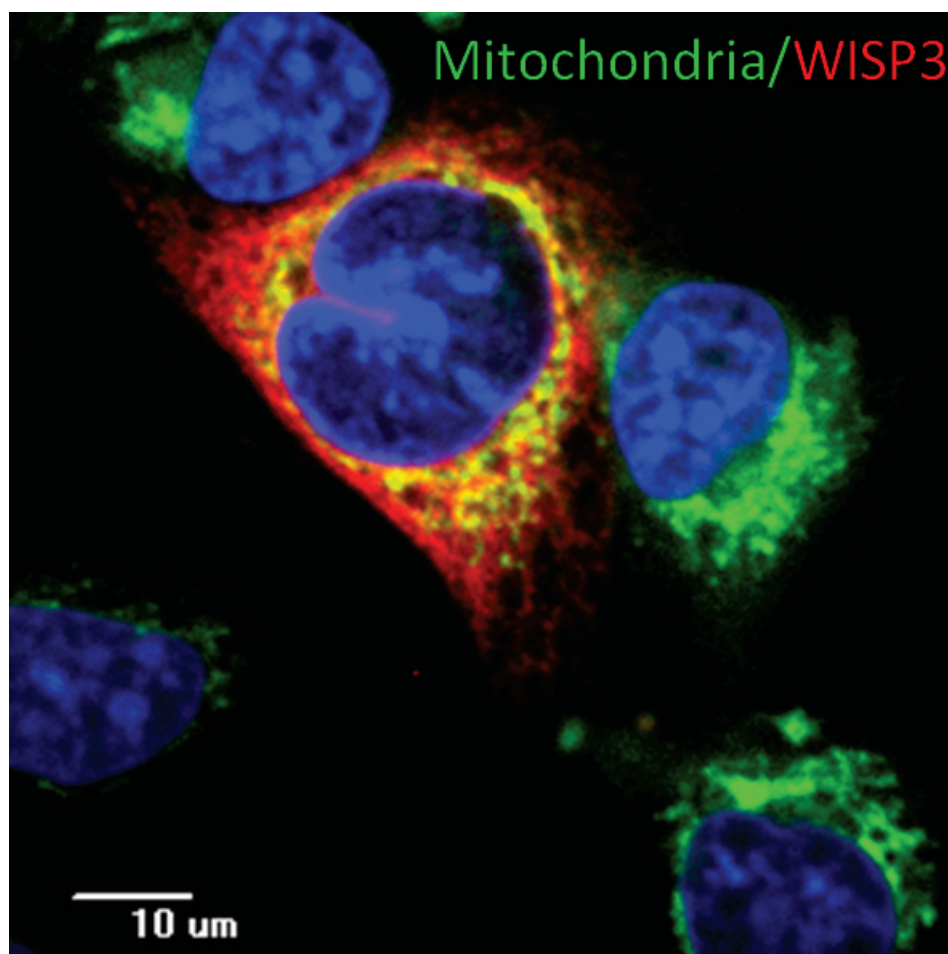


Fig. 2: Confocal microscopy of WISP3-myc transfected chondrocyte line depicts co-localization (yellow) of mitochondria (mitotracker green FM: green) with WISP3-myc (red).

Future Research Plans

To find out role of WISP3 on mitochondrial electron transport and metabolism in zebra fish model.

PUBLICATION

Patra, M., Mahata, S. K., Padhan, D. K., and Sen, M. (2016) CCN6 regulates mitochondrial function. *J Cell Sci* **129**, 2841-2851

EXTRAMURAL FUNDING

Role of Wnt5a in the Initiation and Progression of Sepsis. DBT Govt of India.

Mechanism of metabolic regulation by Wnt-induced secreted protein 3 (WISP3). DST Govt of India.

CONFERENCES / WORKSHOPS ATTENDED

Number of abstract India: 1

INVITED TALKS

Role of WISP3 in mitochondrial metabolism in NEHU, Shillong in International Conference on Molecular Signaling. November 2015. Shillong

Dr. Dipyaman Ganguly

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Role of type I interferons in metaflammation

Participants

SRF: Dr. Pritam Duttagupta, Amrit Raj Ghosh, Roopkatha Bhattacharya, Oindrila Rahaman

JRF: Deblina Raychaudhuri, Chinky Shiu Chen Liu

RA: Dr. Shamik Bhattachary

Collaborator(s)

Name of collaborator outside CSIR-IICB

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Dr. Om Tania

MS FRCS, ILS Hospitals, Kolkata

Dr. Parasar Ghosh

MD DM, Dept. of Rheumatology, Institute of Postgraduate Medical Education & Research, Kolkata

Dr. Gobinda Chatterjee

MD, Dept. of Dermatology, Institute of Postgraduate Medical Education & Research, Kolkata

Dr. Stefan Haak

PhD, Zentrum Allergie und Umwelt (ZAUM), Munich, Germany

Dr. Stephan Meller

MD, Dept. of Dermatology, Heinrich Heine University, Dusseldorf, Germany

Name of collaborator within CSIR-IICB

Dr. Partha Chakrabarti

Cell Biology & Physiology Division

Arindam Talukdar

Organic & Medicinal Chemistry Division

Background

Insulin resistance and type 2 diabetes associated with obesity is a major health problem worldwide. Studies done over the past decade or so have established the visceral adipose tissue (VAT) in the obese individuals as the seat of chronic low-grade inflammation, involving myriad innate and adaptive immune cell subsets, termed metaflammation^{1,2}. Interest in mechanisms of metaflammation grew after finding resident macrophages in visceral adipose tissue of obese individuals³. The chemokine-receptor axis CCL2-CCR2 has been implicated in the recruitment of monocyte-derived macrophages into the adipose tissue^{4,5}. But in obese VAT, as opposed to lean VAT, the resident macrophages show a classically activated proinflammatory M1 phenotype rather than the so-called alternatively activated anti-inflammatory M2 phenotype¹. This switch in macrophage phenotype in response to hyperadiposity cannot be explained by the CCL2-CCR2 axis, as evidence for selective recruitment of M1 macrophages to VAT in response to CCL2 is scanty. A recent study shows that CCL2 rather promotes a M2 phenotype⁶. Therefore the potential mediators for the M2 to M1 switch are probably induced in obese VAT in situ. One of the proposed candidates is circulating free fatty acid (FFA), which has the potential of inducing proinflammatory cytokine production from adipocytes via toll-like receptor 4 (TLR4). These adipose-derived cytokines in turn can affect the macrophage phenotype switch in situ as well as systemic insulin resistance⁸ (Kim, 2006). Fetuin-A, a fatty acid binding glycoprotein secreted from liver, has been implicated in mediating TLR4 activation by FFAs⁹. Interestingly, fetuin-A has also been implicated in recruitment of circulating macrophages to VAT and switching their phenotype to M1 in situ¹⁰. Nevertheless, mechanistic link between the metabolic



deregulation associated with increased adiposity and innate immune initiation of metaflammation remains largely unclear. One of the major adipose-intrinsic deregulation in obesity is change in adipokine expression levels. An imbalance between two such adipokines, leptin and adiponectin, has been found to be instrumental for the metabolic derangements associated with obesity¹¹. Chemerin (expressed by tazarotene-induced gene 2 or TIG2) is another such adipokine that regulates adipocyte development, differentiation and metabolic function¹². Chemerin expression in adipocytes is increased with free fatty acid abundance¹³, accordingly its systemic level has been found to be elevated in obese patients with metabolic syndrome (Ernst and Sinal, 2010; Li et al., 2014). Moreover genetic deficiency of chemokine-like receptor 1 (CMKLR1), the cognate receptor for chemerin, in mice protects them from high-fat diet-induced insulin resistance (Ernst et al., 2012). Of note, chemerin also acts as a chemokine for immune cells acting through CMKLR1, specifically for plasmacytoid dendritic cells (pDCs), the major type I interferon (IFN)-producing cells in the body (Zabel et al., 2005). In autoimmune contexts like psoriasis chemerin has been shown to recruit pDCs in tissues and initiate the cascade of autoreactive inflammation through type I IFNs (Vermi et al., 2005; Ganguly et al., 2009; Ganguly et al., 2013). We wondered if adipose tissue-derived chemerin is in some way involved in linking hyperadiposity to initiation of metaflammation, by playing a similar chemotactic function in obesity as well. To investigate this, we collected visceral adipose samples from obese individuals, and by means of whole tissue gene expression, adipose explant culture and cell culture studies unraveled a hitherto unknown role of chemerin-recruited pDCs and type I interferons in initiating metaflammation.

Aims and Objectives

- Exploring role of plasmacytoid dendritic cells in obesity associated metaflammation
- Exploring role of type I interferons in metaflammation

Work Achieved

In obese individuals the visceral adipose tissue becomes seat of chronic low grade inflammation (metaflammation). But the mechanistic link between increased adiposity and metaflammation remains largely unclear. We report here that in obese individuals deregulation of a specific adipokine, chemerin, contributes to innate initiation of metaflammation, by recruiting circulating plasmacytoid dendritic cells (pDCs) into visceral adipose tissue via chemokine-like receptor 1 (CMKLR1). Adipose tissue-derived high mobility group B1 (HMGB1) protein, activates Toll-like receptor 9 (TLR9) in the adipose-recruited pDCs by transporting extracellular DNA via receptor for advanced glycation endproducts (RAGE) and induces production of type I interferons. Type I interferons in turn help in proinflammatory polarization of adipose-resident macrophages. The level of type I IFN induction in the adipose tissue correlates with insulin resistance in obese individuals. Thus our study reveals a hitherto unknown pathway that contributes to metaflammation and insulin resistance in obesity.

Future Research Plans

Exploring role of type I interferons in a mouse model of obesity associated metaflammation and insulin resistance through loss-of-function and gain-of-function experiments.

Exploring potential therapeutic effect of novel biologic and small molecule based therapies in preclinical models of obesity associated insulin resistance.

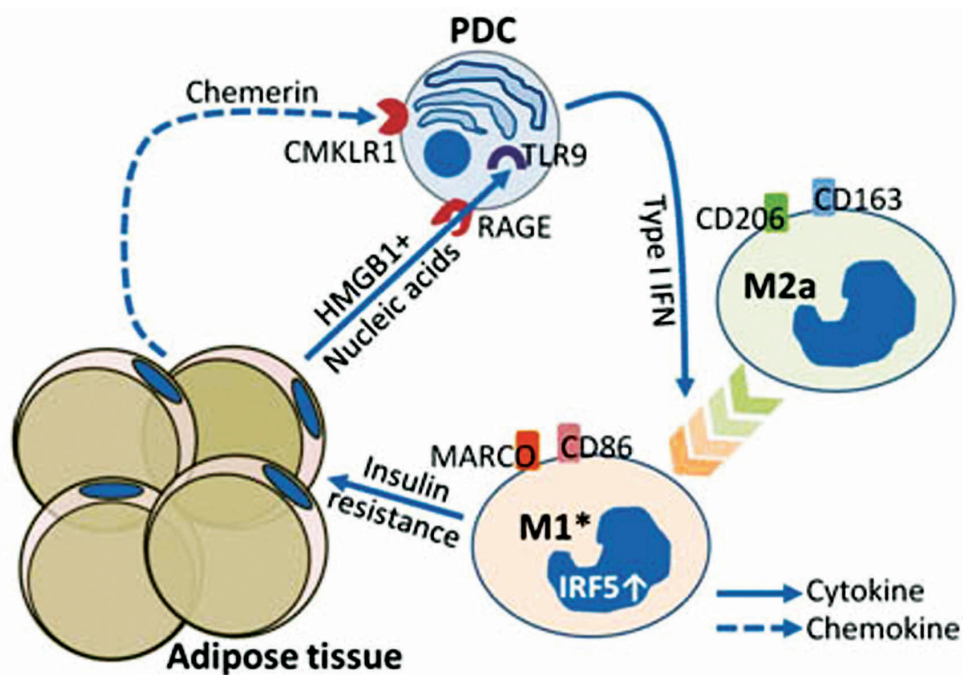


Fig. 1: The model based on our data proposes that visceral adipose tissue (VAT)-derived chemerin recruits circulating plasmacytoid dendritic cells (pDCs) through the CMKLR1 receptor. VAT-recruited pDCs are activated in situ by HMGB1+nucleic acid complex that may access Toll-like receptor-9 (TLR9) in pDCs via RAGE receptors. pDCs thus activated produce type I IFNs in situ, which in turn can fuel in situ polarization of CD206+ M2 macrophages to proinflammatory CD86+ M1 macrophages expressing IRF5 and NOS2. The proinflammatory M1 macrophages in turn contribute to propagation of chronic inflammation in VAT and insulin resistance.

PUBLICATIONS

Meller, S., Di Domizio, J., Voo, K. S., Friedrich, H. C., Chamilos, G., Ganguly, D., Conrad, C., Gregorio, J., Le Roy, D., Roger, T., Ladbury, J. E., Homey, B., Watowich, S., Modlin, R. L., Kontoyiannis, D. P., Liu, Y. J., Arold, S. T., and Gilliet, M. (2015) T(H)17 cells promote microbial killing and innate immune sensing of DNA via interleukin 26. *Nat Immunol* **16**, 970-979

PATENTS FILED / SEALED

Name Surname: DIPYAMAN GANGULY

Patent Title: BLOCKING TOLL-LIKE RECEPTOR 9 SIGNALING WITH SMALL MOLECULE ANTAGONIST

Country(ies) : IN, WO

Patent No. Application No. 201611009670, 2015

Date filed / granted:

Co-inventors and their Institutes

ARINDAM TALUKDAR, DIPYAMAN GANGULY, BARNALI PAUL, AYAN MUKHERJEE, SHAUNAK ROY, SWARNALI ROY, KANTUBHUKTA RAMARAO, SOHAL SATISH, AMRIT RAJ GHOSH, ROOPKATHA BHATTACHARYA, OINDRILLA RAHAMAN, BISWAJIT KUNDU

Patent filed by DBT / CSIR-IICB / another organization
CSIR-IICB

AWARDS / HONOURS / MEMBERSHIPS

Invited to Overseas Outstanding Young Scholars Forum, Sun Yat-sen University & Zongshan Medical School, Guangzhou, Peoples Republic of China.

EXTRAMURAL FUNDING

Ramanujan Fellowship

2013-2018, DST

Co- Investigator: *Probing endosomal toll-like receptor 9 biology using novel small molecule antagonists*

2015-2018, DST

Role of type I interferons in cerebral malaria

2016-2019 (sanction awaited), DBT

CONFERENCES / WORKSHOPS

Number of abstract

India: 2

International: 1

Dr. Amitava Sengupta



Epigenetic regulation of hematopoietic stem/progenitor cell activity in leukemia

Participants

JRF: Liberalis Debraj Boila, Sayantani Sinha **SRF:** Shankha Subhra Chatterjee, Mayukh Biswas, Sayan Chakraborty

Project Assistant: Pranay Saha

Background

Stem cells possess two fundamental properties; self-renewal and differentiation. Bone marrow-resident adult hematopoietic stem cells (HSC) respond to physiological stimuli and regenerate hematopoiesis. Dysregulated self-renewal and arrest in differentiation of HSC and progenitors induce leukemic transformation.

Acute myeloid leukemia (AML) is a global life threatening disease that involves heterogeneity with respect to presentation and clinical outcome. Importantly, AML patients still receive the same chemotherapy treatment developed more than half a century ago, which remits completely in less than 40% of patients. Hence, there is an urgent need to understand underlying transformation mechanisms and develop better therapeutic strategies for AML.

From a translational perspective HSCs draw attention because of their potential use in stem cell and gene therapy. We are interested at understanding the cell-autonomous and non-cell-autonomous molecular determinants that regulate HSC self-renewal, differentiation and interaction with hematopoietic microenvironment in normal and leukemic hematopoiesis.

Aims and Objectives

- Identify cell-autonomous mechanisms of hematopoietic stem cell transformation
- Investigate epigenetic regulation of leukemia stem cell heterogeneity
- Determine microenvironment regulation in hematopoiesis.



Work Achieved

We have identified novel epigenetic dysregulation and mechanistic underpinnings operating within human hematopoietic stem/progenitor cell compartment in patients presenting with myelodysplasia and acute myeloid leukemia. We further characterized bone marrow mesenchymal stromal cell regulation in leukemic hematopoiesis.

Future Research Plans

Future research would be directed to address genetic characterization of myeloid tumor suppressor genes in leukemia. We aim to identify pre-disposing somatic mutations involved in the pathogenesis of AML in Indian cohort with prognostic relevance and characterize epigenetic and functional heterogeneity present within human leukemia cells. The overreaching goal is to eventually provide cost-effective cancer therapeutics and genetic diagnostics to leukemia patients.

EXTRAMURAL FUNDING

Polycomb repressive complex in Myelodysplastic Syndromes, 2014-17, Department of Science & Technology (DST-SERB), Govt. of India.

Rho GTPase signaling in adult Hematopoietic stem cell-Microenvironment interaction, 2011-16, Department of Biotechnology-Ramalingaswami Fellowship (DBT-RLS), Govt. of India.

Understanding Hematopoietic Stem Cell-Aging in Leukemia, Indian Council of Medical Research (ICMR), Govt. of India (approved).

CONFERENCES / WORKSHOPS

<i>Number of abstract</i>	India: 2
	International: 1

CONFERENCES / EVENTS ORGANIZED BY CSIR-IICB

One day hands on Workshop & Technical Presentation on Droplet Digital PCR supported by BIO-RAD, 8th March 2016 @ CSIR-IICB, Translational Research Unit of Excellence (TRUE), Salt Lake Campus, Kolkata.

INVITED TALKS

Dissecting Chromatin remodeling in Hematopoietic Stem/progenitor cell (HSPC) regulation in Leukemia. 17th All India Congress of Cytology & Genetics (AICCG) & International Symposium on Exploring Genomes: The New Frontier, 2015, CSIR-Indian Institute of Chemical Biology, Kolkata.

Bone marrow Microenvironment in Hematopoiesis. 5th Ramalingaswami Fellows' Conclave, 2015, Translational Health Science & Technology Institute (THSTI), NCR, India.

Dr. Shila Elizabeth Besra

shilabesra@iicb.res.in



Evaluation of the molecular mechanism towards anti-cancer and anti-inflammatory activity of different natural products.

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Santanu Basu

Department of Oncology, Employee State Insurance Hospital, Kolkata

Background

Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver. Identification of bioactive molecules with immunostimulant property that induces apoptosis has been the mainstay of anticancer therapeutics for several decades. *Bellamya bengalensis* used as traditional medicine for the cure of a number of ailments such as an arthritis, conjunctivitis etc, but no work has been done so far in the field of cancer with this fresh water snail. Secretion extract of *Bellamya bengalensis* f. *annandalei* (SEBB) possesses significant apoptotic activity against three myeloid cell lines as reported in our previous work. We evaluated the cytotoxic and apoptosis activity on hepatocellular carcinoma cells.

Aims and Objectives

- Evaluation of cytotoxic and apoptosis inducing effect of secretion extract of *Bellamya bengalensis* on hepatocellular carcinoma cell lines.
- Immunostimulant studies with SEBB on mouse murine macrophage cells.
- Wound healing potential of *Lawsonia alba* Lam leaves.
- Formulation of LA extracts into a topical gel.

Work Achieved

SEBB significantly decreased the metabolically viable cells and caused apoptosis, as confirmed by morphologically and by Flowcytometric analysis shows appreciable number of cells in early & late apoptotic stages and cells are arrested in the sub-G1 & G1 phases of cell cycle. The SEBB induces nitric oxide in RAW264.7 cells but when used in combination with recombinant interferon- γ (rIFN- γ), it shows a marked enhancement in NO production in murine macrophages RAW264.7 cells. Elevated NO production was significantly inhibited by pre-treatment with PDTC and

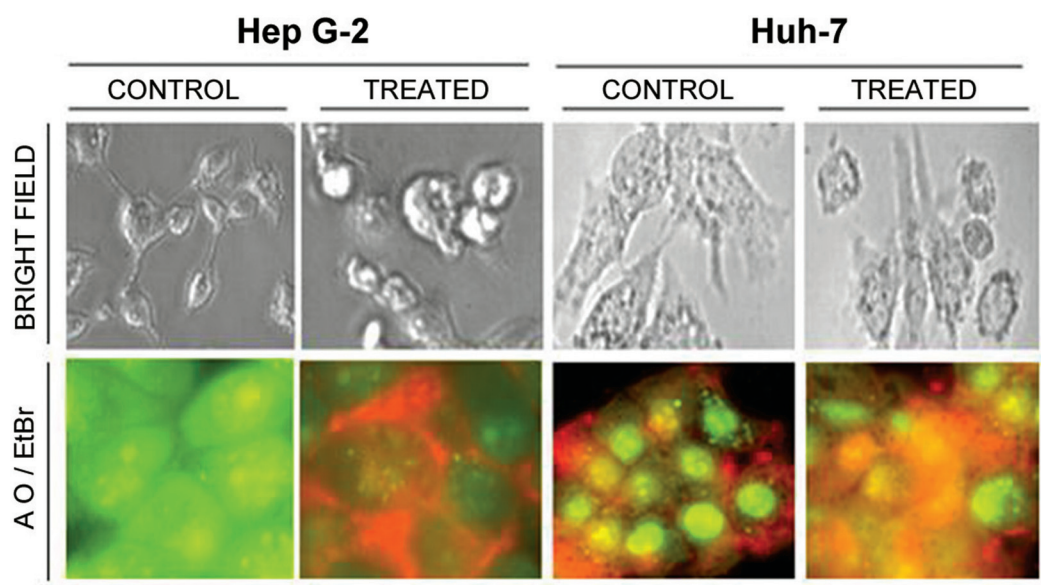


Fig. 1: Light and Fluorescence microscopic images of SEBB treated HepG-2 and Huh-7 cells. The control cells were with intact nuclei and gave bright green fluorescence whereas treated cells showed intense orange-red fluorescence showing signs of apoptosis.

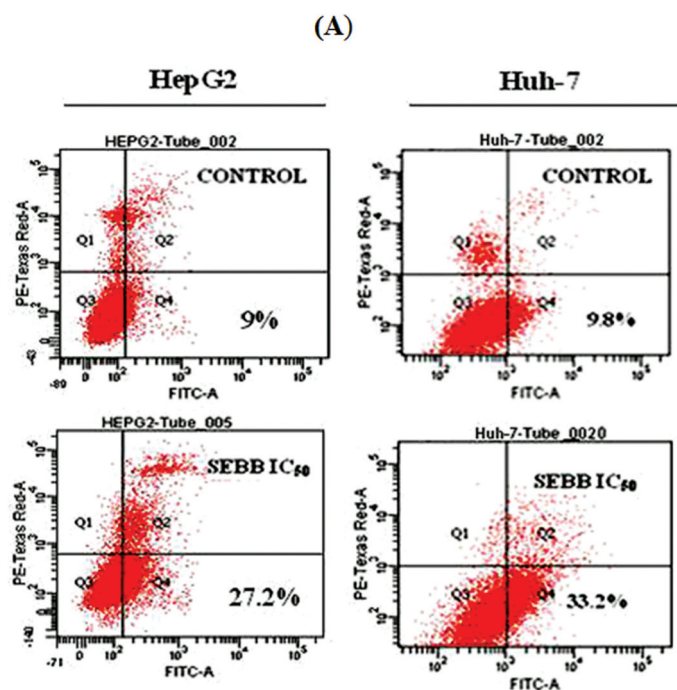


Fig. 2: (A) Detection of apoptosis by Flow cytometric analysis in control and SEBB treated of HepG2 and Huh-7 cells respectively after 18 hrs treatment at IC₅₀ doses with SEBB. Staining was done with Annexin V FITC and Propidium iodide. Dual parameter dot plot of FITC-fluorescence (x-axis) vs. PI-fluorescence (y-axis) shows logarithmic intensity.



Caspase-3 study on HepG-2 and Huh-7 cell lines

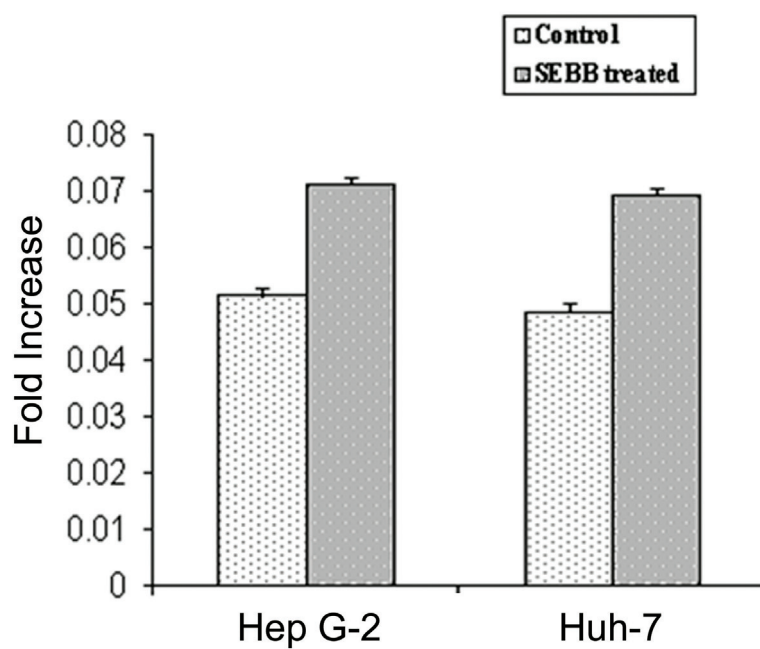


Fig. 2: (B) Fold increase in caspase 3 production in HepG-2 and Huh-7 cell lines after SEBB treatment for 24 hrs at IC50 dose with respect to control.

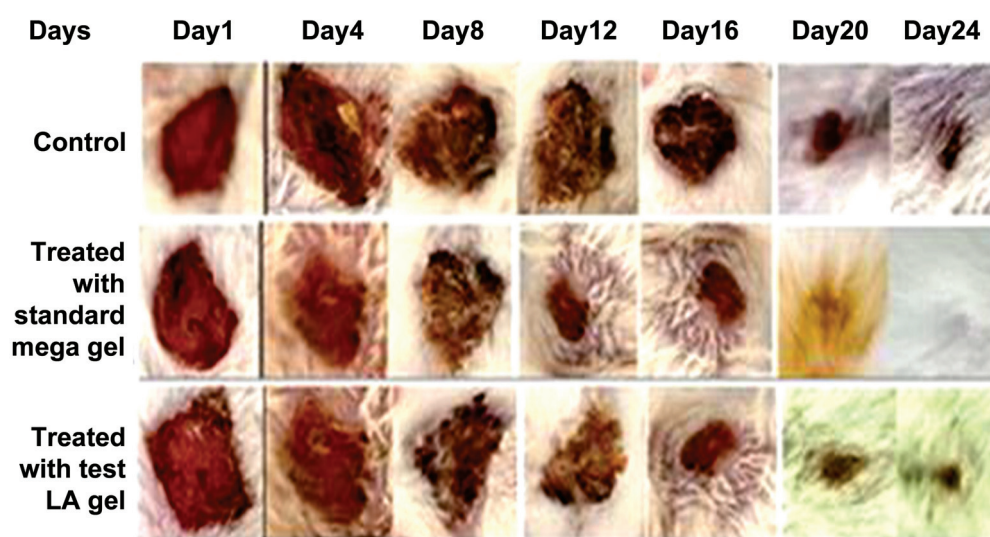


Fig. 3: Wound contraction and comparison of wound healing by ethyl acetate fraction of Lawsonia alba Lam. leaves on different days in standard and test treated groups compared to control.



N GMMA, thus SEBB indicates a role of immunomodulation. MTT assay in RAW264.7 cells revealed that insignificant reduction and apoptosis is mediated through activation of caspase 3.

Future Research Plans

Analgesic, antipyretic and anti-inflammatory study with SEBB/LBB and its mechanism of action on rodent models.

Antileukemic effect of SEBB against PBMNCs of leukemia patients and its mechanistic study.

Anti-cancer activity in skin melanoma and breast cancer cell lines along with identifying the active constituents.

Other Projects-Anti-cancer activity of *Lawsonia alba* Lam. Leaves on hepatocellular carcinoma.

PUBLICATIONS

Besra, A. R., Pal, K., Basu, S., and Besra, S.E. (2015) Anti tumor activities of secretion extract of *Bellamya bengalensis* in human hepatocellular carcinoma cell lines is mediated by caspase-dependent apoptosis and cell cycle arrest. *World J Pharm Res* **4**, 2326-2344

Dutta, S., Besra, S.E., Bhattacharjee, A., and Mukhopadhyay, G. (2016) Wound healing potential of *Helicteresisora* Linn. Fruits extract formulated into a topical gel. *Int J Pharm Eng* **4**, 655-668

Dutta, S., Pattnaik, A.K., and Besra, S.E., (2016) Wound healing potential of methanolic extract and its active fraction of *Lawsonia alba* Lam. leaves formulated in to a topical gel. *World J Pharm Res* **5**, 1091-110

AWARDS / HONOURS / MEMBERSHIPS

Memberships

Life member of All India Congress of Cytology and Genetics (AICCG), 2015.

Student Award

Soumyasree Dutta

Awarded 3rd prize in poster presentation for "Antiproliferative activity of leaves of *Lawsonia alba* Lam. against Hepatocellular carcinoma", National Seminar on Emerging Trends & Innovation in Pharmaceutical Education & Research in India-2015 held at Durgapur, West Bengal, India on 11th April 2015.

CONFERENCES / WORKSHOPS

Number of abstracts India: 6

Dr. Krishna Das Saha

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Protective role of phytocompounds against lung and hepatic disease

Participants

JRF: Sayoni Nag, Tanusree Das, Sujata Das, Moumita Saha,

SRF: Dipayan Bose

Project Assistant: Snehasis Mishra, Saswati Banerjee

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Asim Bhowmik
IACS, Kolkata

Dr. Sanchita Goswami
CU, Kolkata

Dr. Tarun Jh
JU, Kolkata

Dr. Debjani Nath
KU, Kalyani

Dr. Joydev Dinda
Utkal University, Odisha

Dr. Debasish Maity
Tripura University, Tripura

Dr. Rajkumar Duary
Tezpur University, Assam

Name of collaborator within CSIR-IICB

Dr. G. Suresh Kumar
Organic and Medicinal Chemistry Division

Background

Lung and liver are vital organs of the body. Common lung diseases like asthma, lung disorder from inflammation become fatal without proper medication. Again, liver damage over time results a life-threatening condition if not properly treated.

Aims and Objectives

Extract or bioactive component rich fraction of several medicinal plants have been used to examine their protective role against (a) OVA induced allergic asthma or *E. coli* induced lung inflammation and (b) liver damage caused by arsenic or CCl₄.

Plant extract or bioactive component rich fractions have been prepared according to published method.

Protective effect of the bioactive component rich fractions against lung disorder and hepatic damage have been performed.

Work Achieved

Oral treatment of the bioactive component rich fraction of *Andrographolide paniculata*, *Ananas comosus*, or *Nyctanthes arbortristis* (each of 100 mg/kg bwt/dose) from day 15 to 30 of OVA challenge lowered the number of inflammatory cells in the BAL fluid and lung tissues, level of Th2 cytokines and IgE with an increase in Th1 type cytokines and repairment of lung tissue in the OVA challenged mice. The same fractions were also potent to modulate the Th1 type cytokines profile, infiltration of inflammatory cells, lung histology caused by i.p. challenge of heat killed *E.coli*.

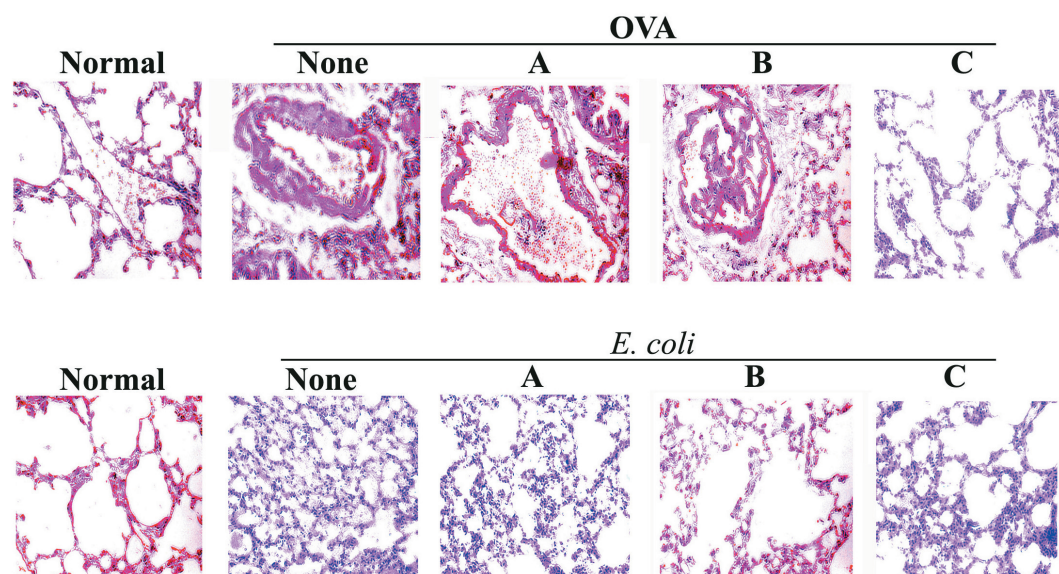


Fig. 1: Lung Histology: A: Methanolic extract of *Nyctanthes arbortristis*, B: Methanolic extract of *Ananas comosus*, C: Pomegranate Extract (each: 100mg/kg bwt/dose).

Treatment of 150 mg/kg bwt/dose of lyophilized form of the extract of pomegranate or tender coconut water on every alternate day for one month along with arsenic exposure showed good hepatoprotective role against arsenic induced toxicity by suppressing liver function markers, and oxidative stress with concomitant rise in the anti-oxidant enzymes.

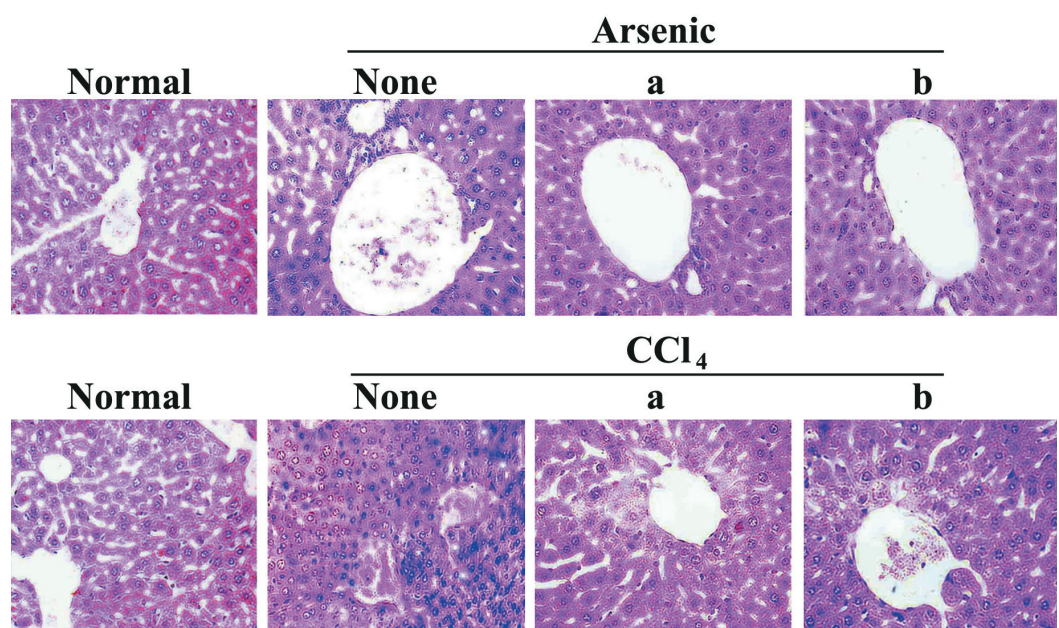


Fig. 2: Liver Histology: a, Methanolic extract of *Andrographolide paniculata*. b, Tender Coconut Water Extract.



Future Research Plans

Finger printing of the fractions will be performed (HPLC-DAD/LC-MS)

Patent filling

Determination of pK values of each active fractions

Pharmacokinetic study of each active fractions

Commercialization

PUBLICATIONS

Das, S., Pradhan, G. K., Nath, D., and Das Saha, K. (2015) Enhanced protective activity of nano formulated andrographolide against arsenic induced liver damage. *Chem Biol Interact.* **242**, 281-9

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Halder, A. K., Mallick, S., Shikha, D., Saha, A., Saha, K. D., and Jha, T. (2015) Design of dual MMP-2/HDAC-8 inhibitors by pharmacophore mapping, molecular docking, synthesis and biological activity. *Rsc Adv.* **5**, 72373-72386

Samanta, T., Munda, R. N., Roymahapatra, G., Nandy, A., Das Saha, K., Al-Deyab, S. S. and Dinda, J. (2015) Silver(I), Gold(I) and Gold(III)-N-Heterocyclic carbene complexes of naphthyl substituted annelated ligand: Synthesis, structure and cytotoxicity. *J Organomet Chem* **791**, 183-191

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Mondal, C., Halder, A. K., Adhikari, N., Saha, A., Das Saha, K., Gayen, S. and Jha, T. (2015) Comparative validated molecular modeling of p53-HDM2 inhibitors as antiproliferative agents. *Eur J Med Chem.* **90**, 860-875

Das, S., Chatterjee, N., Bose, D., Banerjee, S., Jha, T., and Das Saha, K. (2015) Leishmanial sphingolipid induces apoptosis in Sarcoma 180 cancer cells through regulation of tumour growth via angiogenic switchover. *Tumor Biol.* **36**, 3109-3118

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Banerjee, S., Bose, D., Chatterjee, N., Das, S., Chakraborty, S., Das, T. and Saha, K. D. (2016) Attenuated *Leishmania* induce pro-inflammatory mediators and influence leishmanicidal activity by p38 MAPK dependent phagosome maturation in *Leishmania donovani* co-infected macrophages. *Sci Rep* **6**, 22335

Bhowmick, D., Bhar, K., Mallick, S. K., Das, S., Chatterjee, N., Sarkar, T. S., Chakrabarti, R., Das Saha, K., and Siddhanta, A. (2016) Para-Phenylenediamine Induces Apoptotic Death of Melanoma Cells and Reduces Melanoma Tumour Growth in Mice, *Biochem Res Int.*, 3137010.

Bose, D., Banerjee, S., Das, S., Chatterjee, N., and Saha, K. D. (2016) Heat Killed Attenuated *Leishmania* Induces Apoptosis of HepG2 Cells Through ROS Mediated p53 Dependent Mitochondrial Pathway. *Cell Physiol Biochem.* **38**, 1303-18

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EXTRAMURAL FUNDING

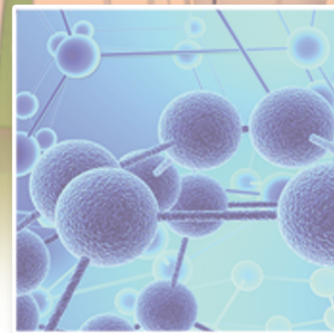
Mechanistic study of effect of Spargulin-A extracted from Glinus oppositifolius on macrophages to raise anti leishmanial host defense. Start date- 14.03.2016 (3 years). DST-SERB, India.

Designing bioactive peptides from whey liquid waste of the dairy industry: Functionality and health benefit in Obesity, Obesity associated disorders with exploration of molecular mechanism. March, 2016 (3 years). DBT- NER, India.

Modulatory role of quercetin on radiation-induced oxidative stress in human colorectal carcinoma cells: Assessment of possible role of certain trace elements. Start date-01.12.2015 (3 years). UGC-DAE, India.

Studies on anticancer activities of extracts (Bromelain and Peroxidase) of different pineapple (Ananas comosus) cultivars of Tripura. Start date- 18.03.2014 (3 years). DBT-NER, India.

Organic and Medicinal Chemistry Division



Dr. P. Chattopadhyay (Head till September 2015), Dr. G. Suresh Kumar, Dr. P. Jaisankar (Head from October 2015 onwards), Dr. Chinmay Chowdhury, Dr. Sharmila Chattopadhyay, Dr. Biswadip Banerji, Dr. Surajit Ghosh, Dr. Indrajit Das, Dr. Sanjay Dutta, Dr. Ranjan Jana, Dr. Arindam Talukdar, Dr. R. Natarajan and Dr. Indu Bhusan Deb

The Organic and Medicinal Chemistry Division - wherein novel designer and functional molecules are being synthesized at will - is the major backbone of the institute. The scientists of this division, in active collaboration with other scientists of the institute, strive to develop drugs and diagnostics for infectious diseases, neuronal diseases, cancer and other ailments. The division has a strong and proven track record of developing natural product based drugs 'Asmon' and 'Prostalyn' currently in the market. The divisional scientists also excel in performing cutting-edge research in basic and applied chemistry aligned towards solving the health problems of social, national and global importance.

The major research themes pursued in the division include isolation of medicinally active natural products from indigenous plants for drug formulation; development of synthetic analogues of bioactive phytochemicals as lead molecules for drugs through structure-activity relationship studies; genetic manipulation of phytochemicals for better medicinal benefits; development of lead molecules from structure-based drug design; design and synthesis of 'new

chemical entities' to examine their biological/biophysical efficacy towards 'new therapeutic entities'; development of economic and efficient reagents for essential and innovative synthetic transformations to obtain heterocyclic bioactive molecules; development of novel chiral and achiral catalytic systems for various organic transformation of functional groups and C-H activation strategies for synthesis to obtain functional molecules, especially, fluorescent and multifunctional molecular probes for affinity based protein profiling; development of novel synthetic methodologies for bioconjugation; design and synthesis of novel synthetic supramolecular receptors of organic and metal-organic in nature to study biomolecular recognition and controlled release; targeting nucleic acids, bacterial and viral RNAs by small molecule natural products and heterocycles; development of small molecules, peptides and peptoids for neurodegenerative diseases; development of small molecules based antibiotics against various resistant bacteria; development of various platforms for studying bio-molecular interactions through surface modification and patterning using liposomes; and, development of peptide-based soft hydrogel for various biomedical applications.

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Design and synthesis of amino acid based pseudo cyclic peptides and studies on their self assembly

Participants

Project Assistant: Avijit Ghorai, Gautam Kulsi

Background

Molecular self-assembly offers unique directions for the fabrication of novel supramolecular structures and advanced materials. The inspiration for the development of such structures is often derived from self-assembling modules in biology, as natural systems form complex structures from simple building blocks such as sugars, amino acids, nucleic acids and lipids. Peptide-based nanostructures are important for the production of ordered nanostructures as several studies had demonstrated their ability to form well organized assemblies. We have planned to synthesise various kinds of sugar based peptidomimetic macrocycles which are expected to undergo self-assembly to form nanostructures. Detailed binding studies of the products to search for the formation of ion channels, catalysts, and drug delivery vehicles etc are envisaged.

We initially plan to synthesise 20-membered triazole/urea based peptidomimetic macrocycles from the readily available starting material diacetone glucose. As peptide bond (i.e. amide) is isostere of (1,4) linked triazole, we also want to synthesise 18-membered cyclic amide/urea macrocycles. Finally, their self-assembly behaviour will be investigated in detail.

Aims and Objectives

To develop synthetic methodology for sugar based triazole/amide macrocycles.

Extension to triazole-urea based peptidomimetics to structures of higher macrodipole and studies on dipole moment controlled self-assembly using NMR, Molecular Modeling/IR/TEM/SEM/AFM/SAED/DSL analyses.

Studies on changes in self-assembly behavior due to insertion of chirality/prochirality in the macromolecules.

Studies of the anion binding properties of these macrocycle.

Work Achieved

Insertion of D- α -amino acid as well as β -amino acid with cis- β -furanoid (1,4)-linked triazole amino acids has been shown to be helpful for the



construction of larger macrocyclic peptides with a predictable self-assembly pattern generating a modified macrodipole (**Fig. 1**). The D- α -amino acid derived macrocyclic pseudo peptide **1** undergoes parallel homo-stacking in solution phase via amide NH and amide carbonyl oxygen H-bonding. Such macrocycles may be used as model systems for artificial ion channels as their unidirectional assembly pattern attributes them with large dipole moments. In contrast, β -amino acid derived product **2** does not undergo self-assembly due to higher flexibility of the peptide backbone.

Future Research Plans

Aminoxy-triazole modified cyclic peptides: Realising that appropriate functionalization may lead to nanotubes with greater selectivity for forming ion channels, catalysts, receptors, or molecule containers, we have planned to synthesise various kinds of sugar based peptidomimetic macrocycles which will undergo self-assembly to form nanostructures. Detailed binding studies of these sugar based peptidomimetic macrocycles towards development of ion channels, catalysts, and drug delivery systems etc are also contemplated.

The advantage of designing aminoxy peptide is that aminoxy amide NH has higher acidity over normal amide NH and hence the products become better binders of anions.

PUBLICATIONS

Kulsi, G., Ghorai, A., Achari, B., and Chattopadhyay, P (2015) Design and Synthesis of Conformationally Homogeneous Pseudo Cyclic Peptides through Amino Acid Insertion: Investigations on Their Self Assembly. *RSC Advance*, **5**, 64675-64681

Ghorai, A., Achari, B., and Chattopadhyay, P (2016) Self-assembly of cyclic peptides and peptidomimetic macrocycles : lining structure with function. *Tetrahedron* **72**, 3379-3387

EXTRAMURAL FUNDING

Synthesis, conformational studies and self assembly behavior of triazole/ urea based peptidomimetic macrocycle; (2013-16)

FDST (Govt. of West Bengal), India

Co- investigator; *Organic reactions in generating innovative and natural scaffolds*

(2014-2015) Individual

CSIR-NETWORK

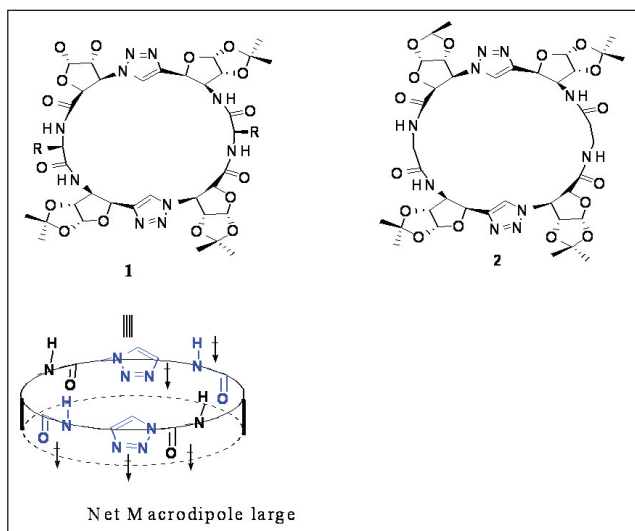


Fig.1: The D- α -amino acid derived macrocyclic pseudo peptide **1** undergoes parallel homo-stacking in solution phase.

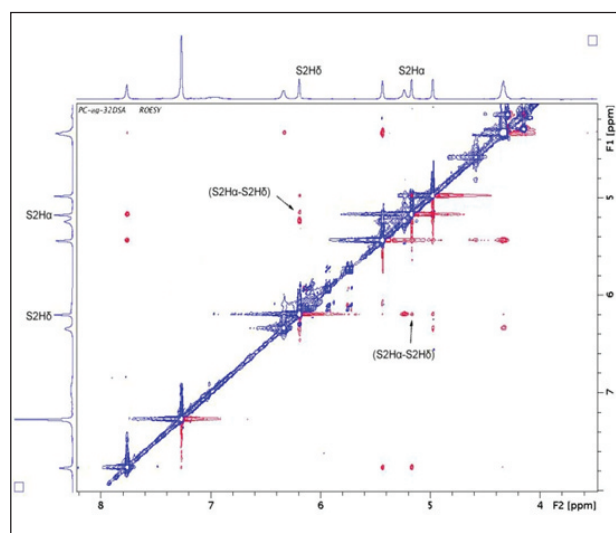
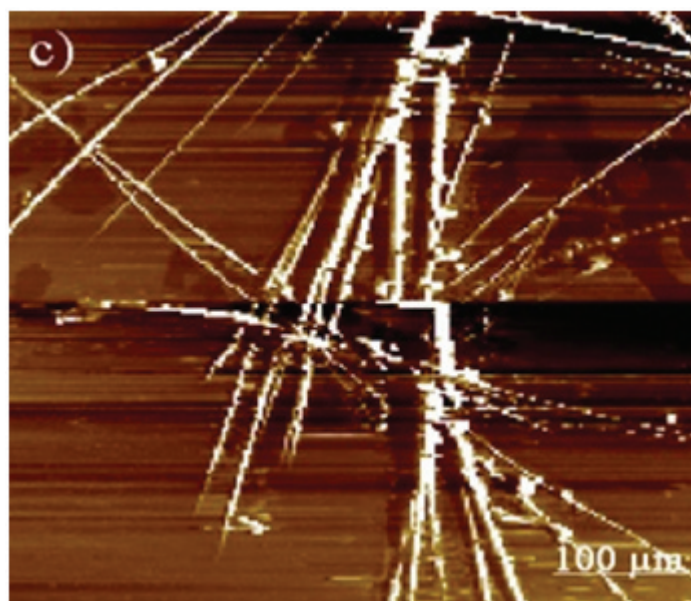
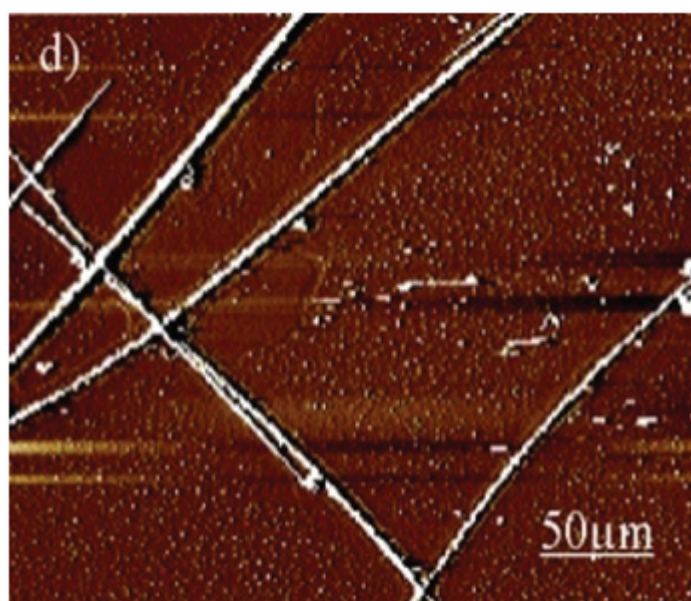


Fig 2: Selected region of the ROESY spectrum of macrocyclic peptide **1** showing parallel-homostacking interaction by cross peaks between SH α -SH δ in (2:3) CDCl₃:CCl₄ (600 MHz, 298K).



AFM images (c) and (d): Rod like assemblies of 1 in (2:3)



$\text{CDCl}_3:\text{CCl}_4$.

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Nucleic acid and protein binding by plant alkaloids, food colorants and small molecules

Participants

JRF: Sabyasachi Chatterjee, Baishakhi Saha

SRF: Anirban Basu, Abhi Das, Asma Yasmee Khan, Debipreeta Bhowmik, Ayesha Kabir, Soumitra Hazra, Chandrima Jash, Pritha Basu

RA: Srabanti Kumar

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Name of collaborator within CSIR-IICB

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Cancer Biology and Inflammatory Disorder Division

Background

The binding of small molecule alkaloids, dyes and drugs to nucleic acids is an important area to understand the molecular aspects of the interaction. This data is required to develop them as nucleic acid targeted drugs. Furthermore, their binding to functional and carrier proteins need to be studied to understand their efficacy in delivering them to specific sites. In order to develop natural product alkaloids and related molecules as therapeutic agents we studied the interaction of a number of small molecule alkaloids, their analogs and other dyes and drugs to nucleic acids and many functional proteins.

Aims and Objectives

Study the structural aspects of interaction of plant alkaloids, dyes and small molecules with RNA, DNA and proteins.

Elucidate the thermodynamics of the interaction. Correlate the structural aspects with energetic data.

Work Achieved

Our laboratory is interested in elucidating the structural and thermodynamic aspects of the interaction of small molecules like natural alkaloids, their analogs, dyes and other molecules with nucleic acids (RNA and DNA) and functional proteins.

We studied the binding of the iminium and alkanolamine forms of the benzophenanthrine alkaloid chelerythrine (**Fig. 1**) to lysozyme (Lyz) using spectroscopy, calorimetry and docking studies. Spectroscopic evidence suggested that Trp-62 and Trp-63 in the beta-domain of Lyz are closer to the binding site; the binding site was evaluated to be at a distance of 2.27 and 2.00 nm from the iminium and alkanolamine forms, respectively, according to the Forster theory of non-radiative energy transfer. The binding constants for the iminium and alkanolamine forms

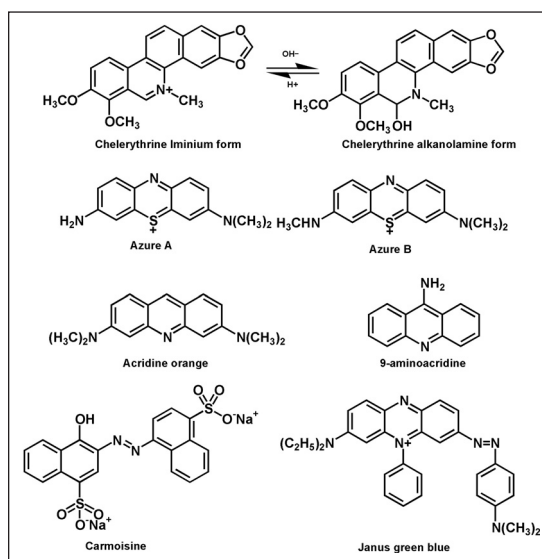


Fig. 1: Chemical structure of the alkaloid chelerythrine (iminium and alkanolamine forms), food colorant carmoisine, acridine dyes acridine orange and 9-aminoacridine phenathazinium dyes azure A and azure B and janus green blue.

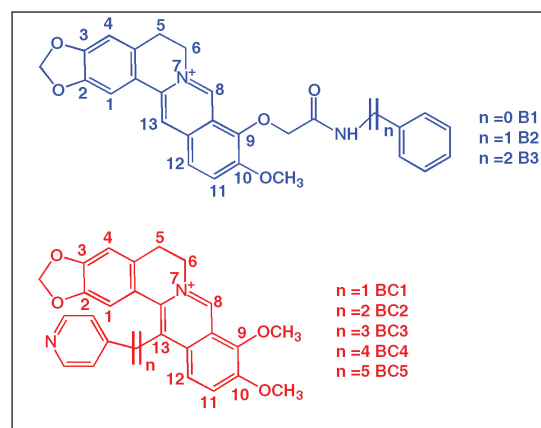


Fig. 3: Structure of 13-pyridinealkyl 9- ω -amino hexyl ether analog berberine analogues.

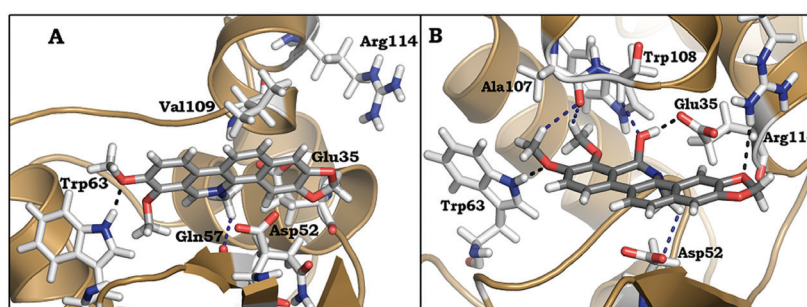


Fig. 2: Crucial H-bond interactions (classical and non-classical) of (A) iminium and (B) alkanolamine (R). Black and blue dotted line denote the classical and the non-classical H-bonds, respectively.

at 298.15 K were evaluated to be 1.29×10^5 and $7.79 \times 10^5 \text{ M}^{-1}$, respectively. The binding resulted in an alteration of the secondary structure of the protein with a distinct reduction of the helical organization. The binding of the iminium was endothermic, involving electrostatic and hydrophobic interactions, while that of the alkanolamine form was exothermic and dominated by hydrogen bonding interactions. Docking studies provided the details pertaining to the binding of both forms of chelerythrine and supported the higher binding in favour of the alkanolamine over

the iminium. **(Fig. 2)** Furthermore, molecular dynamics study provided accurate insights regarding the binding of both chelerythrine forms in accordance with the experimental results. Chelerythrine binding pocket involves the catalytic region and aggregation prone K-peptide region, which are sandwiched between one another. Overall, these results suggest that both the forms of the alkaloid bind to the protein but the neutral form has higher affinity than the cationic form.

Chelerythrine binds to the duplex poly(A).poly(U) and triplex RNA, poly(U). poly(A)*poly(U), in a



cooperative manner with affinity of the order of 10^6 M^{-1} . A weaker binding ($\sim 10^5 \text{ M}^{-1}$) in a non-cooperative mode was found for poly(U). Chelerythrine is more selective towards RNA triplex than its parent duplex.

We also studied a new series of 13-pyridinealkyl berberine analogues (**Fig. 3**) on their DNA binding efficacy using spectroscopic, calorimetric and molecular modeling techniques. Analogues with more than one CH_2 group showed better intercalative binding than berberine. The analogue with one CH_2 group bound DNA weaker than berberine. The binding of the analogue with single CH_2 group was entropy driven, while those with more than one CH_2 group was favoured by both entropy and enthalpy changes. Higher salt concentration and temperature destabilized the binding. A larger contribution from non-polyelectrolytic forces to the Gibbs energy and the involvement of strong hydrophobic interactions were inferred. Molecular modeling pin pointed the specific binding site and the non-covalent interactions in the association. The best DNA binding analogue (BER5) inhibited the growth of hepatocellular and breast carcinoma most efficiently. It induced apoptosis in HepG2 and MCF-7 cells with externalization of phosphatidylserine and reactive oxygen species generation with accumulation of cells in the G0/G1 phase. Furthermore, up regulation of p53 and p21 indicated the role of p53 in BER5 mediated apoptosis. The results suggested that 13-pyridinealkyl berberine analogues intercalated to DNA much stronger than berberine, the chain length of the linker plays an important role for the binding, and they induced ROS mediated apoptosis in HepG2 and MCF-7 cells by p53 modulation. It was also found that the 9- ω -amino hexyl ether analog (**Fig. 3**) of berberine stabilized the human telomeric G-quadruplex structure better than the 13-phenyl alkyl analog (**Fig. 3**) as revealed from

spectroscopic and calorimetric studies.

The binding aspects of the food colorants carmoisine, acridine dyes acridine orange and 9-aminoacridine (**Fig. 1**) to hemoglobin and tartrazine to double stranded deoxyribonucleic acids were elucidated. Proflavine-DNA interaction was characterized by microcalorimetric studies. Spectroscopic and thermodynamic investigation on the binding of phenothiazinium dyes azure A and azure B (**Fig. 1**) to double stranded RNA polynucleotides and that of janus green blue with double stranded DNA was also performed.

Overall new data on the interaction of a wide variety of small molecules to nucleic acid structures, and many functional proteins have been advanced.

Future Research Plans

Structural and thermodynamics studies on the interaction of alkaloids and other small molecules with G-quadruplexes,

PUBLICATIONS

- Basu, A., and Suresh Kumar, G. (2015) Thermodynamic characterization of proflavine-DNA binding through microcalorimetric studies. *J Chem Thermodyn* **87**, 1-7
- Basu, A., and Suresh Kumar, G. (2015) The food colorant carmoisine can bind strongly to hemoglobin: Spectroscopic and calorimetric characterization. *Food Res Int* **72**, 54-61
- Basu, P., and Suresh Kumar, G. (2015) Structural and thermodynamic basis of interaction of the putative anticancer agent chelerythrine with single, double and triple-stranded RNAs. *RSC Adv* **5**, 29953-29964
- Jash, C., Basu, P., Payghan, P.V., Ghoshal, N., and Suresh Kumar, G. (2015) Structural and thermodynamic studies on the interaction of iminium and alkanolamine forms of benzophenanthridine alkaloid chelerythrine with lysozyme. *Phys Chem Chem Phys* **17**, 16630-16645
- Khan, A.Y., and Suresh Kumar, G. (2015) A thermodynamic investigation on the binding of phenothiazinium dyes azure A and azure B to double stranded RNA polynucleotides. *J Chem Thermodyn* **91**, 225-233
- Chatterjee, S., Mallick, S., Buzzetti, F., Fiorillo, G., Syeda, T. M., Lombardi, P., Saha, K.D., and Suresh Kumar, G. (2015) New 13-pyridinealkyl berberine analogues intercalate to DNA and induce apoptosis in HepG2 and MCF-7 cells through ROS mediated P53 dependent pathway: Biophysical, biochemical



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Kundu, S., Banerjee, A., De, A., Khan, A.Y., Suresh Kumar, G., Bhadra, R. and Ghosh, P. (2015) Synthesis, fluorescence spectra, redox property and the DNA binding studies of 7-phenylacene[1,2-b]quinoxalin-7-ium chloride: evidences of the formation of neutral radical analogue. *J Fluorescence* **25**, 1637-1643

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Khan, A.Y., and Suresh Kumar, G. (2016) Spectroscopic studies on the binding interaction of phenothiazinium dyes, azure A and azure B to double stranded RNA polynucleotides. *Spectrochim Acta Part A* **152**, 417-425

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Maity, P., Saha, B., Suresh Kumar, G., and Karmakar, S. (2016) Binding of monovalent alkali metal ions with negatively charged phospholipid membranes. *Biochim Biophys Acta- Biomembranes* **1858**, 706-714

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Saha, B., and Suresh Kumar, G. (2016) Calorimetry and thermal analysis studies on the binding of janus green blue to calf thymus DNA. *J Therm Anal Calorim* **123**, 1993-2001

Guhathakurta, B., Basu, P., Suresh Kumar, G., Lu, L., Zhu, M., Bandyopadhyay, N., and Naskar, J. P. (2016) Synthetic, structural, electrochemical and DNA-binding aspects of a novel oximate bridged copper(II) dimer. *Polyhedron* **110**, 227–234

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Chatterjee, S., and Suresh Kumar, G. (2016) Probing the binding of fluorescent acridine dyes acridine orange and 9-aminoacridine to hemoglobin and elucidation of their molecular recognition by spectroscopic, calorimetric and molecular modeling techniques. *J Photochem Photobiol B* **159**, 169–178

Basu, A., and Suresh Kumar, G. (2016) Studies on the interaction of the food colorant tartrazine with double stranded deoxyribonucleic acid. *J Biomol Struct Dyn* **34**(5), 935-942

Basu, A., and Suresh Kumar, G. (2016) Thermodynamics of the induction of self-structure in polyadenylic acid by proflavine. *J Chem Thermodyn* **100**, 100-105

Book Chapters / Invited Reviews

Khan, A.Y., and Suresh Kumar, G. (2015) Natural isoquinoline alkaloids: Binding aspects to functional proteins, serum albumins, hemoglobin and lysozyme. *Biophys Rev* **7**, 407-420

Bhowmik, D., and Suresh Kumar, G. (2016) Recent advances in nucleic acid binding aspects of berberine analogues and implications for drug design. *Mini Rev Med Chem* **16**, 104-109

Suresh Kumar, G., and Basu, A. (2016) The use of calorimetry in the biophysical characterization of small molecules binding to RNA structures. *Biochim Biophys Acta* **860**, 930-944

AWARDS / HONOURS / MEMBERSHIPS

C.R Krishna Murti Award (2015) by the Society of Biological Chemists

Setaram-ITAS Calorimetry Excellence Award 2016

Students

Dr. Debipreeti Bhowmik

Awards

Dr. Gurdip Singh Best thesis award (2016) by the Indian Thermal Analysis Society

CONFERENCES / WORKSHOPS

Number of abstracts India: 8 International: 3

INVITED TALKS

Nucleic acid interaction of small molecules: From lac repressor protein fragments, mitomycin C to natural alkaloids; BITS Pilani Hyderabad Campus; 14th FAOBMB Congress and 84th annual meeting of SBC(I), 24-30 November 2015, Hyderabad, India.

Thermal analysis and calorimetry as effective tools to Investigate ligand-biomolecular Interactions, BHU; DAE-BRNS 20th Symposium on thermal analysis -THERMANS-2016, 18 -20 January 2016, Varanasi, India.

Thermal analysis and calorimetry as effective tools to Investigate drug-biomolecular Interactions; Jadavpur University, Symposium on Recent Trends in Research in Physics, 21 March 2016 Kolkata, India.

Dr. Parasuraman Jaisankar

jaisankar@iicb.res.in



Racemization barriers of atropisomeric 3, 3'-bipyrroles: An experimental study with theoretical verification

Participants

RA: Dr. Sreya Gupta

Ext. SRF: Mr. Chiranjit Acharya

SRF: Mr. Sourav Chatterjee, Rahul Gajbhiye

Proj. Asst.: Mr. Pinaki Bhattacharjee, Ms. Anushree Achari

Background

Atropisomers are stereoisomers that principally arise due to the constrained rotation of single bonds flanked by a pair of hindered planar groups; the stereogenicity of these molecules originates from the concept of axial chirality. These optically active molecules are widely employed in applications such as medicinal chemistry, molecular devices, electrochemical polymerization, spectrochemical and photophysical investigations, asymmetric catalysis, and organic dyes. The biological activities, toxicities and pharmacokinetics of an individual atropisomer may fluctuate in biological environment due to significant diastereomeric interactions. Although there is immense interest in biaryl atropisomers, one of the major problems associated with their practical application is that their chiral stability is often poor due to an insufficient atropisomerization energy barrier. Thus, an important area of research is to investigate new kinds of atropisomers having significantly higher atropisomerization energy and deduce the process of determination of their thermodynamic properties.

Aims and Objectives

Our objective was to establish a systematic detailed study for the determination of activation barrier of racemization of 3,3'-bipyrrole systems, which could enable us to identify stable enantiomers that may prove useful in biology and materials science.

Work Achieved

In the present study, The significant rotational energy barrier about the stereogenic carbon carbon bond of axially chiral 3,3'-bipyrroles have been investigated by the electronic circular dichroism (ECD) spectroscopy, time dependent HPLC analysis, and computational modeling. A series of experimental studies confirmed the stability of enantiomerically pure atropisomer of 3,3'-bipyrroles at ambient temperature. The activation



barrier of racemization for 3,3'-bipyrroles were experimentally determined to be $\sim 26 \text{ kcal.mol}^{-1}$ which are in good agreement with the computational results. The emerging importance of very slow rate of isomerization of 3,3'-bipyrroles grants an ease of separation and potential for storage of an individual enantiomer without the erosion of its optical purity, which might be useful for numerous advanced studies.

Future Research Plans

Two enantiomers of an atropisomeric mixture may differ in their toxicities, biological activities and pharmacokinetics. These enantiomers can also be interesting for their uses as molecular recognition, molecular clefts etc. in the field of materials science. As the two individual enantiomer of 3,3'-bipyrroles are isolable and significantly stable at room temperature, our further research goal is in the line of detailed study of their electrochemical properties. We will also focus on the investigation of racemization kinetics of other bis-heterocyclic systems.

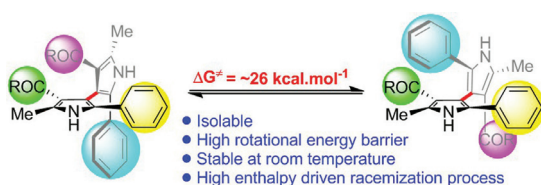


Fig. 1: Activation barrier of racemization of 3,3'-bipyrroles

PUBLICATIONS

Pal, R., Chatterjee, N., Roy, M., El Said A. Nouh, Sarkar, S., Jaisankar P, Sarkar, S., and Sen, A. K. (2016) Reusable palladium nanoparticles in one-pot domino Sonogashira-cyclization: Regio- and stereo-selective syntheses of (Z)-3-methyleneisindoline-1-ones and furo[3,2-h]quinolines in water. *Tetrahedron Lett* **57**, 43-47

Banerjee, T., Kar, D., Krishna, P. R., Prabhakar, S., Nomula, R., Mallula, V. S., Ravindranath, H., Sridhar, G., Adepu, R., Srikanth, G., Mabalirajan, U., Ghosh, B., Jaisankar, P, Johri, R., Chakraborty, D., Mishra, V., Chhabra, J. K., Shukla, M., Paul, B. N., Bandyopadhyay, S., Roy, S., Sharma, G. V. M. and Bandyopadhyay, A. (2015) A Novel Triazine-Aryl-Bis-Indole Derivative Inhibits both Phosphodiesterase IV and Expression of Cell Adhesion Molecules. *RSC Adv* **5**, 70271-70281

PATENTS FILED / SEALED

Name Surname PARASURAMAN

JAISANKAR AND SNEHASIKTA SWARNAKAR

Patent Title: 3-INDOLYL FURANOIDS AS INHIBITORS OF MATRIX METALLOPROTEINASE-9 FOR PREVENTION OF GASTRIC ULCER AND OTHER INFLAMMATORY DISEASES

Country: United States

Patent No.: Applied for filing

Date filed / granted: Applied for filing

Co-inventors and their Institutes: SOURAV CHATTERJEE (CSIR-IICB), SUGREEV VERMA (CSIR-IICB), MADHUMITA MANDAL (CSIR-IICB), SUSHRI RAY CHAUDHURI (CSIR-IICB)

Patent filed by: CSIR-IICB

AWARDS / HONOURS / MEMBERSHIPS

Awards

Indian National Science Academy (INSA) Award, 2015 for International Collaboration/Exchange Programme at Taiwan

Student

Sourav Chatterjee

Award

Best poster award in ISCBDD-2016 sponsored by ACS Chemical Biology

CONFERENCES / WORKSHOPS

Number of abstract India: 1 Taiwan: 1

INVITED TALKS

• *Modification of indomethacin as inhibitors of matrix metalloprotease-9 for prevention of gastric ulcer and other inflammatory diseases.* International Conference on Molecular Signalling: Recent Trends in Biosciences, North-Eastern Hill university (NEHU), 20-22 November 2015. Shillong, India.

• *Challenges and Strategies in Natural Product Research (Division of Pharmacognosy)* AICTE SPONSORED Quality Improvement Program 2015 organized by BIT. 26 November – 9 December 2015. Mesra, Ranchi.

Dr. Chinmay Chowdhury

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Synthesis and biological evaluation of a novel betulinic acid derivative as inducer of apoptosis in human colon carcinoma cells (HT-29)

Participants

SRF: Priyanka Kundu, Moumita Jash, Amrita Mondal

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Santanu Paul

Calcutta University

Name of collaborator within CSIR-IICB

Dr. Padma Das

Cancer Biology and Inflammatory Disorder Division

Background

Betulinic acid (BA) is found to be cytotoxic towards a variety of cancer cell lines such as lung, ovarian, cervical, neuroblastoma, and glioblastoma including head and neck carcinomas. It has low toxicity and high safety profile in normal cell lines, and is safe for use even at a dose of 500 mg/Kg body weight. This feature calls for its development as anticancer drug in preference to other natural products like taxol, camptothecin, ellipticine, etoposide, vinblastin and vincristin etc. Besides, BA acts as potent inhibitor of eukaryotic topoisomerase I and II. Despite such encouraging results, the poor solubility of BA preventing blood serum solubilizations and its low bioavailability have limited its potential to be used as a drug candidate. In order to overcome this lacuna, efforts are being made for structural modifications through judicious manipulation of the functional groups present in the molecule. In continuation of our studies on structural modulations of bioactive natural products for the development of lead(s) having better efficacy and less toxicity than the parent compound, we chose betulinic acid to prepare an analogue library.

Aims and Objectives

To synthesize a number of 1,2,3-triazole derivatives (at C3) of betulinic acid and to assess the potency of these compounds and the parent compound (BA) for the induction of cell death in five different cancer cell lines along with normal epithelial cells. This may result into the identification of lead molecule(s) for further development

Establish the apoptotic properties of the lead molecule using technique like ROS generation, the externalization of phosphatidylserine, loss in mitochondrial membrane potential, induced expression of pro and antiapoptotic proteins, and appreciable DNA fragmentations etc.

To study the mechanism of action of the lead molecule to provide insight into anticancer activity.

To study the binding efficacy and mode of binding with DNA of the lead molecule.



Work Achieved

Betulinic acid (**1**, **Fig. 1**) used in this study was isolated in bulk quantity (~ 50 g) from methanolic extracts of the *Dillenia indica* fruits. A novel family of betulinic acid analogues (**2**, **Fig. 1**), carrying a triazole unit at C-3 attached through a linker, was

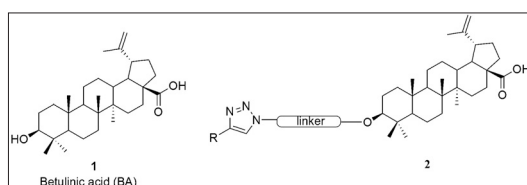


Fig. 1: Betulinic Acid (**1**) and its designed analogues **2**

synthesized by the application of azide-alkyne "Click reaction". The requisite azide intermediate was prepared in two steps comprising (a) treatment of the betulinic acid (**1**) with chloroacetyl chloride in the presence of *N,N*-diisopropylethylamine (DIPEA) and 4-dimethylaminopyridine (cat. DMAP) followed by (b) azidation of the resulting compound by using sodium azide in dry DMF. The cytotoxic activity of betulinic acid analogues (**2a-l**) was studied using MTT assay on cultured cancer cells such as U937, HT-29, Jurkat, HepG2, MCF-7 as well as normal human PBMC cells. 5-Fluorouracil was used as the reference compound. Compound **2c** (**Fig. 1**), R=CH₂OH) was found as the most potent inhibitor of cell line HT-29 with IC₅₀ value 14.9 μM. Its role as an inducer of apoptosis was investigated in this cell line by Annexin-V/PI binding assay and by following its capability for ROS generation, depolarization of mitochondrial transmembrane potential, activation of caspases, PARP cleavage, nuclear degradation and expression of pro- and anti-apoptotic proteins. Besides, the treatment of the HT-29 cells with 14.9 μM of compound **2c** resulted in the induction of chromatin condensation, fragmentation, membrane blebbing and clear apoptotic bodies that were visualized in confocal microscopy (**Fig. 2**).

Future Research Plans

Preparation of the nanoencapsulated betulinic acid analogue (**2c**) and its apoptotic study in human

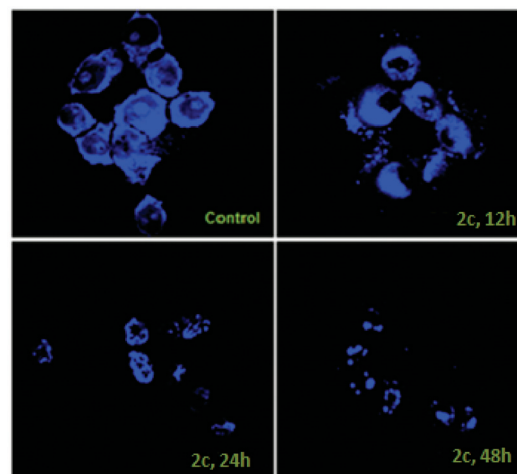


Fig. 2: Nuclear degradation induced by **2c**. Control and **2c** treated (14.9 μM; 0-48 h) HT-29 cells (2.5 x 10⁵/mL) were stained with Hoechst 33258 and observed under Leica confocal microscope (100x).

colon carcinoma (HT-29) cells.

Synthesis of benzo[a]carbazoles via Pd(II)-catalyzed hetero- and carboannulations in one-pot.

Development of a palladium-catalyzed method for the synthesis of 2-(α -styryl)quinazolin-4(3H)-ones and 3-(α -styryl)-1,2,4-benzothiadiazine-1,1-dioxides.

PUBLICATIONS

Chakraborty, B., Dutta, D., Mukherjee, S., Das, S., Maiti, N. C., Das, P., and Chowdhury, C. (2015) Synthesis and biological evaluation of a novel betulinic acid derivative as inducer of apoptosis in human colon carcinoma cells (HT-29). *Eur J Med Chem* **102**, 93-105

Kundu, P., Mondal, A., Das, B., and Chowdhury, C. (2015) A Straightforward Approach for the stereoselective synthesis of (E)-2-aryl/vinylmethylidene-1,4-benzodiazepines and -1,4-benzodiazepin-5-ones through palladium/charcoal-catalyzed reactions, *Adv Synth Catal* **357**, 3737-3752

Kumar, D., Das, B., Sen, R., Kundu, P., Manna, A., Sarkar, A., Chowdhury, C., Chatterjee, M., and Das, P. (2015) Andrographolide Analogue Induces Apoptosis and Autophagy Mediated Cell Death in U937 Cells by Inhibition of PI3K/Akt/mTOR Pathway. *PLoS One* **10**, e0139657

Dutta, D., Chakraborty, B., Sarkar, A., Chowdhury, C., and Das, P. (2016) A potent betulinic acid analogue ascertains an antagonistic mechanism between autophagy and proteasomal degradation pathway in HT-29 cells. *BMC Cancer* **16**, 23

EXTRAMURAL FUNDING

Co-Principal Investigator: Chinmay Chowdhury

Study of the anti-leukemic and anti-oxidant potential of some wild edible mushrooms of West Bengal: Leading to chemical identifications of the lead molecules. 2014-2017 (DBT, Govt of West Bengal).

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Plant Biology: Crosstalk of GSH with other phytohormones to combat environmental stress *In planta*

Participants

JRF: Asma Sultana, Soumi Biswas, Priyanka

SRA: Dr. Rajgouvab Ghosh

SRF: Saptarshi Hazra, Deepak Kumar, Aparupa Bose Mazumder

Project Assistant: Anuja Joseph

Collaborator(s)

Name of collaborator outside CSIR-IICB

Prof. P. S. Chaudhuri, Professor of Zoology, Tripura University, Tripura

Name of collaborator within CSIR-IICB

Dr. Saikat Chakraborty & Dr. Sucheta Tripathy

Structural Biology and Bioinformatics Division

Background

Plants are consistently exposed to unfavourable growth conditions throughout their life cycle. To ensure survival, plants must effectively and efficiently sense, respond, and adapt to their ever-changing environment. Abiotic stresses viz. drought, temperature fluctuations, salinity, radiation, nutrient deprivation etc. adversely affect growth, development and productivity. Considering biotic challenges, plants are also continuously threatened by a wide range of harmful pathogens and pests, including viruses, bacteria, fungi, oomycetes, nematodes and insect herbivores. To defend themselves, plants evolved sophisticated surveillance systems. Understanding the molecular basis of perception of stress and transduction of signals is of great interest to plant researchers. Classic phytohormones, viz. ABA, auxins, cytokinins, ET and gibberellins, but small signalling molecules such as brassinosteroids, jasmonates (JAs) and salicylic acid (SA) also recognized as phytohormones, interact with each other in a synergistic and/or antagonistic fashion to resist unfavourable environmental stress conditions. Glutathione, being an almost ubiquitous molecule, fulfils various important roles in plant functioning making it a dynamic biomolecule. It is fair to note that although most of our current knowledge concerning the participation of GSH in the environmental stress tolerance is established; however, the intricate mechanism of GSH's participation in the multifarious signalling network is yet to be known.

Aims and Objectives

To unravel the dynamic complexity of plant disease resistance mechanism and crosstalk of GSH with other established signaling molecules to combat environmental stress's *in planta*.

To elucidate the biosynthetic pathways of plant secondary metabolites viz. podophyllotoxin.



Work Achieved

To this end, our investigation indicated that GSH-mediated resistance occurs via an ET-mediated pathway to challenge necrotrophic infection and salt-stress (**Fig. 1**). We have also demonstrated a

dual-level regulation of ET biosynthesis by GSH during stress.

Medicinal Plant & Metabolic Engineering: Cloning of podophyllotoxin biosynthetic pathway gene/s from *Podophyllum hexandrum* Royle and establishment of transgenic lines (**Fig. 2**).

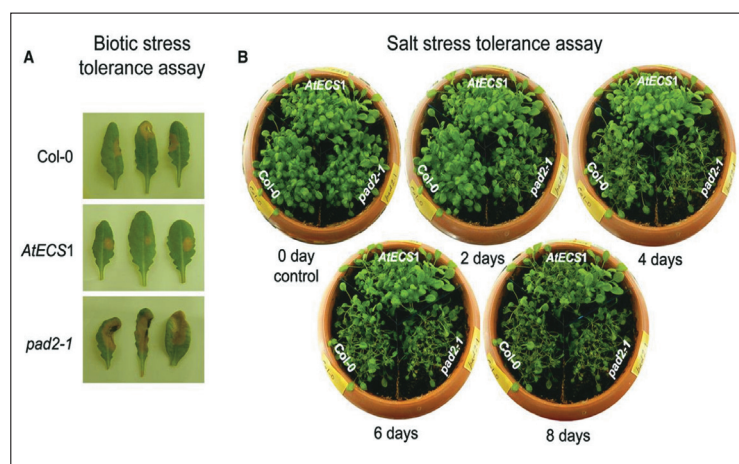


Fig. 1: Stress response assay of Col-0, *AtECS1*, and *pad2-1* plants. **A** Biotic stress assay in response to *Botrytis cinerea* infection. **B** Abiotic stress assay in response to salt stress. The *AtECS1* transgenic plants exhibited resistance against both the stresses, while the *pad2-1*, the GSH mutant, was susceptible.

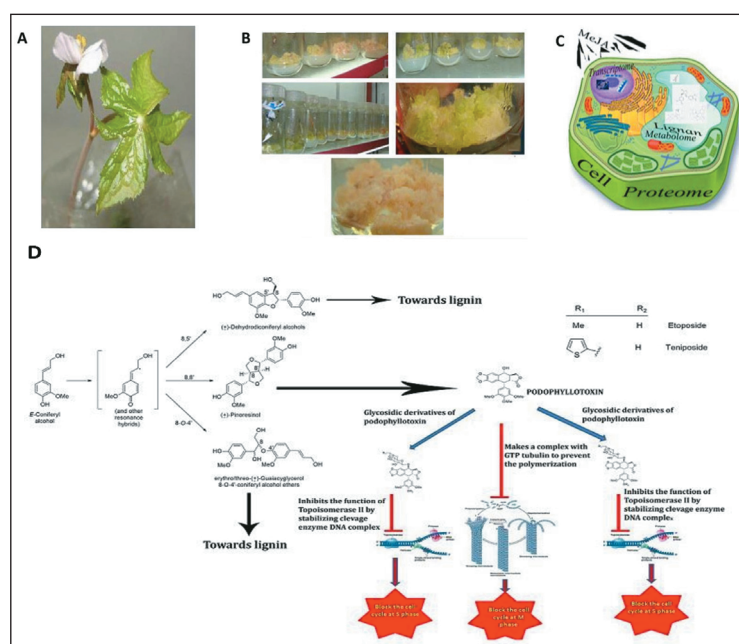


Fig. 2: **A.** A flower twig of *P. hexandrum*; **B** Leaf derived green & brown callus of *P. hexandrum*; **C** Exogenous application of MeJA to cell suspension cultures of *P. hexandrum*; **D** Trafficking of Coniferyl alcohol, a precursor of podophyllotoxin, by regio and stereospecific coupling towards lignin and lignan biosynthesis.



Future Research Plans

Proteomic profiling of stress treated *pad2.1*, a GSH mutant.

Exploring the mechanism of interaction between HSPs and GSH in stress management.

PUBLICATIONS

Datta, R., and Chattopadhyay, S. (2015) Changes in the proteome of *pad2-1*, a glutathione depleted *Arabidopsis* mutant, during *Pseudomonas syringae* infection. *J Proteom* **126**, 82-93

Kalim, M.D., Dutta, D., Das, P., and Chattopadhyay, S. (2015) Evaluation of phytochemicals interrelated to the antioxidant potential of Unani plants. *Int J Pharma and Bio Sci* **6**, 330 – 342

Bhattacharyya, D., and Chattopadhyay, S. (2015) Characterization of podophyllotoxin biosynthetic pathway and future prospect of podophyllotoxin production from *Podophyllum hexandrum* Royle. *Chem Biol Let* **2**, 12-21

Datta, R., Kumar, D., Sultana, A., Hazra, S., Bhattacharyya, D., and Chattopadhyay, S. (2015) Glutathione regulates ACC synthase transcription via WRKY33 and ACC oxidase by modulating mRNA stability to induce ethylene synthesis during stress. *Plant Physiol* **169**, 2963-2981

Bose Mazumder A., and Chattopadhyay, S. (2015) Sequencing, De novo assembly, functional annotation and analysis of *Phyllanthus amarus* leaf transcriptome using the Illumina platform. *Front Plant Sci* **6**, 1199

Hazra, S., and Chattopadhyay, S. (2016) An overview of lignans with special reference to podophyllotoxin, a cytotoxic lignan. *Chem Biol Let* **3**, 1-8

EXTRAMURAL FUNDING

Crosstalk of GSH with other signaling molecules to combat biotic stress in *planta*

2014-2017

SERB (formerly DST), New Delhi, India

CONFERENCES / WORKSHOPS

Number of abstracts India: 1, International: 1

INVITED TALKS

Environmental stress tolerance potential of transgenic mint with enhanced GSH content Invited talk. University Paris Diderot-Paris 7/3rd International Symposium on Plant Signaling and Behavior, 29 June – 2 July, 2015, Paris, France.

Interplay of glutathione with salicylic acid and ethylene to combat biotic stress. Department of Botany, University of Calcutta, / National Seminar on "Genomic Perspectives of Host-Pathogen Interaction, 3 December 2015, Kolkata, India.

Cross talk of Glutathione with ethylene to combat environment stress conditions. CSIR-NBRI/37th Annual Meeting of PTCA (India) & National Symposium on Plant Biotechnology for Crop Improvement, 25-27 February 2016, Lucknow, India.

Dr. Biswadip Banerji

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Regioselective synthesis of quinazolinone-phenanthridine fused heteropolycycles by Pd-catalyzed direct intramolecular aerobic oxidative C-H amination from aromatic strained amides

Participants

SRF: Suvankar Bera, Satadru Chatterjee, Sunil K Killi, Saswati Adhikary

Background

A new route for the expedient synthesis of specific regioisomer of quinazolinone and phenanthridine fused heterocycles through a palladium-catalysed regioselective intramolecular oxidative C-H amination from cyclic strained amides of aromatic amido-amidine systems (quinazolinone), has been developed. Amine functionalization of an aromatic C-H bond from strained amide nitrogen, involved in aromaticity has been a challenging work so far. More importantly, fusion of two heterocyclic cores, quinazolinone and phenanthridine can occur in two different fashions (linear and angular), but under the condition reported here, only linear type isomer is exclusively produced. However, this approach provides a variety of substituted quinazolinone & phenanthridine fused derivatives in moderate to excellent yields. Further, these fused molecules show excellent fluorescent property and have great potential to be a new type of fluorophores for the use in medicinal and material science.

Aims and Objectives

Design and synthesis of 'New Chemical Entities' (NCE) and study their biological/biophysical efficacy to produce 'New Therapeutic Entities' (NPT).

Efficient Synthetic Organic Methodologies to deliver 'Hot Molecule' for Future 'Biomaterials'.

Nanoformulation of small Peptide/non-peptidic molecules and study their Biophysical properties to cater different therapeutic application.

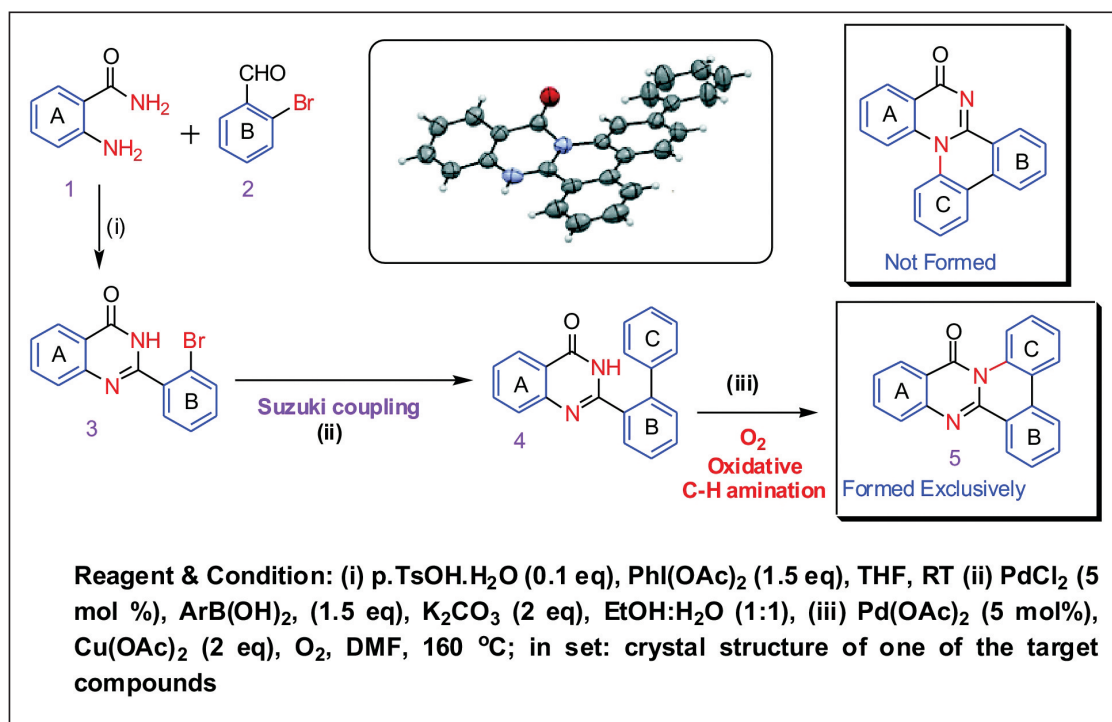


Fig. 1: Regioselective Synthesis of Quinazolinone-Phenanthridine Fused Heteropolycycles by Pd-Catalyzed Direct Intramolecular Aerobic Oxidative C-H Amination

PUBLICATIONS

Banerji, B., Bera, S., Chatterjee, S., Killi, S.K., and Adhikary, S. (2016) Regioselective Synthesis of Quinazolinone-Phenanthridine Fused Heteropolycycles by Pd-Catalyzed Direct Intramolecular Aerobic Oxidative C-H Amination from Aromatic Strained Amides. *Chem-A Eur Journal* **10**, 3506-3512

EXTRAMURAL FUNDING

Targeting HSP-90 as cancer therapy: Design and synthesis of mahanine

Derived Second-Generation lead molecules. Year: 2016 - 2019 (SERB-DST, India)

Dr. Surajit Ghosh

sghosh@iicb.res.in



Peptide-based therapeutics for Alzheimer's Diseases (AD)

Participants

JRF: Krisnangsu Pradhan, Surajit Barman Gaurav Das

SRF: Abhijit Saha, Batakrishna Jana, Prasenjit Mondal, Saswat Mohapatra, Debmalya Bhunia, Anindyasundar Adak

Project Fellow: Subhajit Ghosh

Collaborator(s)

Name of collaborator outside CSIR-IICB

Prof. Kankan Bhattacharyya & Prof. Arindam Banerjee

IACS Kolkata

Prof. Sandeep Verma

IIT Kanpur

Prof. D Mal

IIT Kharagpur

Prof. Yoshio Aso & Prof. Takeshi Sato

Osaka University, Japan

Prof. Siddhartha Roy

Bose Institute

Dr. Kaustabh Kumar Maiti

CSIR, IIIST-Trivandrum

Name of collaborator within CSIR-IICB

Dr. Samit Chattopadhyay

Cancer Biology and Inflammatory Disorder Division

Dr. Subhash Chandra Biswas

Cell Biology and Physiology Division

Dr. R. Natarajan

Organic and Medicinal Chemistry Division

Dr. N. C. Maiti

Structural Biology and Bioinformatics Division

Background

In last three decades, Alzheimer's disease (AD) has become a major threat for elderly people around the globe and millions of people are suffering in this devastating disease. Amyloid-beta ($A\beta$) peptide plays central role in AD, misfolds into the β -sheet rich conformation, forms long unbranched fibers and becomes insoluble inside the cellular milieu, which deposits as amyloid plaques followed by disruption of neuronal networks. $A\beta$ fiber is also known to disrupt intracellular microtubule networks. Therefore, development of novel inhibitor for $A\beta$ fibrillizations is extremely important for potential therapy of AD. Till date, there are no approved therapies for inhibiting amyloid fibrillizations. However, many small molecules including one octapeptide (NQ: NAPVSIQ) inhibit fibrillizations *in vitro*. Among them, small molecule clioquinol inhibits *in vivo* $A\beta$ fibrillizations and NQ inhibits *in vivo* tau hyperphosphorylation. Interestingly, Shoichet group and others have found that many fibrillization inhibitors like molecules form spontaneous chemical aggregates, which are colloidal like particles with varying sizes from 50 to 600 nm. Recently, we have also found that NQ, which is known to inhibit tau hyperphosphorylation *in vivo*, spontaneously forms amyloid like fibrils and inhibits amyloid fibril formation *in vitro*. Although there are few molecules, like clioquinol and NQ inhibit $A\beta$ fibrillizations and show potential in *in vivo* studies, but success rate in clinical stage is still poor. Therefore, development of potential amyloid inhibitor is extremely important for the treatment of AD. Currently, our group is working on this field and actively searching for new peptide and peptoid based therapeutics against AD.

Aims and Objectives

To develop peptide/peptoid-based therapeutics for Alzheimer Disease.

To develop small molecule based neuroprotecting agent.



Work Achieved

Microtubule plays important role in eukaryotic cell division and function. In addition, microtubule also plays important role in signal transduction in brain and during Alzheimer's disease (AD) microtubules are severely disrupted. Therefore, microtubule is the key target for development of both anti-cancer and anti-alzheimer therapeutics. We have developed peptides and various small molecules for controlling microtubule dynamics using *in vitro* assays, 2D and 3D-Spheroid cell culture-based assays and *in vivo* mice model. Our high quality work has been published in top international journals chemical biology area. [Jana *et al.*, ACS Appl. Mater. Interfaces, 2016, Just Accepted, Adak *et al.*, Chem. Commun. 2016, Just Accepted, Saha *et al.*, RSC Adv. 2015, Jana *et al.*, Chem. Commun. 2015, Nair and Mohapatra *et al.*, Chem. Commun. 2015].

We have developed peptides, peptoids and small molecules for neuroprotection against damage caused due to Alzheimer's disease (AD). Our achievements resulted in patents (*Under process in US Office*) and high quality research articles [Biswas *et al.*, ACS Chem. Neuroscience, 2015; Biswas *et al.*, Chem. Commun. 2014, Ghosh *et al.*, US patent filed; Ghosh *et al.*, PCT patent under preparation; Ghosh *et al.*, PCT patent under preparation; Saha *et al.*, Chem. Commun. 2013, Saha *et al.*, Chem. Commun. 2015].

Reconstitution of biological events or structure is extremely important to understand the detailed function of the key important player when they work in a group. For this purpose, highly biocompatible platforms are required, which help to reconstitute various biological events. We have developed two platforms (a) novel biocompatible chemically functionalized 2D micropattern surfaces for the reconstitution of chromosome and centrosome surface, (b) artificial cell like system using liposome for the reconstitution of amyloid beta peptide aggregation and its propagation. Our

achievements were published in high quality international journals and few of them highlighted in cover-page of the issue [Biswas *et al.*, ChemBioChem, 2013, Soft Matter, 2014, Saha *et al.*, Chem. Commun. 2013

Future Research Plans

Development of small molecules, peptides and peptoids for Alzheimer Diseases (AD) and neuron cell generation from stem cell.

Development of small molecule and peptide based anti-cancer therapeutics targeted to microtubule and Kinesin 5 (Eg5).

Development of small molecules based antibiotics against various resistant bacteria.

Development of various platforms for studying bio-molecular interactions through surface modification, patterning and using liposome.

Reconstitution of kinesin mediated cargo (nanomaterial) transport and microtubule dynamics.

Peptide-based soft scaffold (Hydrogel) for various biomedical applications.

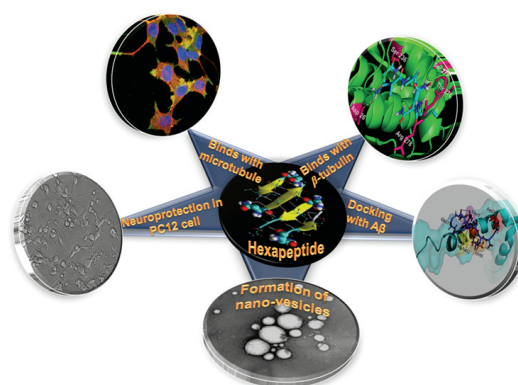


Fig. 1: Hexapeptide shows excellent neuroprotection: MD simulation, molecular docking and *in vitro* experiments reveal that a novel hexapeptide spontaneously self-assembles to form nano-vesicles, interacts with tubulin and microtubule. It also interacts with A β peptide and inhibits its fibrillization as well as exhibits excellent neuroprotection against A β toxicity.

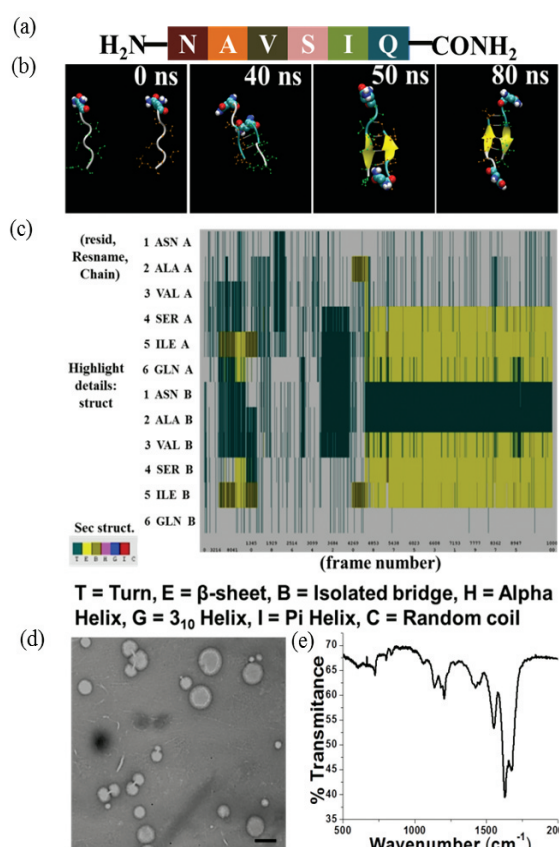


Fig. 2: Confocal images reveal binding of NV with intracellular tubulin/microtubule networks of PC12 cells. (a) Red coloured microtubule networks of PC12 cells at 561 nm channel (b) Green tiny particles are distributed along the microtubule networks and all over the PC12 cells at 488 nm channel. (c) Blue coloured nucleus of PC12 cells at 405 nm channel. (d) Yellow coloured merged image reveals that NV binds along the intracellular microtubules of PC12 Cells. Scale bar corresponds to 30 μm .

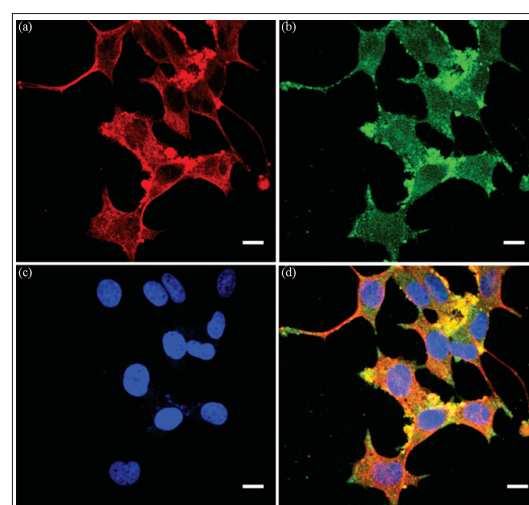


Fig. 3: (a) Amino acid sequence of NV. (b) Snapshots from a MD simulation movie of NV demonstrating how it assembles rapidly to antiparallel β -sheet structure. (c) Secondary structure with the change of time reveals that Ala, Val, Ser, Ile and Gln of NV are involved in antiparallel β -sheet structure formation. (d) NV self-assembles to form nano-vesicles (Scale bar corresponds to 100 nm). (e) FT-IR spectrum of one hour incubated sample of NV reveals β -sheet structure.

PUBLICATIONS

- Chattoraj, S., Amin, Md. A., Jana, B., Mohapatra, S., Ghosh, S., and Bhattacharyya, K. (2015) Selective Killing of Breast Cancer Cells by Doxorubicin Loaded Fluorescent Gold Nano-Cluster: Confocal Microscopy and FRET. *ChemPhysChem* **17**, 253-259
- Saha, A., Mohapatra, S., Kurkute, P., Jana, B. Sarkar, J., Mondal P., and Ghosh, S. (2015) Targeted delivery of novel peptide-docetaxel conjugate to MCF-7 cell through Neuropilin-1 receptor: Reduced toxicity and enhanced efficacy of docetaxel. *RSC Adv* **5**, 92596-92601
- Bhunia, D., Chowdhury, R., Bhattacharyya, K., and Ghosh, S. (2015) Fluorescence Fluctuation of Antigen-Antibody Complex: Circular Dichroism, FCS and smFRET of Enhanced GFP and its Antibody. *Phys Chem Chem Phys* **17**, 25250-25259
- Biswas, A., Kurkute, P., Saleem, S., Jana, B., Mohapatra, S., Mondal, P., Adak, A., Ghosh, S., Saha, A., Bhunia, D., Biswas, S. C. and Ghosh, S. (2015) Novel Hexapeptide Interacts with Tubulin and Microtubules, Inhibits A β Fibrillation, and Shows Significant Neuroprotection. *ACS Chem Neurosci* **6**, 1309-1316.



Jana, B., Sarkar, J., Mondal, P., Barman, S., Mohapatra, S., Bhunia, D., Pradhan, K., Saha, A., Adak, A., Ghosh S., and Ghosh, S. (2015) A short GC rich DNA derived from microbial origin targets tubulin/microtubule and induces apoptotic death of cancer cell. *Chem Commun* **51**, 12024-12027

Basu, K., Baral, A., Basak, S., Dehsorkhi, A., Nanda, J., Bhunia, D., Ghosh, S. Castelletto, V., Hamley, I. W., and Banerjee, A. (2016) Peptide based hydrogels for cancer drug release: Modulation of stiffness, drug release and proteolytic stability of hydrogels by incorporating D-amino acid residue(s). *Chem Commun* **52**, 5045-5048

Nair, J. B., Manu M. J., Mohapatra, S., Safeera, M., Ghosh, S., Sreelekha, T. T., and Maiti K. K. (2016) A Dual-Targeting Octaguanidine-Doxorubicin Conjugate Transporter for Inducing Caspase-Mediated Apoptosis on Folate-Expressing Cancer Cells. *ChemMedChem* **11**, 702-712

Chatteraj, S., Amin, Md. A., Mohapatra, S., Ghosh, S. and Bhattacharyya, K. (2016) Cancer Cell Imaging by In Situ Generated Gold Nano-clusters. *ChemPhysChem* **17**, 61-68

PATENTS FILED / SEALED

Name Surname: SURAJIT GHOSH

Patent Title: A HEXAPEPTIDE INTERACTS WITH TUBULIN/MICROTUBULE AND EXHIBITS SIGNIFICANT NEUROPROTECTION AGAINST A β TOXICITY THEREOF

Country: US

Patent No.: 15/062773

Date filed / granted: Filing date: 7th March 2015

Co-inventors and their Institutes ATANU BISWAS, PRASHANT KURKUTE, SURAIYA SALEEM, BATAKRISHNA JANA, SASWAT MOHAPATRA, PRASENJIT MONDAL, ANINDYASUNDAR ADAK, SUBHAJIT GHOSH, ABHIJIT SAHA, DEBMALYA BHUNIA, SUBHASH CHANDRA BISWAS FROM CSIR IICB.

Patent filed by DBT / CSIR-IICB / another organization: CSIR-IICB

Name Surname: SURAJIT GHOSH

Patent Title: "A LIPOSOMAL COMPOSITION OF PHOTO SYSTEM-I FOR TREATMENT OF CANCER"

Country: PCT and Others

Patent No. 0058NF2016

Date filed: 7th March 2016

Co-inventors and their Institutes: ABHIJIT SAHA, SUBHAJIT GHOSH, SASWAT MOHAPATRA, BATAKRISHNA JANA, DEBMALYA BHUNIA FROM CSIR IICB.

Patent filed by CSIR-IICB

AWARDS / HONOURS / MEMBERSHIPS

Associate Editor of Royal Society of Chemistry (RSC Advances)

Fellow of Royal Society of Chemistry (FRSC)

EXTRAMURAL FUNDING

Development of anti-alzheimer peptide from taxol binding pocket of β -tubulin. 2016 - 2018. (DST, India)

INVITED TALKS

A short GC rich DNA derived from microbial origin targets tubulin/microtubule and induces apoptotic death of cancer cell at CSIR-IICB Research festival 5 June 2015 Kolkata

Microtubule targeted chemically functionalized graphene oxide micro/nano particle. 4th International Conference on Advanced Nanomaterials and Nanotechnology (ICANN2015), on 08-11 December 2015 at the Indian Institute of Technology Guwahati.

Microtubule targeted chemically functionalized graphene oxide micro/nanoparticle

17th All India Congress of Cytology and Genetics. 22 -24 December 2015.

Microtubule targeted neuroprotective peptide. Sixth International Conference on Metals in Genetics, Chemical Biology and Therapeutics (ICMG-2016), from 17-21 February 2016 at IISc Bangalore.

Chemical tools for understanding/perturbing various biological events at the National level Symposium Facets of Chemistry in Biology-2016 at St. Xavier's College, on 22-23 February 2016, Kolkata.

Development of novel delivery vehicles for targeted delivery of docetaxel the International symposium on Chemical Biology and Drug Discovery at Hotel Taj, on 1-3 March 2016. Kolkata.

Dr. Indrajit Das

Id@csiriicb.in



Tandem chemoselective sulfur migration in γ -ketothioesters: direct approach to substituted butenolides

Participants

JRF: Sandip Naskar

SRF: Kanchan Mal

Collaborator(s)

Name of collaborator within CSIR-IICB

Dr. Ramalingam Natarajan

Organic and Medicinal Chemistry Division

Background

Sulfanyl group migration is an important chemical transformation and is extensively studied in the synthesis of modified carbohydrates, heterocycles as well as acyclic compounds. Several elegant approaches have been developed for the 1,2-migration of the thio group in the past few years. Among the numerous methods developed, the most common route reported so far proceeds mainly through a key thiiranium intermediate, which undergoes rearrangement, elimination, or substitution reactions. Unlike 1,2-migration of the thio group, there has been limited success in 1,4-sulfanyl group migration. The most common route reported so far proceeds through the thiolanium intermediate. To the best of our knowledge, there are no reports of tandem chemoselective 1,2-/1,4-migration of the thio group from a ketothioesters. On the other hand, substituted butenolides with one or more quaternary centres are privileged structural motifs occurring in a plethora of biologically active natural products and pharmaceutically important molecules. However, chemical synthesis of such molecules is very challenging and remains a dynamic area of research for the past few decades. Several elegant approaches have been developed for their synthesis, which are mostly limited to the direct functionalization of pre-existing substituted butenolide scaffolds. Therefore, general approaches for the construction of these essential scaffolds, under metal/ligand-free conditions, are still highly desirable.

Aims and Objectives

Sulfanyl group migration: Development of a general approach

Synthesis of substituted butenolides having one or more tertiary centers



Work Achieved

We report herein an efficient and mechanistically unique tandem chemoselective 1,2-/1,4-migration of the thio group in ketothioesters that provides substituted butenolides in moderate to excellent yields. Thus, γ -ketothioesters in the presence of stabilized phosphonate carbanions undergo tandem 1,2-sulfur migration, whereas 1,4-migration of the thio group has been achieved with the same thioesters after the treatment with Wittig reagents followed by $\text{BF}_3 \cdot \text{OEt}_2$ -catalyzed tandem reaction. Parallely, visible light-induced 1,2-sulfur migration has also been observed in α -ketothioesters for accessing substituted butenolides. This two examples are the first such instances where 1,2-/1,4-migration of the thio group proceeds without any conventional intermediate. As substituted butenolides are privileged structural motifs in plethora of biologically active natural products and pharmaceutically important molecules. On the contrary, methods for their preparation are scarce and very challenging, and mostly limited to the direct functionalization of pre-existing substituted butenolide scaffolds. Therefore, the development

of synthetic methods that lead to these essential structural motifs is of particular importance (see Fig. 1).

Future Research Plans

Research is currently in progress to develop the asymmetric version of these tandem reactions and to reiterate the superior reactivity of the ketothioesters towards the synthesis of biologically active heterocycles.

PUBLICATIONS

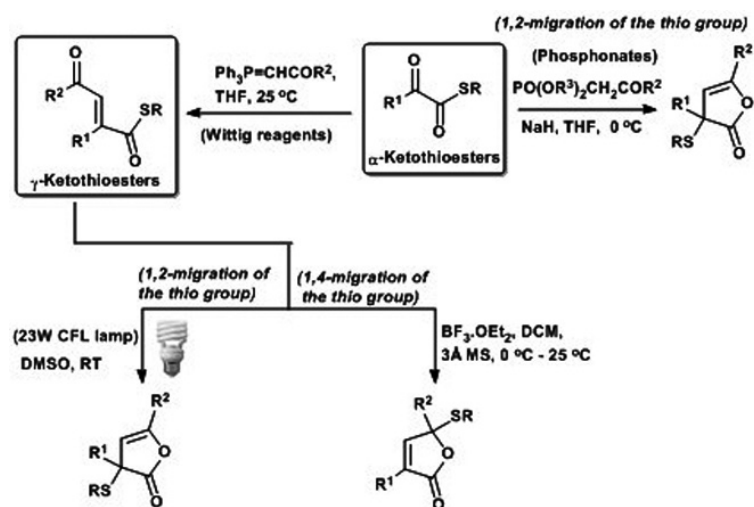
Mal, K., and Das, I. (2016) Base Induced Chiral Substituted Furans and Imidazoles from Carbohydrate-Derived 2-Haloenones. *J Org Chem* **81**, 932-945

Mal, K., Kaur, A., and Das, I. (2015) Chirally Substituted 3-Formylfurans from Carbohydrates: An Expedient Route via NBS-Mediated Electrophilic Cyclization. *Asian J Org Chem* **4**, 1132-1143

Mal, K., Kaur, A., Haque, F., and Das, I. (2015) $\text{PPh}_3 \cdot \text{HBr} \cdot \text{DMSO}$: A Reagent System for Diverse Chemoselective Transformations. *J Org Chem* **80**, 6400-6410

EXTRAMURAL FUNDING

N-Heterocyclic Carbene Catalyzed Diastereoselective Synthesis of Substituted Cyclohexanones from Modified Carbohydrates: Application to the Total Synthesis of Conduramines and Phenanthridone Alkaloids. 2013 - 2016. (DST-SERB, India).



(Fig. 1)

Dr. Sanjay Dutta

sanjaydutta@icb.res.in



Development of novel small molecules targeting nucleic acids (DNA and RNA) and their fluorescent conjugates which can be utilized as small molecule probes, diagnostics and therapeutics (antiviral and antibiotics)

Participants

JRF: Dipendu Patra, Jeet Chakravarty

SRF: Tridib Mahata, Ajay Kanungo, Subhadeep Palit

RA: Sanghamitra Mukherjee

Collaborator(s)

Name of collaborator outside CSIR-IICB

Prof. Gautam Basu

Department of Biophysics, Bose Institute, Kolkata 700054

Dr. S. K. Pal

Department of Chemical, Biological and Macromolecular Sciences S. N. Bose National Centre for Basic Sciences, Kolkata 700 098

Name of collaborator within CSIR-IICB

Dr. Prakash R. Maulik, CSIR-IICB

Organic & Medicinal Chemistry Division

Background

Quinoxaline antibiotics, containing two quinoxaline moieties attached to an octadepsipeptide ring (**Fig. 1A**), are able to bis-intercalate double-stranded DNA (dsDNA) in a sequence-specific manner. In addition to studies on synthetic derivatives, potent anticancer agents have been designed using the depsipeptide-biquinoxaline scaffold. In contrast, known DNA-binding monoquinoxaline scaffolds are either metal chelates or contain a fused quinoxaline moiety. The DNA binding affinity of the only reported simple synthetic monoquinoxaline DNA-binding scaffold, however, was only moderate. There is a need to develop simpler monoquinoxaline DNA-intercalating small molecules since they can be easily synthesized and derivatized for modulating DNA affinity and targeted delivery. Herein we report the design, synthesis, and DNA binding properties of a series of synthetically accessible small molecules derived from an unfused monoquinoxaline scaffold, and we identify a unique benzyl switch which controls their DNA-binding modes.

Aims and Objectives

Targeting nucleic acids (DNA & RNA) by small molecules based on natural products, carbohydrates and heterocycles.

Targeting viral RNA (Hepatitis C Virus) and bacterial RNA, development of RNA targeted therapy.

Exploring the mechanisms of actions of natural compounds targeting DNA, which will ultimately be utilized for targeting particular diseases and discovery of drug like molecules.

Targeting cellular receptors for drug delivery to liver.

Work Achieved

Quinoxaline antibiotics intercalate dsDNA and exhibit antitumor properties. However, they are difficult to synthesize and their structural complexity impedes a clear mechanistic



understanding of DNA binding. Therefore design and synthesis of minimal-intercalators, using only part of the antibiotic scaffold so as to retain the key DNA-binding property is extremely important. Reported is a unique example of a monomeric quinoxaline derivative of a 6-nitroquinoxaline-2,3-diamine scaffold which binds dsDNA by two different modes. While benzyl derivatives bound DNA in a sequential fashion, with intercalation as the second event, nonbenzyl derivatives showed only the first binding event. The benzyl intercalation switch provides important insights about molecular architecture which control specific DNA binding

modes and would be useful in designing functionally important monomeric quinoxaline DNA binders and benchmarking molecular simulations.

Future Research Plans

Elucidation of the unusual DNA structure formed. Development of effective noncovalent DNA binders and anticancer agents. Study of the DNA damage mechanisms of these quinoxaline compounds. Cellular delivery of DNA damaging agents. Development of RNA binding small molecules with fluorescent properties.

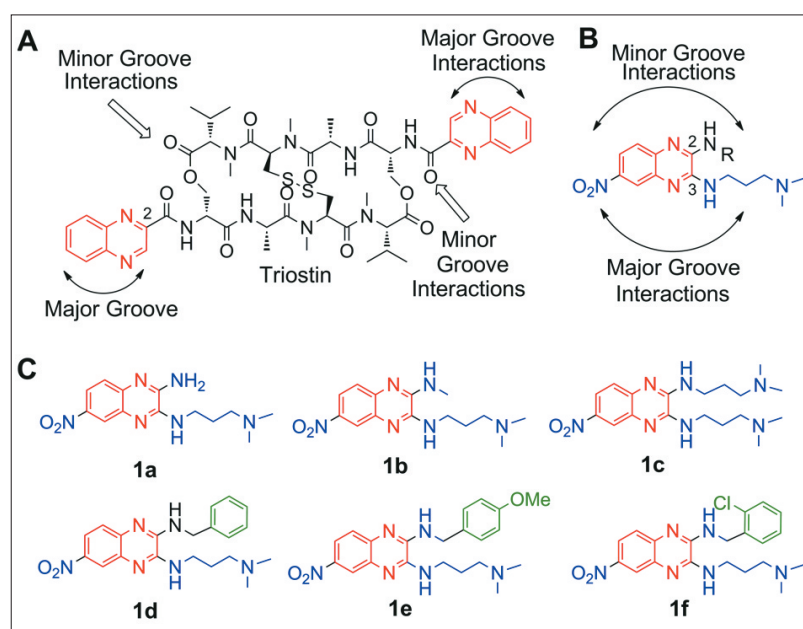


Fig. 1. **A)** Structure of quinoxaline antibiotic triostin **(A)** depicting key DNA interactions. **B)** The nitroquinoxaline-diamine scaffold used in this study with plausible DNA interactions. **C)** Structures of the six molecules used in this work.



PUBLICATIONS

Kanungo, A., Patra, D., Mukherjee, S., Mahata, T., Maulik, P.R., and Dutta S. (2015) Synthesis of a Visibly Emissive 9-nitro-2, 3-dihydro-1Hpyrimido[1,2-a]quinoxalin-5-amine Scaffold with Large Stokes Shift and Live Cell Imaging. *RSC Adv* **5**, 70958-70967

Mahata, T., Kanungo, A., Ganguly, S., Modugula, E. K., Choudhury, S., Pal, S.K, Basu, G., and Dutta, S. (2016) A benzyl

moiety in a quinoxaline-based scaffold acts as a DNA intercalation switch. *Angew Chem Int Ed* **55**, 7733-7766

EXTRAMURAL FUNDING

Discovery of RNA binding ligands-targeting Hepatitis C Virus RNA

Grant Title. July 2015 – July 2018. (DBT, India)

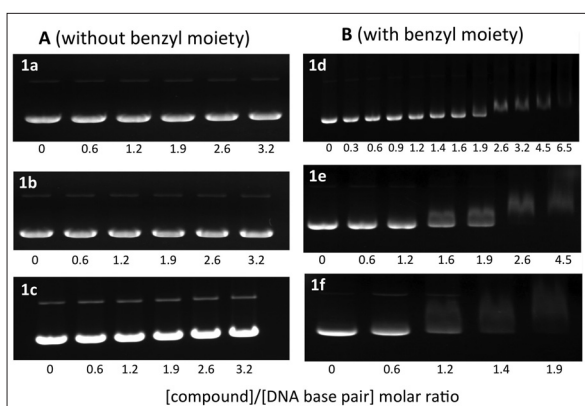


Fig. 2: Agarose gel shift assay of supercoiled DNA with the compounds 1a–c (A) and compounds 1d–f (B).

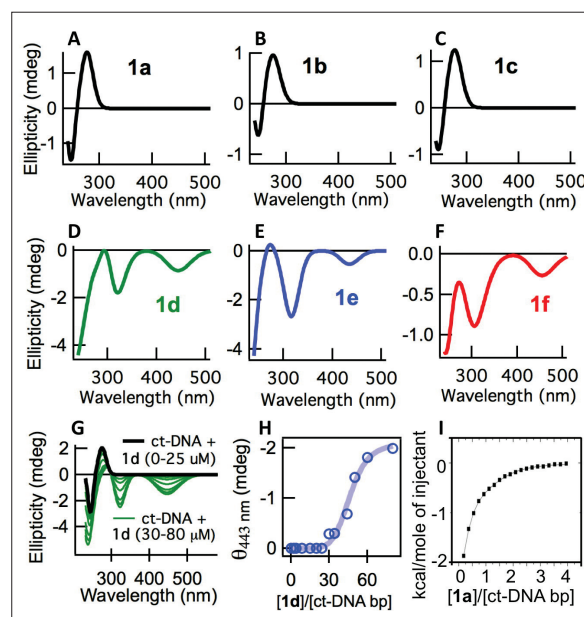


Fig. 3: CD spectra of 50 nm 1a(A), 1b(B), 1c(C), 1d(D), 1e(E), and 1f(F) in the presence of 10 μM ct-DNA (bp) in buffer A (10 mM phosphate buffer pH 7.0 with 10 mM NaCl and 1% DMSO) at 25°C. The compounds 1a–f did not show ICD at this concentration in the absence of DNA. G) Titration of ct-DNA (15 μM) by 1d. H) θ_{443} nm versus [1d]/[DNA] from (G). I) Difference in integrated heat from ITC titrations of 1a against 50 μM ct-DNA and buffer A as a function of [1a]/[ct-DNA].

Dr. Ranjan Jana

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A combined late stage C-H functionalization and affinity-based protein profiling strategy for the identification of highly selective kinase inhibitors in breast cancer cell lines

Participants

SRF: Bijaya Kumar Singh, Asik Hossian, Manash Kumar Manna, Samir Kumar Bhunia, Arghya Polley

RA: Dr. Ashok Behera

Background

The establishment of drug resistance following treatment with chemotherapeutics is strongly associated with poor clinical outcome in patients, and drugs that target chemoresistant tumors have the potential to increase patient survival. In an effort to identify biological pathways of chemoresistant breast cancers that can be targeted therapeutically, a small molecule screen utilizing metastatic patient-derived breast cancer cells is extremely essential.

Aims and Objectives

1. Synthesis of basic pharmacophores and their late-stage diversification via site-selective C-H activations.
2. Initial phenotypic screen of this library of compounds against MCF-7 primary breast cancer cell line and the corresponding MCF-10A normal cell line in 3D cell culture for hit optimization.
3. Affinity-based protein profiling for target identification, validation and hit to lead optimization through structure modifications.

Work Achieved

We have initiated and optimized the synthesis of basic scaffolds through C-H activation. We have accomplished a palladium-catalyzed synthesis of 2-arylindoles, and indolines from readily available and inexpensive aryl ureas and vinyl arenes merging C-H activation and alkene difunctionalization at room temperature. The reaction initiates with a urea-directed electrophilic *ortho* palladation, alkene insertion, and β -hydride elimination sequences to provide the Fujiwara-Moritani arylation product. Subsequently, aza-Wacker cyclization, and β -hydride elimination provide the 2-arylindoles in high yields. Intercepting the common σ -alkyl-Pd intermediate, corresponding indolines are also achieved. The 2-arylindole moiety has been extended to the dibenzofused carbazole system through multiple C-H activations. The molecular affinity probe for pull down experiment has also been synthesized.



Future Research Plans

Evaluation of these molecules against breast cancer and other cell lines are undergoing. Affinity-based protein profiling (ABPP) for the identification of highly selective inhibitor is the future goal of this project.

PUBLICATIONS

Manna, M.K., Hossian, A., and Jana, R., (2015) Merging C–H Activation and Alkene Difunctionalization at Room Temperature: A Palladium-Catalyzed Divergent Synthesis of Indoles and Indolines, *Org Lett* **17**, 672-675

Tohasib, T.Y., Hossian, A., Manna, M.K., Jana, R. (2015) Chemo-, Regio-, and Stereoselective Heck-Matsuda Arylation of Allylic Alcohols under Mild Conditions. *Org Biomol Chem* **13**, 4841-4845

Bhunia, S.K., Polley, A., Natarajan, R., and Jana, R. (2015) Through-Space 1,4-Palladium Migration and 1,2-Aryl Shift: Direct Access to Dibenzo[a,c]carbazoles through a Triple C–H Functionalization Cascade. *Chem Eur J* **21**, 16786-16791

Singh, B.K.S., and Jana, R. (2016) Ligand-Enabled, Copper-Promoted Regio- and Chemoselective Hydroxylation of Arenes, Aryl Halides, and Aryl Methyl Ethers. *J Org Chem* **81**, 831-841

Hossian, A., Bhunia, S.K., and Jana, R. (2016) Substrate-Dependent Mechanistic Divergence in Decarboxylative Heck Reaction at Room Temperature, *J Org Chem* **81**, 2521-2533

Singh, B.K.S., Polley, A., and Jana, R. (2016) Copper(II)-Mediated Intermolecular C(sp²)–H Amination of Benzamides with Electron-Rich Anilines. *J Org Chem* **81**, 4295–4303

EXTRAMURAL FUNDING

A Combined Late Stage C–H Functionalization and Affinity-Based Protein Profiling Strategy for the Identification of Highly Selective Kinase Inhibitors in Breast Cancer Cell Lines

2014-2018, DST, SERB, Govt of India, Project # SR/S2/RJN-97/2012

Molecular Diversity through Cascade C–H Activations

2015-2018, DST, SERB, Govt. of India, Project # EMR/2014/00469

CONFERENCES / WORKSHOPS

Number of abstracts India: 1

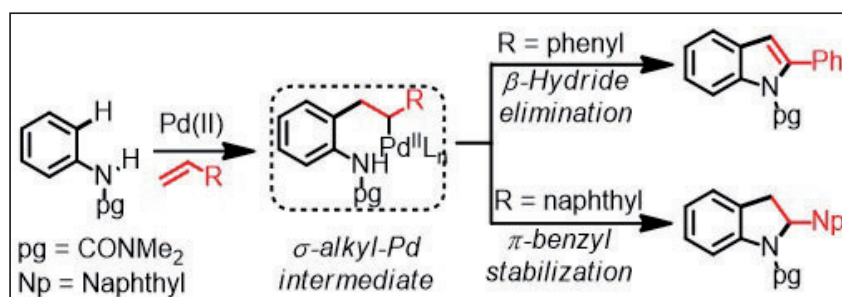


Fig. 1. Divergent synthesis of indole and indolines

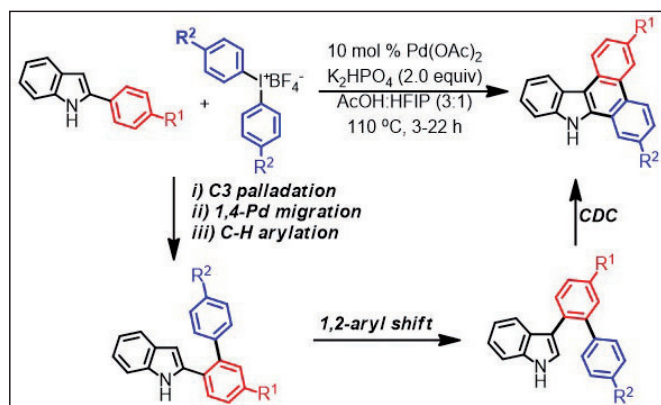


Fig. 2. Synthesis of dibenzofused carbazoles through triple C–H activation / migration cascade

Dr. Arindam Talukdar

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Probing endosomal Toll-like receptors 9 (TLR9) with small molecules

Participants

SRF: Barnali Paul, Swarnali Roy, Ayan Mukherjee

Collaborator(s)

Name of collaborator within CSIR-IICB

Dr. Dipyaman Ganguly

Cancer Biology and Inflammatory Disorder Division

Background

TLRs are members of the larger family of evolutionarily conserved pattern recognition receptors which are critical first line of defence for self-nonsel self discrimination by the host immune response. Aberrant endosomal TLR activation is implicated in autoreactive inflammation in different autoimmune diseases.

Aims and Objectives

To design selective inhibitors for the nucleic acid-recognizing TLRs for devising novel therapeutic strategies in relevant clinical contexts.

To propose a binding mode hypothesis based on computational analysis as no crystal structure available.

Work Achieved

Obtained DST-SERB project to fund the research.

A set of diverse small molecule library has been synthesized by structure guided method with $IC_{50} < 100$ nM constituting specific molecular geometry and varying basicity.

Filed a patent application to protect the research finding.

Various publications have been communicated to journals.

Future Research Plans

To check the selectivity of these potent TLR9 inhibitor with other endosomal TLRs.

To synthesize potent small molecule TLR7 inhibitor.

To validate the small molecule binding region.

To extend our knowledge to other structurally diverse core for synthesis of small molecule library.

To determine functional mechanism of TLR9 antagonism.

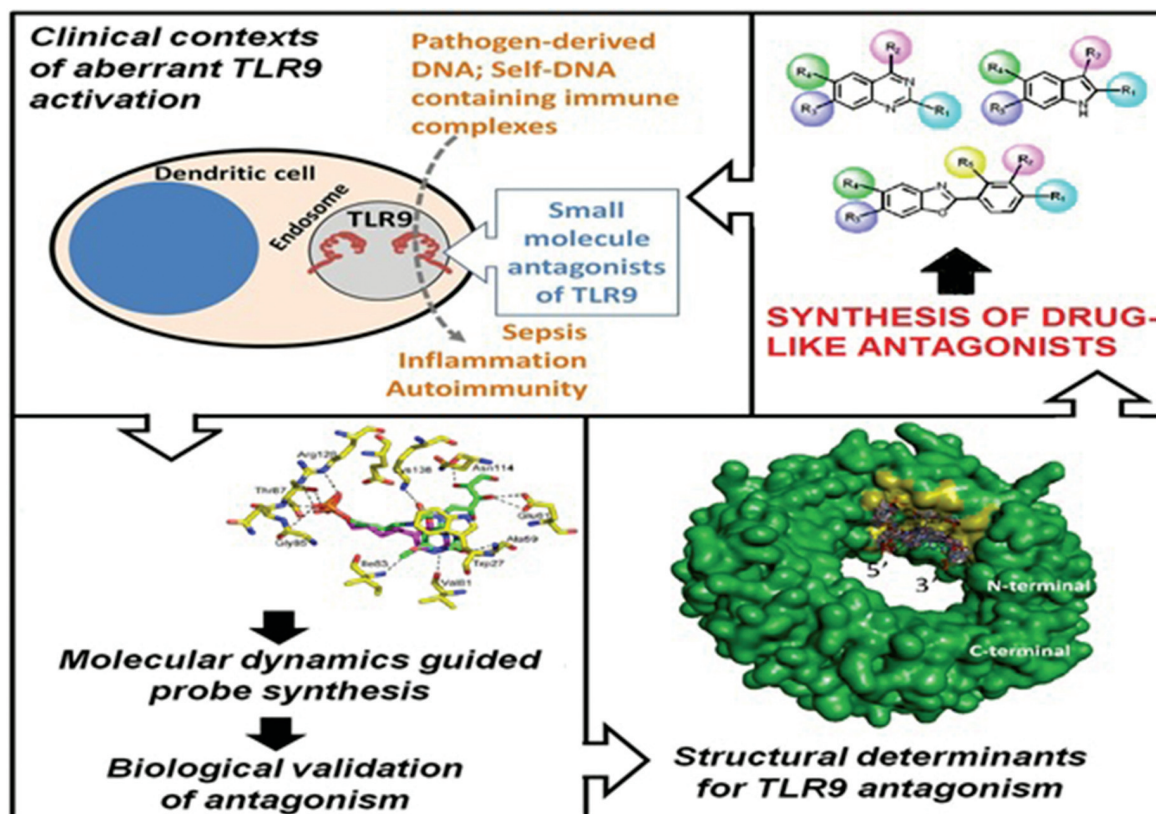


Fig. 1: Exploring the functional mechanism of TLR9 antagonism

PATENTS FILED / SEALED

Name Surname: ARINDAM TALUKDAR

Patent Title: BLOCKING TOLL-LIKE RECEPTOR 9 SIGNALING WITH SMALL MOLECULE ANTAGONIST.

Country: India

Patent No. 201611009670

Date filed / granted 21/03/2016

Co-inventors and their Institutes DIPYAMAN GANGULY, BARNALI PAUL, AYAN MUKHERJEE, SHOUNAK ROY, SWARNALI ROY, AMRIT RAJ GHOSH, ROOPKATHA BHATTACHARYA, OINDRILA RAHAMAN, BISWAJIT KUNDU, CSIR-IICB

Patent filed by DBT / CSIR-IICB / another organization: CSIR-IICB

AWARDS / HONOURS / MEMBERSHIPS

Memberships

Chemical Biology Society, India (Life Membership)

EXTRAMURAL FUNDING

Probing endosomal toll-like receptor 9 biology using novel small molecule antagonists. October 2015 to September 2018 (EMR/2015/000117), DST-SCIENCE & ENGINEERING RESEARCH BOARD, India

CONFERENCES / WORKSHOPS

Number of Abstract India: 2

Dr. R. Natarajan

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Novel synthetic receptors and ligands for biomolecular recognition and biomedical relevance

Participants

JRF: Krishanu Samanta

SRF: Jayanta Samanta, Shovan Kumar Sen

Project Fellow: M Vasmi Krishna

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Swapan Majumdar

Tripura University

Dr. Subal Chandra Manna

Vidyasagar University

Name of collaborator within CSIR-IICB

Dr. Indrajit Das, Dr. Surajit Ghosh, Dr. Ranjan Jana, & Dr. Nirup B. Mandal

Organic and Medicinal Chemistry Division

Dr. M. C. Denbath

Infectious Diseases & Immunology Division

Dr. Subhas C. Biswas

Cell Biology and Physiology Division

Dr. Krishnananda Chattopadhyay

Structural Biology and Bioinformatics Division

Background

Firstly, synthetic receptors, capable of recognizing ligands such as carbohydrates, peptides, inorganic ions and polycyclic aromatic hydrocarbons, and delivering the chosen drug molecules in the desired site in controlled manner, play a crucial role in several crucial events of environmental and biological significance. Development of novel receptor towards recognition of specific ligands in solvents of necessity and choice, either aqueous or organic, is greatly challenging. The nature of receptors can be purely organic or metal-organic, with cyclic or acyclic convergent recognition surface, each of which has associated challenges and advantages. Further, the metal-organic receptor can be either discrete or polymeric. However, design, synthesis of novel receptor and demonstration of its specific desired function holds several practical utilities.

Secondly, design and synthesis of specific ligands, capable of modulating the aggregation of specific peptides and proteins towards desired biological functions play a crucial role in developing therapeutic agents for neurodegenerative diseases. One of the primary reasons of Alzheimer's disease is due to undesired aggregation and folding of A β peptide. Control over its aggregation, with an aid of small molecule ligands, towards neuronal cell protection is crucial in developing therapeutic agents. Parallely, identification of early stage oligomeric species by spectral means is also crucial for the early detection of the disease.

Thirdly, structural determination of small molecules by single crystal x-ray diffraction is a crucial tool in development of drug design. Despite the advancement of computational tools and automation, structure solution and refinement is a challenging task in several instances and requires significant scientific skill.



Aims and Objectives

Design and synthesis of novel organic cages and macrocycles, soluble in water and organic solvents, for biomolecular recognition.

Design and synthesis of novel metal-organic frameworks (MOFs) and metal-organic cages from endogenous organic ligands for biomolecular recognition and controlled delivery.

Design and synthesis of novel ligands for amyloid forming peptides and proteins to engineer their aggregation towards neuronal cell protection in neurodegenerative diseases.

Structure solution and refinement of challenging and non-trivial small molecules by single crystal x-ray diffraction.

Work Achieved

We have designed and synthesized a novel cage-like organic receptor, using Cu(I)-catalyzed azide-alkyne cycloaddition. The cage functions as excellent receptor for carcinogenic polycyclic aromatic hydrocarbons in solution and solid state. The detection and removal of them in the environment is a challenging task. The synthetic receptor can function as scavenger of the toxic pollutants.

We have made significant progress in design and synthesis of metal-organic framework and cage, based on an endogenous chiral organic ligand. We have also made significant progress in design and synthesis of novel small molecules capable of binding A peptide towards therapeutic agents for Alzheimer's disease.

We have accomplished the structure determination of a few significant small molecules, synthesized by our collaborators, by single crystal x-ray diffraction techniques.

Future Research Plans

Study on the ability of the newly synthesized metal-organic cages towards drug delivery.

Study on the ability of the newly synthesized designer small molecules on neuroprotection.

PUBLICATIONS

Majumdar, S., Hossain, J., Natarajan, R., Banerjee, A. K., and Maiti, D. K. (2015) Phthalate tethered strategy: carbohydrate nitrile oxide cycloaddition to 12–15 member chiral macrocycles with alkenyl chain length controlled orientation of bridged isoxazolines. *RSC Adv* **5**, 106289-106293

Bhunia, S. K., Polley, A., Natarajan, R., and Jana, R. (2015) Through-Space 1,4-Palladium Migration and 1,2-Aryl Shift: Direct Access to Dibenzo[a,c]carbazoles through a Triple C-H Functionalization Cascade. *Chem Eur J* **21**, 16786-16791

Bharitkar, Y. P., Das, M., Kumarib, N., Kumari, M. P., Hazra, A., Bhayye, S. S., Natarajan, R., Shah, S., Chatterjee, S., and Mondal, N. B. (2015) Synthesis of bis-pyrrolizidine fused di-spiro oxindole analogs of curcumin via one pot azomethine ylide cycloaddition: Experimental and computational approach towards regio and diastereoselection. *Org Lett* **17**, 4440 - 4443

Nayak, D. K., Baishya, R., Natarajan, R., Sen, T., and Debnath, M. C. (2015) Tricarbonyl $^{99m}\text{Tc}(\text{I})$ and $\text{Re}(\text{I})$ -thiosemicarbazone complexes: synthesis, characterization and biological evaluation for targeting bacterial infection. *Dalton Trans* **46**, 16136-16148

EXTRAMURAL FUNDING

Metal-Organic Frameworks (MOFs) from Bile Acid Derivatives as Carriers for Drug Delivery. 2013-2016. (Science and Engineering Research Board (SERB), India

Ramanujan Fellowship. 2013-2017. (Science and Engineering Research Board (SERB), India

Dr. Indu Bhusan Deb

indubhusandeb@gmail.com



Development of new catalytic system using transition metals (Pd, Fe, Ni, Ru & Rh) to perform C–H/C–X bond cleavage for the synthesis of functionalized biologically important small molecules

Participants

JRF: Aniket Mishra, Surendar Meher

Project Assistant: Tripta Kumari, Anupama Roy

Collaborator(s)

Name of collaborator within CSIR-IICB

Dr. Subhas C. Biswas

Cell Biology and Physiology Division

Dr. Subhajit Biswas

Infectious Diseases & Immunology Division

Dr. Uday Bandyopadhyay

Infectious Diseases & Immunology Division

Background

The ubiquitousness of indole, azaindole and pyrrole skeletons in various natural products, pharmaceuticals and synthetic materials make them immensely valuable heterocycles. Hence development of new and efficient methods for their synthesis and derivatization assumes high significance. Our group is actively involved in designing methodology to synthesize functionalized bioactive heterocycles employing transition metal (Pd, Fe, Ni, Ru & Rh) catalyzed C–H/C–X bond activation concept.

Aims and Objectives

Development of methodology for Indolyl/pyrrolyl-3-phosphonates.

Development of transition metal catalyzed C–H activation methodology for azaindole functionalization.

Synthesis of small molecules against AD and PD.

Work Achieved

We have demonstrated that a PdCl₂/Cu(OAc)₂ catalytic system allows the formation of indolyl-3-phosphonates and pyrrolyl-3-phosphonates in good to excellent yields via oxidative cyclization (dual C–H activation) of the corresponding imino/enamino phosphonates with a broad range of substrates depicted in **Fig. 1**.

Very recently, We have developed an efficient, highly regioselective and scalable ruthenium-catalyzed ortho aryl C–H mono cyanation of *N*-aryl-7-azaindoles to form *N*-(2-cyanoaryl)-7-azaindoles through N-directed ortho C–H activation using easily accessible and non hardus *N*-cyano-*N*-phenyl-*p*-toluene sulfonamide as cyanating reagent in presence of AgOTf and NaOAc in DCE. A range of substrates has furnished cyanated azaindoles in good to excellent yields under the simple reaction conditions depicted in **Fig. 2**. The structure of the heterocycles was further verified by single X-ray crystallography.

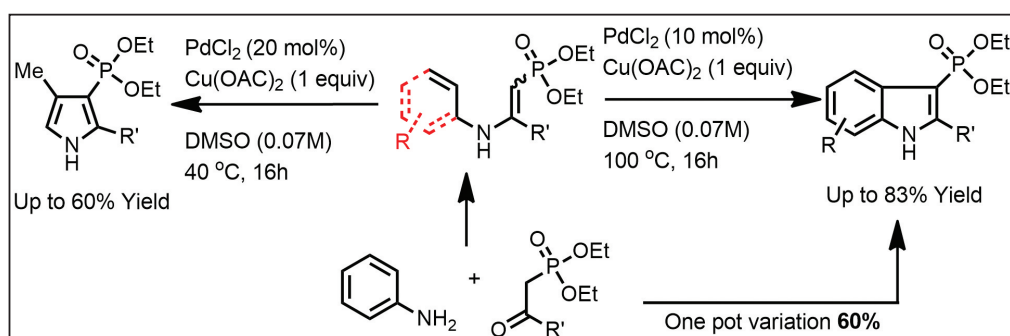


Fig. 1: Indole/pyrrole synthesis using dual C–H activation methodology

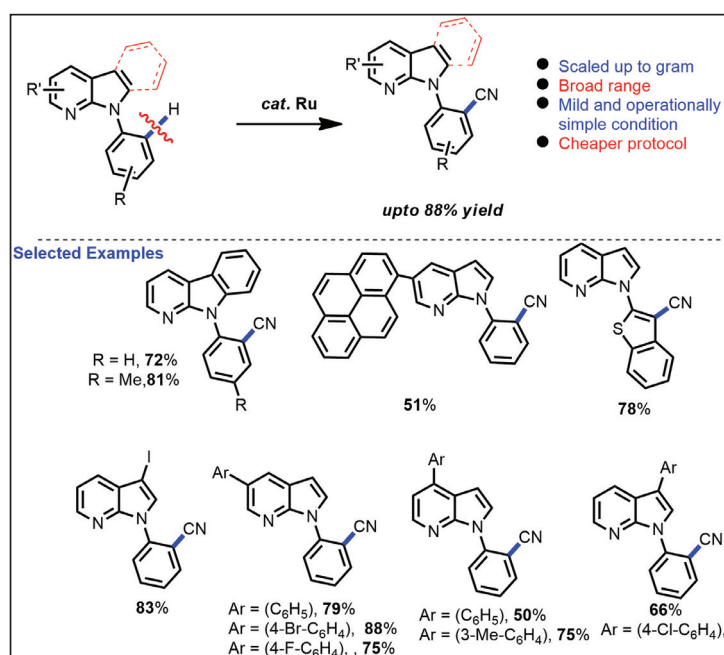


Fig. 2: Cyanation reaction employing ruthenium catalyzed C–H activation concept

Future Research Plans

Development of transition metal catalyzed C–H bond activation methodology for the synthesis of biologically important heterocycles. Synthesis of chalcogen containing biologically important functionalized heterocycles. Photophysical study and bioactivity study of newly synthesized molecules will be pursued.

AWARDS / HONOURS / MEMBERSHIPS

Bristol Mayer Squibb Research Fellowship-USA

Memberships

Life member of Chemical Biology society

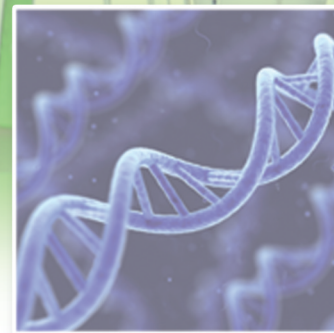
EXTRAMURAL FUNDING

Bristol Mayer Squibb research Grant. 2015-2017. (BMS-USA)

CONFERENCES / WORKSHOPS

Number of abstract India: 1

Molecular and Human Genetics Division



Dr. Samit Adhya, Dr. Suvendra Nath Bhattacharyya (Head) and Dr. Debabrata Biswas

This department has mandates to identify the role of pathogens in modulating small RNAs in the host; to find whether telomere length or senescence factors are responsible for the carcinogenic effects of arsenic; to determine the molecular basis of gene delivery to mitochondria, and to understand the eukaryotic transcriptional regulatory mechanisms and their role in human diseases.

Previous work led to the development of a novel carrier-based protocol for mitochondrial RNA therapy; in the following years we propose to explore the mechanism of uptake and intracellular targeting of the carrier complex and RNA to mitochondria in animal model. Emphasis will be placed on determination of the function of microRNAs in parasitic disease (leishmaniasis) and also in cancer.

One objective of this department is poised to identify the mechanisms that regulate activity of different miRNAs in mammalian cancer and immune cells and to relate these to disease onset and progression. Mechanistic understanding and regulation transcription process at molecular level is also under investigation. Using a combination of basic and applied approaches we will study the molecular basis of genetic disease and its therapy.

Dr. Samit Adhya

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Post-transcriptional Regulation of cyclin D1 mRNA in serum-stimulated myoblasts by microRNA-Argonaute complexes

Background

Mammalian Argonaute proteins (AGO1-4), in combination with microRNAs (miRs), bind to target mRNAs to initiate degradation and/or translation repression, but the relationships between these two effects is unclear. Although the AGO isoforms of *Drosophila* and plants perform different functions, mammalian AGO isoforms are considered to be functionally degenerate in terms of miR loading and downstream silencing effects.

Aims and Objectives

Our objective was to study the interactions between cyclin D1 mRNA and Argonaute-microRNA complexes in serum-stimulated myoblasts.

Work Achieved

We found that, in quiescent (G0) rat myoblasts transiting to the G1 phase, cyclin D1 (*Ccnd1*) mRNA was associated with two functionally distinct AGO-miR complexes. While AGO1-miR-1 downregulated the mRNA level, AGO2-let-7 delayed the timing of translation. Knockdown (KD) of AGO2, or antisense-mediated depletion of Let-7, caused *Ccnd1* translation to occur earlier, but had no significant effect on mRNA abundance. Conversely, downregulation of either AGO1 or miR-1, resulted in elevated *Ccnd1* mRNA levels at early times, but failed to affect the timing of translation. These results show that the two miR-mediated silencing effects, viz. mRNA decay and translation repression, are independent processes induced by individual AGO isoforms in association with specific miRs.

Future Research Plans

We plan to examine the possible involvement of other RNA binding proteins in positioning of Argonaute complexes on cyclin D1 mRNA.



PUBLICATIONS

Ghosh, U., and Adhya, S. (2016) Non-equivalent roles of AGO1 and AGO2 in mRNA turnover and translation of cyclin D1 mRNA. *J Biol Chem* **291**, 7119-712

PATENTS FILED / SEALED

Name Surname SAMIT ADHYA

Patent Title: COMPOSITIONS AND METHODS FOR DELIVERY OF PROTEIN-CODING RNAS TO CORRECT MITOCHONDRIAL DYSFUNCTION

Country(ies) USA

Patent No. : 9127080

Date granted : 08/Sep/2015

Co-inventors and their Institutes

Patent filed by CSIR-IICB

Dr. Suvendra N. Bhattacharyya

suvendra@iicb.res.in



Identification of the mechanism of miRNA activity modulation in mammalian cancer and immune cells

Participants

JRF: Bartika Ghoshal, Avijit Goswami, Dipayan De, Saikat Banerjee, Diptankar Banerjee, Susanta Chatterjee

SRF: Kamalika Mukherjee, Bahnisikha Barman, Somi Patranabis, Yogaditya Chakraborty, Mainak Bose

Pool Officer: Dr. Sudarshana Basu

RA: Dr. Arnab Das

Project Assistant: Tanay Roy

Collaborator(s)

Name of collaborator outside CSIR-IICB

Prof. Saumitra Das

Indian Institute of Science, Bangalore

Background

miRNAs are tiny regulatory RNAs that regulate more than half of genes expressed in mammalian cells. These regulatory RNAs repress the synthesis of proteins from the target mRNAs by imperfectly base pairing to them and by inducing translational repression and degradation of target messages. In human cells the activity and levels of miRNAs are also known to be regulated at several steps during their biogenesis, function and turnover.

Aims and Objectives

Our objective was poised to indentify the mechanisms that regulate activity of different miRNAs in ammalian cancer and immune cells and to relate these to disease onset and progression.

Work Achieved

We are engaged in understanding the mechanism of miRNA function in animal cells. A major part of our research is focused on pathogen mediated changes in miRNA activity in host cells. In this context we have earlier published a pioneering work where we described how *Leishmania donovani*, a pathogenic parasite, modulates miRNA-122 in the host tissue during infection and how it is essential for parasite's survival in the host. We also have identified miRNA-122 as a unique therapeutic molecule against visceral leishmaniasis. Working on miRNAs role in immune response, we have also identified a transient phase during proinflammatory response when miRNA activities get impaired. Apart from that, we work on exosome mediated intercellular miRNA transfer and have reported a new approach to curtail growth of cancer cells by exosomal delivery of anti-proliferative miRNAs.

Our recent work has revealed how human cells sense their environments and control cellular miRNA levels and activities by exporting excess miRNAs out of the cells to ensure senescence or proliferation of mammalian cells. Working on the



same line we have discovered how compartmentalization of target mRNAs to Endoplasmic Reticulum is prerequisite for miRNA mediated repression in mammalian cells.

Future Research Plans

We have planned to explore the pathway and proteins that regulate exosomal export of miRNAs to control their activity in mammalian cells.

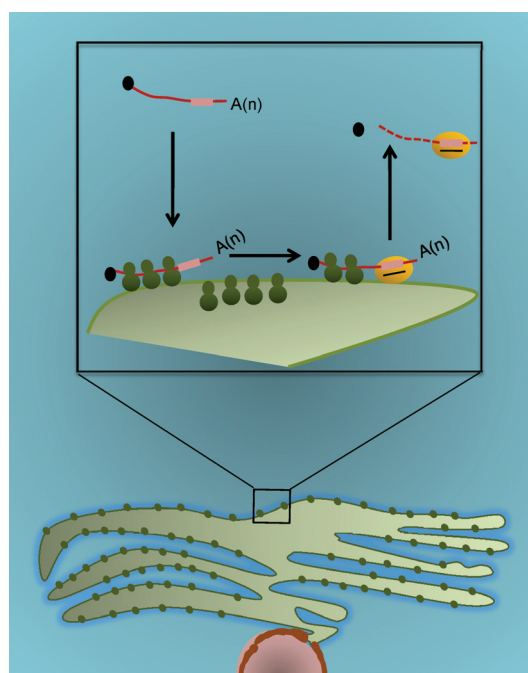


Fig.1: miRNA-mediated repression precedes targeting of mRNAs to polysomes attached with endoplasmic reticulum

PUBLICATIONS

Barman, B., and Bhattacharyya, S.N. (2015) mRNA targeting to Endoplasmic Reticulum precedes Ago protein interaction and miRNA-mediated translation repression in mammalian cells. *J Biol Chem* **290**, 24650-24656

Ghosh, S., Bose, M., Ray, A., and Bhattacharyya, S.N. (2015) Polysome arrest restricts miRNA turnover by preventing their exosomal export in growth retarded mammalian cells. *Mol Biol Cell* **26**, 1072-1083

Patranabis, S., and Bhattacharyya, S.N. (2016) Phosphorylation of Ago2 and subsequent inactivation of let-7a miRNPs control differentiation of mammalian sympathetic neurons. *Mol Cell Biol* **36**, 1260-1271

CONFERENCES / WORKSHOPS

Number of abstracts International: 1

INVITED TALKS

Intercellular transfer of miR-122 and reciprocal anti-miR-122 signal: Tug of war for proliferation and growth arrest between hepatic cells; 2nd ISEV research seminar on EV-RNA "Extracellular Vesicle-associated RNA: is there a purpose?" 24-25 September 2015. Utrecht, Netherlands.

Extracellular miRNAs: Potentials for use in diagnostics and therapy; "Conference on microRNA and Biomarkers" on 21 December at Medica Superspecialty Hospital, 21 December 2015, Kolkata.

Reciprocal control of intercellular transfer of miR-122 and an anti-miR-122 signal in proliferating and growth arrested hepatic cells; 17th All India Congress of Cytology and Genetics and the Symposium on "Exploring Genomes: The New Frontier". 22 -24 December 2015, CSIR-IICB, Kolkata.

Exosome mediated intercellular transfer of miRNAs in mammalian cells; Indian Institute of Science Education and Research, 23 February 2016 Thiruvananthapuram.

Regulation of miRNA activity by different intrinsic and extrinsic factors in mammalian cells; Tata Institute for Fundamental Research (TIFR), 28 March 2016, Mumbai.

Post-transcriptional regulations of miRNA activity in mammalian immune and neuronal cells; ACTREC, 29 March 2016, Mumbai.

Dr. Debabrata Biswas

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Mechanistic understanding of transcriptional regulation and leukemogenesis by human DBC1 complex

Participants

SRF: Mahesh Barad, Dipika Yadav

JRF: Subham Basu, Kaushik Ghosh, Nidhi Kumari, Dheerendra Pratap Mall, Sundaram Acharya, Md. Abul Hassan

Project Assistant: Arijit Nandy

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Benu Brata Das

Indian Association for Cultivation of Science, Kolkata

Name of collaborator within CSIR-IICB

Dr. Surajit Ghosh

Organic and medicinal Chemistry

Background

As part of our on-going work, we have observed novel interactions between the MLL fusion partners with DBC1 and FKBP5 proteins. Both the human DBC1 and FKBP5 proteins have been described to be involved in multiple disease pathogenesis including leukemia. However, mechanisms of these disease pathogenesis by these two factors are not known. Using various *in vitro* biochemical and *in vivo* cell biological studies, we would like to explore the role of these two proteins in MLL fusion partner-mediated transcriptional regulation. We would like to further explore the importance of these mechanistic understanding in MLL fusion-mediated leukemogenesis.

Aims and Objectives

Identifying the stable DBC1 protein complex and associated components.

Further understanding of role of some of these components in SEC-mediated transcriptional regulation.

Detailed understanding of role of FKBP5 in SEC complex-mediated transcriptional regulation.

EXTRAMURAL FUNDING

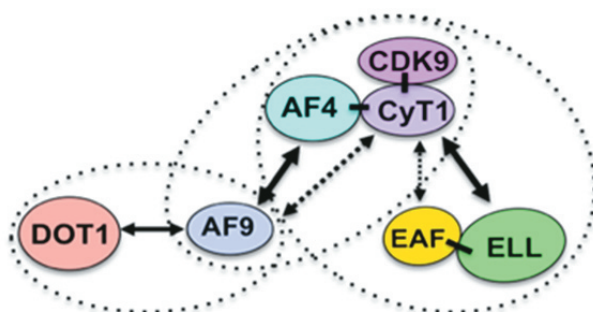
Functional Characterization of human DBC1 complex in transcriptional regulation and leukemogenesis. December 2014 - November 2019. Wellcome-Trust DBT India Alliance, a collaborative effort by Dept. of Biotechnology, Govt. of India and Wellcome-Trust, London, United Kingdom

CONFERENCES / WORKSHOPS

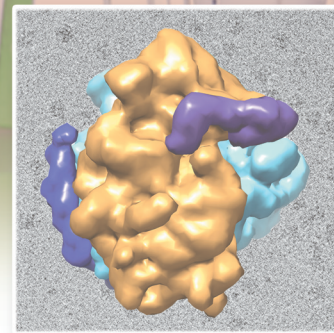
As a participating member of CSIR-IICB, organized the ICYB - 2015 (International Conference of Yeast Biology -), 9-12 December 2015, Jadavpur University, Kolkata

INVITED TALKS

Understanding of Eukaryotic Transcriptional Regulatory Mechanisms and Their Role in Human Diseases. 17th AICCG., All India Congress of Cytology and Genetics, CSIR-Indian Institute of Chemical Biology. Dec 2015 Kolkata, India



Structural Biology & Bioinformatics Division



Dr. Chitra Dutta (Head), Dr. Debasish Bhattacharyya, Dr. Subrata Adak, Dr. Soumen Datta, Dr. Krishnananda Chattopadhyay, Dr. Jayati Sengupta, Dr. Saikat Chakrabarti, Dr. Nakul C. Maiti, Dr. Sujoy Mukherjee, Dr. Sucheta Tripathy and Dr. Siddhartha Roy

With a view to understand cellular functions and dysfunctions in human health and disease, researchers at the Structural Biology & Bioinformatics Division studies attempt to probe into the structural and mechanistic features of various proteins, macromolecular complexes and cellular pathways, using integrative, trans-disciplinary approaches. Basic as well as translational research is being carried out on protein functions, protein-protein interactions, protein-nucleic acid interactions, applying state-of-the-art technologies like X-ray crystallography, Nuclear Magnetic Resonance (NMR), Cryo-EM, Fluorescence Correlation Spectroscopy (FCS), Raman spectroscopy, mass spectrometry, Nano-separation technology etc. Bioinformatic studies involving big data analysis, genome/proteome data mining, molecular dynamic simulations, molecular docking and pathway analysis are also being pursued. Special emphasis is given on macromolecules and small molecules of therapeutic interest against diseases like leishmaniasis, tuberculosis, malaria, Alzheimer's Disease, Parkinson's Disease and other amyloid-related neurodegenerative diseases, systemic diseases like cancer and diabetes and microbial infections. Specific objectives of these studies include

- (i) identification of non-native conformers and oligomers in neurodegenerative diseases,
- (ii) delineation of the key processes/factors involved in protein misfolding, aggregation and amyloid formation,

- (iii) elucidation of cellular defenses against aberrant protein folding,
- (iv) development of novel strategies for amelioration of protein misfolding disorders,
- (v) studying sequence aspects of intrinsically disordered proteins and their plausible implications in diseases.
- (vi) studying ribosomal RNA-assisted folding of denatured proteins in yeast and leishmania
- (vii) investigating oxidative stress responses in Leishmania.
- (viii) harvesting cyanobacterial & fungal genomes in search of commercially important enzymes,
- (ix) metagenomic and pan-genomic analysis of human microbiome components in an attempt to explore their plausible roles in human health and diseases.
- (x) studying parasitic (e.g.malaria) and systemic disease (e.g. cancer) interactomes for identification of novel drug targets,
- (xi) development of nove software tools for NGS data mining, pathway analysis and other big data analysis and
- (xii) design and development of biological knowledgebases of clinical/societal relevance.

Dr. Chitra Dutta

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Studies on human microbiome – Identification of pathogen-specific and habitat-specific genes in microbiome components

Participants

SRF: Aranyak Goswami, Utpal Bakshi, Vinod K. Gupta

RA: Dr. Munmun Sarkar, Dr. Rachana Banerjee

Project Assistant: Narendrakumar M. Chaudhari, Abhishake Lahiri

TO: Dr. Subhagata Ghosh, Dr. Aparna Laskar

Senior Technician: Mahua Bhattacharya

Background

The human body is inhabited by a vast number of microbes that outnumber human somatic and germ cells by 10 to 1. Collectively known as the 'human microbiota', this resident microflora plays a fundamental role in human health and disease. The intricate relationship between these microbes and our health is the focus of a growing number of research initiatives and a perception is just beginning to emerge that studying the human genome only will not be sufficient to comprehend the biology of the human being. Release of reference genome sequences from the microbial flora of diverse anatomical niches by Human Microbiome Project (HMP) consortium has offered a treasure-trove for *in silico* data mining and analysis of the complexity and diversity of the human-microflora ecosystem at the molecular level. Genome analysis of microbiome members may provide unique insights into their virulence or symbiosis, host adaptation and evolution. It is in this context that our group has started microbiome data mining using various bioinformatic and statistical approaches.

Aims and Objectives

Pan genome analysis of microbiota members

Identification and characterization of their core gene complements and the species-specific/orbit niche-specific variations in gene repertoire

Comparative genome/proteome analyses of closely related virulent and avirulent microorganisms in an attempt to identify novel virulent markers

Design and development of novel software packages for microbiome data analysis

Work Achieved

Assessment of virulence potential of uncharacterized Enterococcus faecalis strains using pan genomic approach: Enterococcus faecalis, though traditionally regarded as a gut commensal, has currently emerged as a leading nosocomial



pathogen. Despite considerable efforts, no clear demarcation could be made yet between the *gene content* of pathogenic and non-pathogenic *E. faecalis*. To this end, we conducted a *pan* genome analysis of 36 *E. faecalis* strains of known genome sequences, including 11 pathogens, 3 commensals and 22 strains of unknown pathogenic character. The pan genome of *E. faecalis* is still open, though the core genome has reached almost a closed

state. The strains were clustered using *in silico* multi-locus sequence typing, core genome SNPs, binary pan-matrix and Pathogenicity Island (PAI) gene content. 8 uncharacterized *E. faecalis* strains that co-segregated with reported pathogens in both pan-matrix-based and PAI-based clustering were predicted as potential pathogens. The module A of PAI containing four pathogen-specific genes seems to be the major discriminating factors

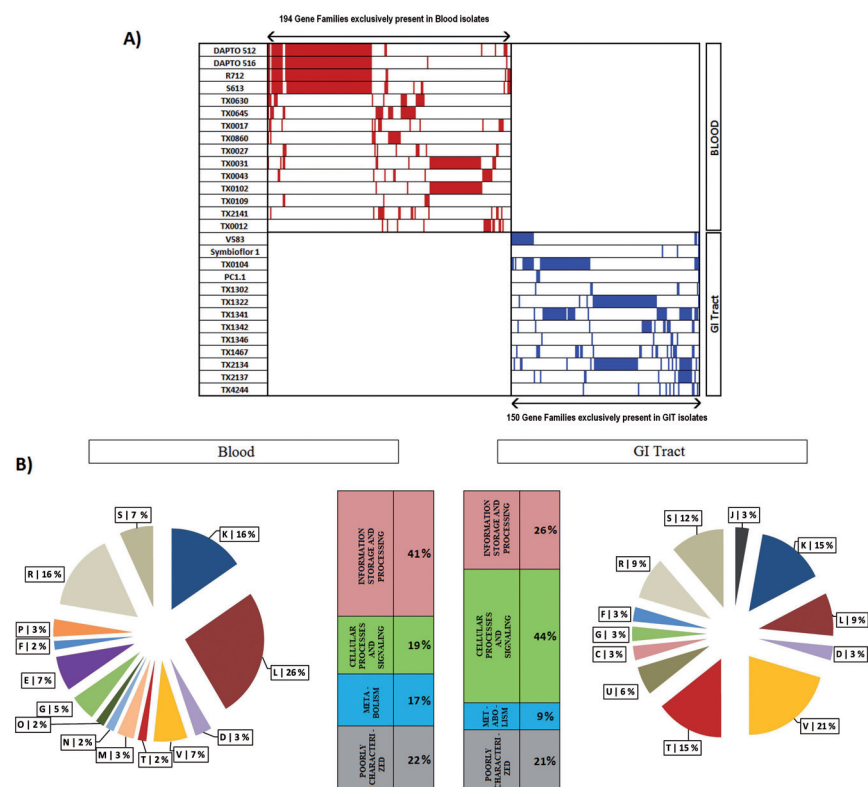


Fig. 1: 194 and 150 gene families specific to Blood and GI Tract niches are shown in red and purple color, respectively. B) Comparative functional analysis of Cluster of Orthologous Groups (COGs) frequencies between Blood and GI Tract niches. COG functional categories represented by one letter code are-J: Translation, ribosomal structure and biogenesis, K: Transcription, L: Replication, recombination and repair, D: Cell cycle control, cell division, chromosome partitioning, V: Defense mechanisms, T: Signal transduction mechanisms, M: Cell wall/membrane/envelope biogenesis, N: Cell motility, U: Intracellular trafficking, secretion, and vesicular transport, O: Posttranslational modification, protein turnover, chaperones, C: Energy production and conversion, G: Carbohydrate transport and metabolism, E: Amino acid transport and metabolism, F: Nucleotide transport and metabolism, H: Coenzyme transport and metabolism, I: Lipid transport and metabolism, P: Inorganic ion transport and metabolism, Q: Secondary metabolites biosynthesis, transport and catabolism, R: General function prediction only, S: Function unknown. Frequencies of four major COG groups are also shown in these two niche.



between virulent and avirulent *E. faecalis*. Four genes in module A of the PAI exist in all reported and putative pathogens, but not in three commensals and other PAI-deficient strains. These four genes were subjected to *in silico* prediction of Intrinsically Disordered Regions (IDR), as presence of IDRs, if any, in these pathogen-specific proteins may enhance their potential as therapeutic targets. Among the four pathogen-specific gene-products, two hypothetical proteins seem to contain intrinsically disordered regions throughout their length, which enhances their potential as novel therapeutic targets. We have found 194, 150, 4 and 1 genes to be exclusive to the blood, GIT, UGT, oral and lymph node isolates of *E. faecalis*, respectively. Further analyses revealed significantly different niche-specific trends in distribution of certain COG categories among these genes (**Fig. 1**), suggesting possible implication of distinct genetic strategies by *E. faecalis* for adaptation to distinct body habitats within human hosts.

Future Research Plans

Pan-microbiome analysis of HMP sequence data and construction of core, accessory and niche-specific microbiomes of human

Mapping of habitat-specific and pathogen-specific genes to KEGG metabolic pathways with a view to identify habitat-specific or virulence-specific variations in microbiome metabolism

Addition of new modules to the in-house pan genome analysis pipeline BPGA (available at <http://www.iicb.res.in/bpga/index.html>)

PUBLICATIONS

Chaudari, N. M., Gupta, V. K. and Dutta, C. (2016) BPGA- an ultra-fast pan-genome analysis pipeline. *Sci Rep* **6**, 24373

COPYRIGHT FILED

Chaudari N M, Gupta V K and Chitra Dutta. (2015) Algorithm of BPGA (Bacterial Pan Genome Analysis tool) (filed by CSIR-IICB)

AWARDS / HONOURS / MEMBERSHIPS

Member, Board of Governors, IIT, Guwahati

Member, Scientific Advisory Committee (SAC), National Institute of Biomedical Genomics (NIBMG), Kalyani

CONFERENCES /WORKSHOPS

Chaired a session, at the symposium "Exploring Genomes: The New Frontier" at CSIR-IICB on 22-24 December 2015

CONFERENCES / EVENTS ORGANIZED BY CSIR-IICB

17th All India Congress of Cytology and Genetics, CSIR-IICB Organizing Committee 22-24 December 2015

Dr. Debasish Bhattacharyya

debasish@iicb.res.in



Biochemical characterization of the drug 'Sterodin'

Participants

JRF: Rajanya Bhattacharyya

SRF: Dr. Payel Bhattacharjee (upto August 2015), Kanika Sharma, Namrata Singh, Chaitali Mukherjee

RA: Dr. Debashree De

Project Assistant: Sromona Das

Collaborator(s)

Name of collaborator within CSIR-IICB

Dr. Subhas Biswas

Cell Biology and Physiology Division

Background

M/s Union Drugs Ltd. Kolkata manufactures 'Sterodin' – a nonspecific immuno-stimulatory drug. This drug is also used as a wound healer. It is constituted of solvent extract of nine different bacterial metabolites along with solvent extract of ox bile lipids. Since neither the composition nor functional molecules of the drug nor their mechanisms of action are known, the company entered into a collaborative research program with this laboratory in two consecutive phases 2012-2014 and 2014-2016 to have insight into its working principles.

Aims and Objectives

While investigating the drug 'Sterodin', two strategies were followed. Since the biochemistry of wound healing and immuno-stimulation are fairly well documented, we followed whether the drug could positively influence those identified pathways. Alternately, presence of such biomolecules that are known to stimulate those biochemical processes was searched for. In either strategy, we had successful findings.

In the protein aggregation studies related to neurological disorders, nontoxic small molecular weight peptides that are assumed to penetrate blood brain barrier were designed and their efficacy against destabilization of β -amyloid fibrils was demonstrated. We advanced our studies to a more complicated system of destabilization of β -amyloid – fibrin coaggregate that has relevance to cerebrovascular diseases.

Work Achieved

In relation to the drug 'Sterodin', limited information is available on the bacterial metabolite. In contrast, very little is known about the other constituent - bile lipids. We made an attempt to identify all components present in the solvent extract of bile lipid that is used in the drug. Partial resolution of the components was achieved by reverse phase HPLC system where 12 fractions were separated. Each of these fractions was



analyzed by mass spectrometric analysis. After matching with mass data, 58 components were identified that include several major bile acids, bile pigments and sulphate conjugates. This provided finger printing of the bile lipids used in the drug.

Previous citations in literature have indicated that bile lipids can regulate oxidative properties of a biological system. To check such regulatory properties, if any, in these fractions of bile prepared from RP-HPLC was evaluated. Estimation of reactive radicals in the H₂O₂-induced HepG2 cells was followed by four specific fluorescent dyes H₂DCF DA, MitoSOX red; Amplex red and DAF-2 DA. Among the separated bile acids, tauroursodeoxycholic acid, glyoursodeoxycholic acid and ursodeoxycholic acid prevented the cells from oxidative damage. Result indicated that hydrophilic bile acids have anti-oxidative properties.

Proteases play regulatory roles in different phases of wound healing. Proteinase K is a aggressive proteases of microbial origin. It was observed that in presence of the drug 'sterodin', autodigestion of Proteinase K was prevented as the functionality of the enzyme could be restored even after a month after incubation at 37°C. While analyzing individual components of the drug, it was observed that cholesterol and its derivatives reversibly inactivate Proteinase K and the activity could be restored in presence of an excess of protein substrate like BSA. Since cholesterol is a major component of cell membrane, reversible inactivation of Proteinase K by cholesterol bound to cell surface was verified. The result was positive. It now appears that cells exposed to *Engyodontium album* (formerly *Tritirachium album*) invasion could absorb some of the Proteinase K molecules to reduce load of proteases in the system. Afterwards, the protease could be released by its natural protein substrates. This might be one of the processes of regulation of protease activity after *Engyodontium album* invasion.

Future Research Plans

In the 'Sterodin' project, we have already predicted some of the mechanisms by which the drug works. Some studies are ongoing. At present the drug house can address some of the questions frequently asked by the physicians. This is an example of translational research carried out in this laboratory.

PUBLICATIONS

Bhattacharjee, P., and Bhattacharyya, D. (2015) An Enzyme from *Aristolochia indica* Destabilizes Fibrin-beta Amyloid Co-Aggregate: Implication in Cerebrovascular Diseases. *PLoS One* **10**, e0141986

Singh, N., and Bhattacharyya, D. (2015) 'Evaluating the presence of reduced nicotinamide adenine dinucleotide phosphate in bacterial metabolites used as an immunostimulator and its role in nitric oxide induction. *Microbiol Immunol* **59**, 311-321

Sharma, K., and Bhattacharyya, D. (2015) Immunoglobulin isotype isolated from Human Placental Extract does not interfere in complement mediated bacterial opsonization within the wound milieu. *FEBS Open Bio* **5**, 369-377

Singh, N., and Bhattacharyya, D. (2016) Identification of the anti-oxidant components in a two step solvent extract of bovine bile lipid: Application of reverse phase HPLC, mass spectrometry and fluorimetric assays. *J Chromat B* **1019**, 83-94

AWARDS / HONOURS / MEMBERSHIPS

Prize from St Peter's University, Madras for outstanding contribution in applied sciences in 2016.

Student

Namrata Singh

Award

Best oral presentation at the 14th Annual Meeting of SFRR-India and 'International Conference on Translational Research in Ionizing Radiation, Free Radicals, Antioxidants and Functional Food' during 7th -9th January, 2016.

EXTRAMURAL FUNDING

Biochemical Characterization of the drug 'Sterodin' 2014-2016. M/s Union Drugs Ltd., Kolkata, India

Growth inhibition and destabilization of β -amyloid aggregate by protease derived peptides. 2012-2015. DST (CSI program), India.

CONFERENCES / WORKSHOPS

Number of abstract India: 1

Conducted workshop at Biotechnology Hub, Tripura University, Agartala during 6 - 10 March 2016 on techniques of protein purification.

Dr. Subrata Adak

adaks@iicb.res.in



Leishmania NAD(P)H cytochrome b5 oxidoreductase deficiency results in dramatically impaired parasite survival

Participants

JRF: Saroj Biswas, Priya Das

SRF: Jayasree Roy, Aditi Mukherjee, Ayan Adhikari

Background

Leishmania infection results into severe, life-threatening disease and is a growing public health concern in many countries including India. Resistance to existing drugs has created demand for new drug targets. Our laboratory has had a long-standing interest in *Leishmania* biology for identifying new genes, specific for the parasite that can be potential target sites for drug development. One of the new parasite specific proteins is NAD(P)H cytochrome *b*₅ oxidoreductase Ncb5or. It has been already established that Ncb5or deficiency results in impaired $\Delta 12$ desaturation in *Leishmania*, thus, regulating a crucial step in polyunsaturated fatty acid biosynthesis.

Aims and Objectives

We are interested to find-out the role of this protein in virulence on infection with activated macrophages as well as inoculation into BALB/c mice.

To find out the exact molecular mechanism and signaling pathways involved in linoleate deficient *Leishmania* infected macrophage.

Work Achieved

To investigate its exact physiological role in *Leishmania*, we have created knockout mutants by gene replacement in *L. major* strains. Null mutant cells exhibit a marked decrease in virulence on infection with activated macrophages as well as inoculation into BALB/c mice. Infection is significantly increased when the KO cells are pretreated with BSA bound linoleate. Real time PCR studies and ELISA assay demonstrate a higher proinflammatory cytokines with a concomitant fall in anti-inflammatory cytokines expression during macrophage infection with LmNcb5or null cell line. Together these findings suggest that decreased linoleate concentration in LmNcb5or null cell infected host cells are the major cause for higher proinflammatory cytokines with a concomitant fall in anti-inflammatory cytokines expression.



Future Research Plans

We are also interested to reveal the exact signaling pathways involved in linoleate deficient *Leishmania* infected macrophage. Blocking of linoleate synthesis causes dramatic drop in parasites infectivity. Thus, targeting Ncb5or gene could be a promising field for developing new drugs for treatment of leishmaniasis.

PUBLICATIONS

Roy, J., Sen Santara, S., Adhikari, A., Mukherjee, A. and Adak, S. (2015) Control of catalysis in globin coupled adenylate cyclase by a globin-B domain. *Arch Biochem Biophys* **579**, 85-90

EXTRAMURAL FUNDING

Examine mechanism of electron transfer from ascorbate or cytochrome c to heme ferryl in the ascorbate peroxidase from *Leishmania major* (LmAPX) by site directed mutagenesis. 2013-2015 (DBT, India)

CONFERENCES / WORKSHOPS

Number of abstract India: 1

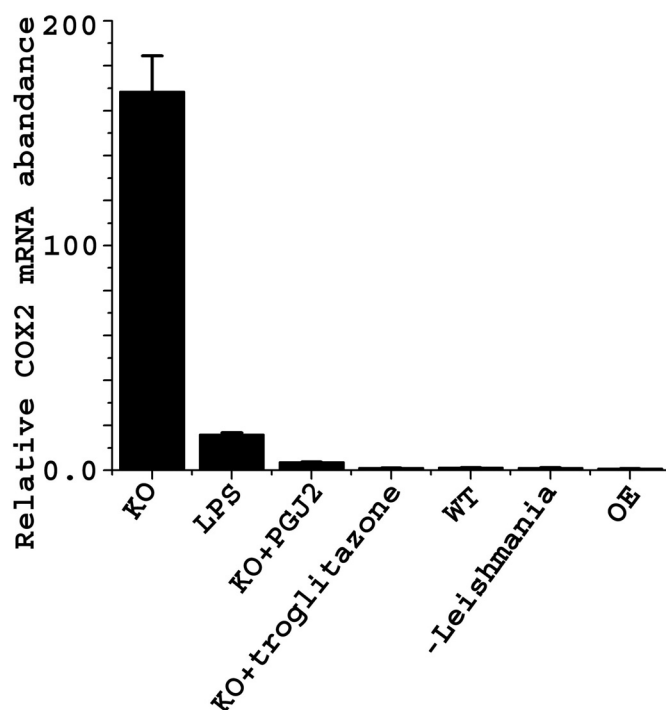


Fig. 1: mRNA status of cyclooxygenase 2 genes in *Leishmania* infected macrophages. Measurements of gene transcript abundance were analyzed by using quantitative RT-PCR. LPS, lipopolysaccharides; PGJ2, 15-deoxy delta(12,14) prostaglandin J2; WT, wild type *Leishmania*; KO, NAD(P)H cytochrome b5 oxidoreductase gene knockout *Leishmania*; OE, NAD(P)H cytochrome b5 oxidoreductase gene overexpressing *Leishmania*; cells. All data were normalized using beta actin as the endogenous control. Data show the mean \pm S.D. of three independent experiments. * p, 0.05, compared with WT sample. All the data are representative of three independent transfection experiments.

Dr. Saumen Datta

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Structural and functional investigation of proteins of Type III secretion system (T3SS) and pantothenate or vitamin B5 synthesis pathway

Participants

JRF: Rajeev Kumar, Arkaprabha Choudhury

SRF: Pranab Halder, Basavraj Khanppavar, Ritapa Chaudhuri

RA: Rakesh Chatterjee

Project Assistant: Chittran Roy, Abhishek Mandal

Background

Many gram negative pathogenic bacteria use type three secretion systems (TTSS) to inject virulent proteins into the host cells through a specialized device called injectisome. After getting injected, these proteins disrupt cell's cytoskeletal assembly and impair immune system; take control of the cell machinery for bacterial survival, replication and dissemination; and at the last promote cell death. These bacterial infestations are manifested by several diseases in animals and plants starting from mild gastroenteritis, dysentery, diarrhea to the acute and life-threatening typhoid fever, bubonic plague, and pneumonia. The virulent proteins do not have any identified secretory signal and the translocation of them directly facilitated by few dedicated chaperones. Genetically all the proteins of TTSS except effectors are well conserved. Translocators, form the top part of the T3SS injectisome, make a pore in the host cell and then facilitate and regulate the transfer of virulent proteins in the host cell. The structural characterization of these proteins are therefore utmost important to clearly understand their hostile activity in side the host cell.

Aims and Objectives

Structure and function of effector and translocator proteins of T3SS

Work Achieved

Pseudomonas aeruginosa and *Yersinia enterocolitica* both posses T3SS. V-antigen of T3SS, a hydrophilic translocator is highly important for its regulatory role on secretion. The V-antigen from *Pseudomonas aeruginosa* and *Yersinia enterocolitica* are PcrV and LcrV respectively. These hydrophilic translocators, with in bacterial cell, are



chaperoned by PcrG and LcrG respectively. Very little is known about the inter-genus complexes of these proteins. We have characterized LcrV-PcrG, PcrV-LcrG, LcrV-LcrG and PcrV-PcrG complex, using size exclusion chromatography (SEC), chemical crosslinking, dynamic light scattering (DLS), Far and near UV circular dichroism (CD), thermal denaturation of proteins and surface plasmon

resonance (SPR) analysis. By bioinformatic analysis, we have stressed on the structural and sequence similarity within Ysc family of hydrophilic translocators, and their regulators. Finally, we have projected an effect of calcium ion on the LcrV-LcrG, PcrV-PcrG, LcrV-PcrG and PcrV-LcrG complexes, which constitutes an important step of regulation of secretion of TTSS.

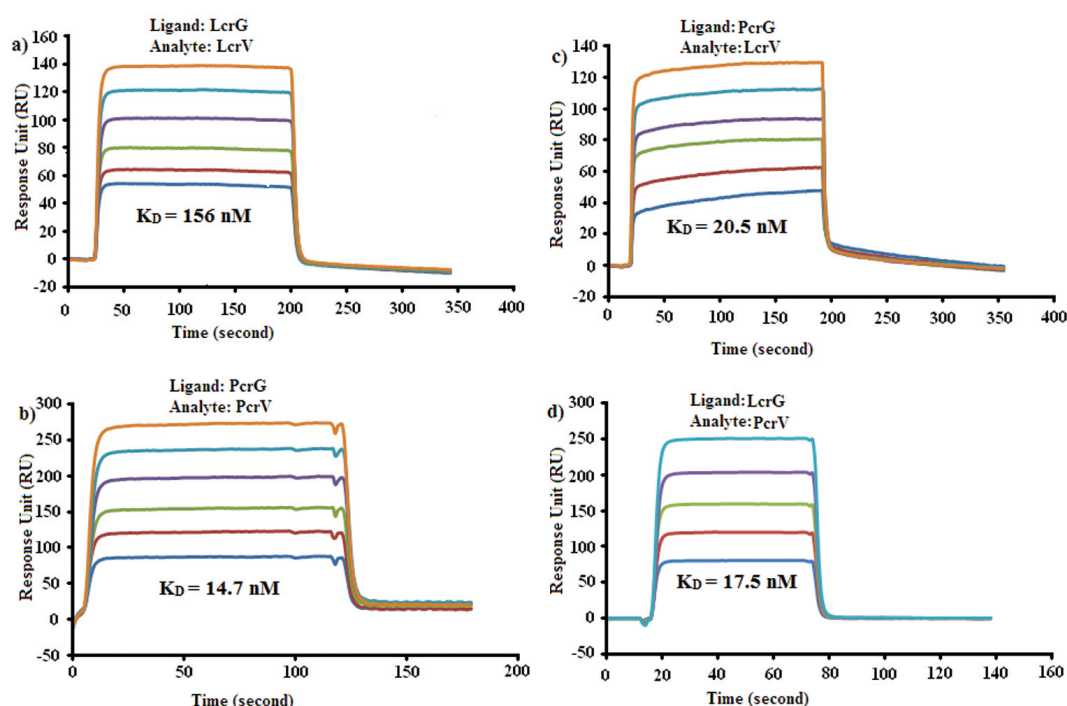


Fig. 1: Molecular Docking studies show the model of LcrV-LcrG₍₁₋₇₀₎ interaction is identical to PcrV-PcrG₍₁₃₋₇₂₎ interaction and mediated by conserved domains of the proteins. (a) Cartoon representation of the model of LcrG₍₁₋₇₀₎, where helices are shown in cyan and loops are shown in salmon. (b) Cartoon representation of the model of LcrV-LcrG₍₁₋₇₀₎, where LcrG₍₁₋₇₀₎ is represented in cyan and LcrV is presented by orange colour, shows that the first two helices of LcrG₍₁₋₇₀₎ and the long helices of LcrV are the sites of interaction. (c) Spacefill model of LcrV-LcrG₍₁₋₇₀₎ interaction with LcrV and LcrG₍₁₋₇₀₎ shown in salmon and purpleblue, respectively, depicts that LcrG₍₁₋₇₀₎ localizes within the groove formed in between two terminal globular domains of LcrV.

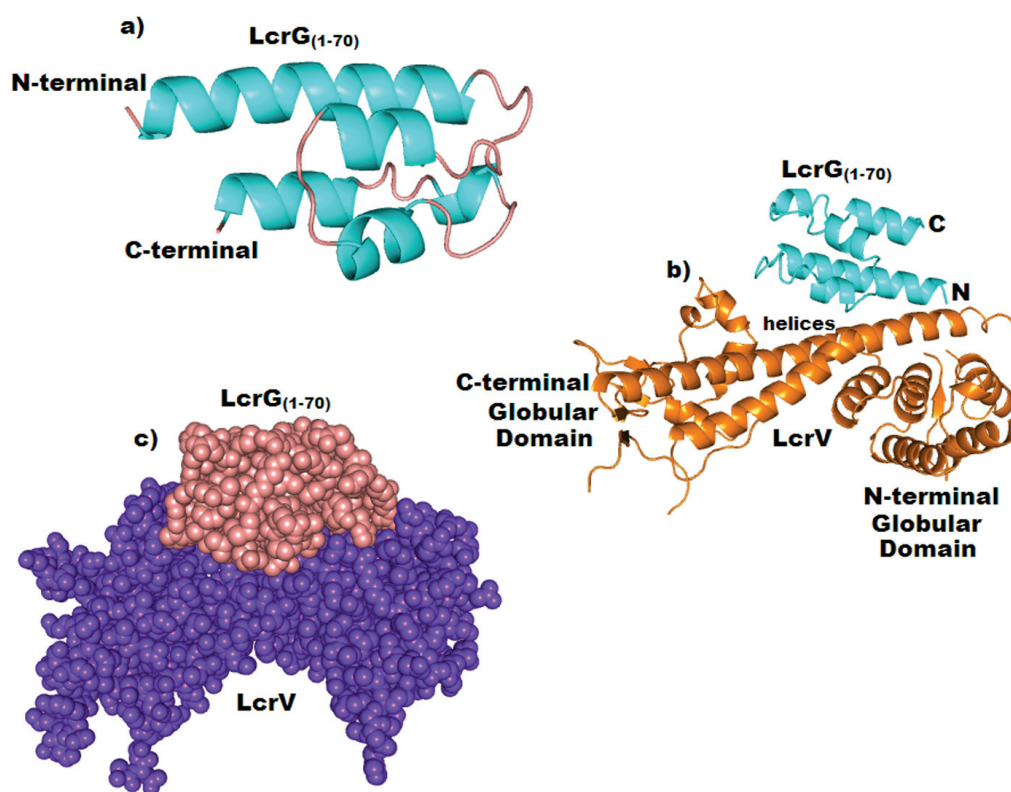


Fig. 2: Calcium ion does not alter the affinity of interaction between V-antigen and its regulator. SPR sensogram of (a) LcrV-LcrG (b) PcrV-PcrG (c) LcrV-PcrG (d) PcrV-LcrG interaction with corresponding K_D values in presence of calcium.

PUBLICATIONS

Basu, A., Das, A., Mondal, A., and Datta S. (2016) Structural analysis of inter-genus complexes of V-antigen and its regulator and their stabilization by divalent metal ions. *Eur Biophys J* **45**, 113-28

EXTRAMURAL FUNDING

Structural and Functional Elucidation of T3SS Effectors with or without their Cognate Chaperone/Target Proteins from Pathogenic Bacteria, 2015 – 2018, DST-SERB, India

Dr. Krishnananda Chattopadhyay



Protein folding, dynamics and aggregation... one molecule at a time

Participants

JRF: Achinta Sannigrahi, Ritobrita Chakraborty, Arnab Bandyopadhyay

SRF: Simanta Sarani Paul, Pallabi Sil, Amrita Kundu, Sumanta Ghash, Sourav Chowdhury

RA: Sangeeta Kundu, Amrita Banerjee, Sayantani Chatterjee

Collaborator(s)

Name of collaborator outside CSIR-IICB

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Presidency University, Kolkata

Dr. Goutam De

CSIR-Central Glass and Ceramic Research Institute, Kolkata

Background

Protein aggregation has been implicated in several neurodegenerative diseases. In addition, protein aggregation may create serious complications in Biologics formulations. One of the major bottlenecks of protein aggregation research arises from the heterogeneity of protein folding/aggregation landscape. In addition, the aggregation kinetics often goes through a lag phase and the present detection techniques seem to be inadequate to understand the events, which occurs in the lag phase of aggregation. 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.

Aims and Objectives

To detect, characterize and investigate in details the early folding pathways of proteins involved in different neurodegenerative diseases.

To Study early stages of aggregation of intrinsically disordered proteins (IDPs) *in vitro* and inside live cells using fluorescence correlation spectroscopy (FCS).

Work Achieved

We have been studying protein conformation, dynamics and aggregation using different biophysical. Previously, 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. Using FCS and other biophysical methods we have shown that the secondary function of a protein (many proteins carry out additional secondary function in addition to their primary functions) depends on the subtle change in the surface charge distributions.

We have now developed ways to detect oligomeric molecules, which populate in the early events of alpha synuclein aggregation pathways. The aggregation of alpha synuclein has been implicated strongly in the pathology of Parkinson's disease (PD). These oligomers are now believed to be responsible for the cellular toxicity, although they are transiently populated and hence uncharacterized by traditional methods. In addition, we have developed methods to directly visualize aggregated protein inclusions inside live neuroblastoma cells using confocal imaging. The effect of solution crowding (either inside cells or by using synthetic crowding agents) on protein folding and stability has been extensively studied at single molecule resolution.

Future Research Plans

To study the conformational stability of SOD1, a key participant of anti-oxidant defense mechanism. Structure determination of transient oligomeric species, which form early in the aggregation process of several proteins, using a host of structure biology techniques.

PUBLICATIONS

- Mukherjee, M., Ghosh, R., Chattopadhyay, K., and Ghosh, S. (2015) . *J Biomol Struct Dyn* **33**, 2145-2160
- Paul, S.S., Sil, P., Haldar, S., Mitra, S., and Chattopadhyay, K. (2015) Subtle change in the charge distribution of surface residues may affect the secondary functions of cytochrome c. *J Biol Chem* **290**, 14476-14490
- Paul, S. S., Sil, P., Chakraborty, R., Haldar, S., and Chattopadhyay, K. (2016) . *Biochemistry* **55**, 2332-2343
- Kundu A., Ghosh, S., and Chattopadhyay, K. (2016) *Biophysical Journal* **110**, 533a
- Mukherjee, M., Ghosh, R., Chattopadhyay, K., and Ghosh, S. (2016) . *RSC Adv* **6**, 61077-61087

AWARDS / HONOURS / MEMBERSHIPS

Student

- Sayantani Chall
- Best poster award in Trombay Symposium in Radiation and Photophysics 2016 (TSRP), BARC, Mumbai.
- Amrita Kundu
- Member of Biophysical Society (BPS), USA.
- Sourav Chowdhury
- Member of Society for Biological Chemists India (SBCI).

CONFERENCES / WORKSHOPS

Number of abstract India: 3 International :1

INVITED TALK

- Department of Chemistry, Hooghly Mohsin College, 11 February 2016. Hooghly, India.
- Department of Chemical Sciences, Tata Institute of Fundamental Research, 29 June 2015, Mumbai.

Dr. Jayati Sengupta

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Elucidating functional mechanisms of macromolecules from their 3D structures determined by cryo-electron microscopy

Participants

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Project Fellow: Shirin Akbar

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Background

The research of my lab is focused on the structure and dynamics of the molecular machine, ribosome. All living organisms utilize ribosome to translate messenger RNA (mRNA) into proteins. The ribosome's function is one of the most fundamental processes of life, and intense efforts are going into elucidating the underlying mechanisms of ribosome-related processes.

Our group primarily uses structural biology (cryo-electron microscopy (Cryo-EM) in conjunction with Single Particle Reconstruction technique) tools to delineate yet-unknown interactions of several regulatory factors (potential targets for antimicrobial drugs) with the bacterial ribosome, particularly the proteins involved in the ribosome biogenesis (e.g. conserved GTPase HflX), and enzymes involved in nascent polypeptide chain processing (e.g. N-terminal deformylation (PDF) and methionine excision (MetAP)).

We also have initiated structural studies employing cryo-EM on other macromolecules involved in crucial cellular functions (in collaboration with other groups).

Aims and Objectives

From the 3D structures of the complexes of ribosome and its subunits we aim to:

- Understand probable role of the ribosome-associated conserved GTPase HflX in ribosome biogenesis and assembly process
- Elucidate the deformylation mechanism of nascent polypeptide chain N-terminal methionine by the enzyme Peptide deformylase (PDF)
- Identify the binding site and functional role of the extra copy of the enzyme methionine aminopeptidase (MetAP) present in *Mycobacterium*.



Work Achieved

Several GTPases likely play a critical role in ribosome biogenesis of individual subunits and their assembly processes. HflX is a GTP binding protein and belongs to a relatively unexplored family. Interestingly, it exhibits GTPase as well as ATPase activities.

Accumulating experimental data indicate functional role of HflX in the biogenesis of the 50S subunit of bacterial ribosome. However, the specific molecular mechanism of the protein's interaction with the ribosomal subunits has not been fully unveiled yet. Our structural study shows interaction of HflX with both the 50S (**Fig. 1A**) and the 30S subunits (**Fig. 1B**) indicating its probable role in ribosome biogenesis/assembly of both the subunits. Apparently, it acts as an 'anti-association factor' (preventing subunit joining to form 70S ribosome) by binding to the intersubunit faces of the subunits.

Future Research Plans

Achieving higher resolution for the already reconstructed 3D cryo-EM maps of HflX-bound ribosomal subunit complexes.

Determining 3D cryo-EM structures of PDF- and MetAP-bound *E. coli* as well as mycobacterium 70S ribosome complexes.

PUBLICATIONS

Shasmal, M., Dey, S., Shaikh, T.R., Bhakta, S., and Sengupta, J. (2016) *E. coli* metabolic protein aldehyde-alcohol dehydrogenase-E binds to the ribosome: a unique moonlighting action revealed. *Sci Rep* **6**, 19936

Chakraborty, B., Bhakta, S., and Sengupta, J. (2016) Disassembly of yeast 80S ribosomes into subunits is a concerted action of ribosome-assisted folding of denatured protein. *Biochem Biophys Res Commun* **469**, 923-9

EXTRAMURAL FUNDING

Processing of the Nascent Polypeptide Chain on Mycobacterium 70S Ribosome: Structural and Functional Studies. 2015-2018, DST-SERB, India

CONFERENCES / WORKSHOPS

Number of abstract India: 2

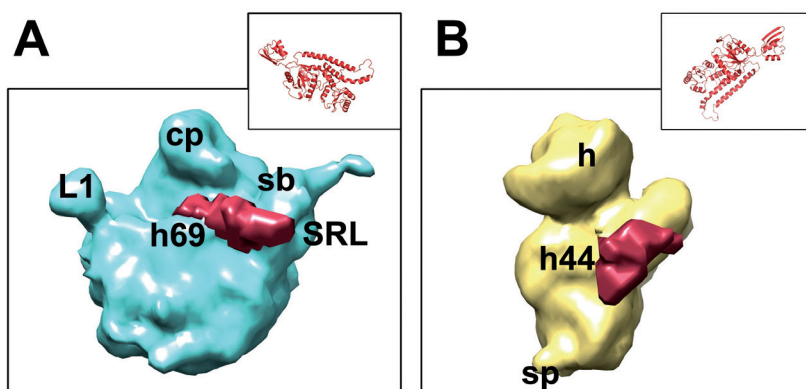


Fig. 1: Intersubunit views of the HflX-bound 50S subunit (A) and 30S subunit (B) complexes (in presence of ATP and GTP nonhydrolyzable analogs) showing HflX (red) binding on the helix 44 region of 30S subunit (yellow) while it binds at the groove of H69 and SRL region of the 50S subunit (cyan). Landmarks for the 30S subunit: h, head; sp, spur; h44, helix 44 of the 16S rRNA. Landmarks for the 50S subunit: CP, central protuberance; SRL, sarcin ricin loop; sb, L7/L12 stalk base; L1, large subunit protein L1; H69, helix 69 of the 23S rRNA. Insets show the HflX structure in 50S (A) and 30S (B) subunit-bound orientations.

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Understanding the molecular mechanisms underlying systemic diseases and host-pathogen interactions

Participants

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Cancer Biology and Inflammatory Disorder Division

Dr. S.N. Bhattacharyya

Molecular and Human Genetics Division

Dr. Partha Chakrabarti

Cell Biology and Physiology Division

Background

Our laboratory research interests are to study the structure, function and evolution of proteins involved in different diseases especially those mediated by a) pathogens and b) involving multiple pathways and processes, such as cancers using computational approaches.

Aims and Objectives

To construct and analyse the protein-protein interactions (PPI) of host-pathogen system.

To understand the hidden properties of systemic disease via using network biology and graph theoretical approaches.

Work Achieved

A) System biology of host pathogen interaction

Network analysis in Plasmodium: During the last few years we have assembled and curated the intra PPI networks of a very important human pathogen, *Plasmodium falciparum*. Using network biological approach we have successfully identified several key regulators of these PPI (**Fig. 1**). Their importance is further demonstrated by a novel network perturbation method developed for this purpose. Further we are addressing the issues related to dynamic change of the whole interactome leading to the transition of life cycle stage of the malarial parasite.

Network analysis in Leishmania: Our group is also investigating another human pathogen, *Leishmania* sp. proteins in order to gain more insight into the pathogenicity of leishmaniasis. We have initiated the compilation and analysis of whole protein interactome data of *Leishmania* sp. so as to study their protein interaction properties both at the systems and molecular level. We have implemented combined bioinformatics and experimental tools providing powerful analytical approaches towards identification and further characterization of the parasitic (e.g., leishmania) virulence factors.



Structure analysis of host-pathogen protein complexes: We have simultaneously carrying out an elaborative study to understand the sequential and structural properties of host-pathogen protein complexes, in an aim to predict host-pathogen protein-protein interactions from sequence and structural data in near future.

B) System biology of Cancer

Similar approaches are also applied to identify key important interactions, proteins and pathways involved in various cancer scenarios utilizing genomics, transcriptomics, and proteomics data generated in collaborators laboratories. Our meta-interaction analyses have shown significant prospects in understanding the complex cellular interaction dynamics during cancer scenario.

Meta-interaction network in complex diseases: We have developed a computational systems biology approach to build a meta-interaction network of proteins and signaling pathways within cellular systems using text mining, network assembly and graph theory approach to understand the complex diseases (e.g., brain cancer). Our objective is to represent a holistic picture of cellular interactome by integrating different types of biological processes at the level of signaling, transcriptional regulation and metabolic networks. In this regard we have developed a pathway assembly tool named PALM-IST (Pathway Assembly from Literature Mining – an Information Search Tool), a platform combining both text mining and data mining methodologies to generate meta-pathways from biomedical

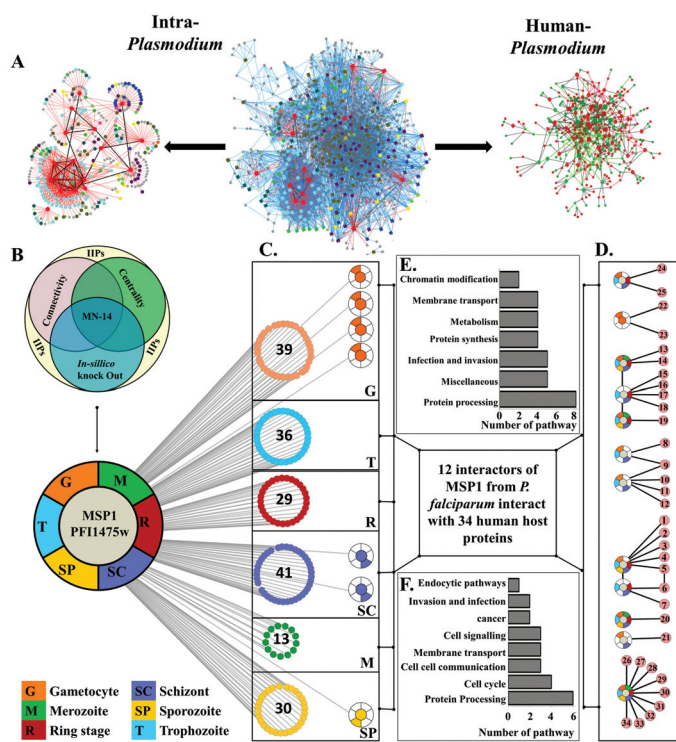


Fig. 1: Identification of IIPs in human Plasmodium interaction. (A) Among the three networks, middle one is intra pathogen PPIN and right one in the host pathogen PPIN. Interaction network mediated by important interacting proteins (IIPs) is shown in the left. (B) A schematic Venn diagram for identification of important proteins. PFI1475w (MSP1) is one of the IIPs identified using this protocol and presented here as an example. (C) Intra Plasmodium stage specific interactions of MSP1 are represented as schematic circular networks in six different boxes where each box represent a particular life cycle stage marked at the bottom right corner of the box. Unique stage specific interactors are marked separately in the boxes. (D) Human partners of these MSP1 interacting proteins are presented as red orange circles. (E and F) Pathways of the Plasmodium interactors (from panel C) and human proteins (from panel C) are represented as two bar charts. The proteins are represented here as small circles and their corresponding stages are represented as a circular colour pattern at the circumference of the circle. The stage(s) where the particular protein is expressed is filled with corresponding colour and other stage(s) are left blank.



abstracts with an objective to identify key crosstalk and bottleneck proteins from the plethora of protein signaling network information (**Fig. 2**).

C) Molecular Modelling and Dynamic Simulation

Our laboratory has assembled and maintained a resource of 4.2 Teraflops of computational power and we have successfully utilized this resource into intensive computational calculations of molecular dynamic simulations, molecular docking, molecular-modeling and sequence alignment programs to solve intricate biological problems. In one such example, our team is investigating the effect of cholesterol during leishmaniasis on human MHC-II protein embedded within a lipid bilayer membrane using molecular dynamic simulations (**Fig. 3**). In another instance of molecular dynamic

simulation, we are exploring the effect of different single site mutations on the Cytochrome P450B1 enzyme structure, leading to the development of glaucoma in human. Extensive molecular modeling and docking analysis is also carried out to understand the interaction between sulfonoquinovosyldiacylglyceride (SQDG) isolated from *Azadirachta indica* against topoisomerase-I enzyme. From the last year onwards, we have extended our research interest to field of RNA biology also. We have started to analyze the RNA-RNA interaction properties between bacterial small RNAs and their target genes. We have developed a method to identify such small RNAs and their target genes and investigating their role in pathogenicity.

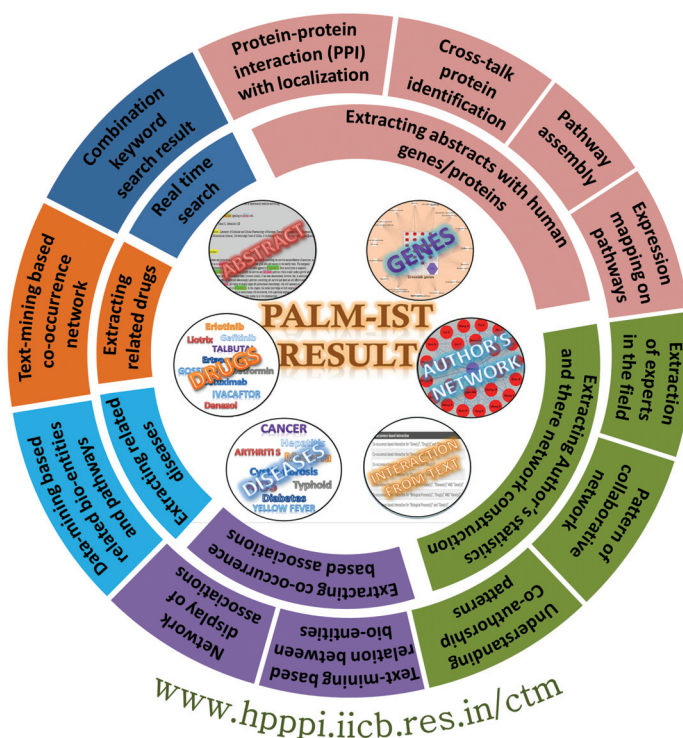
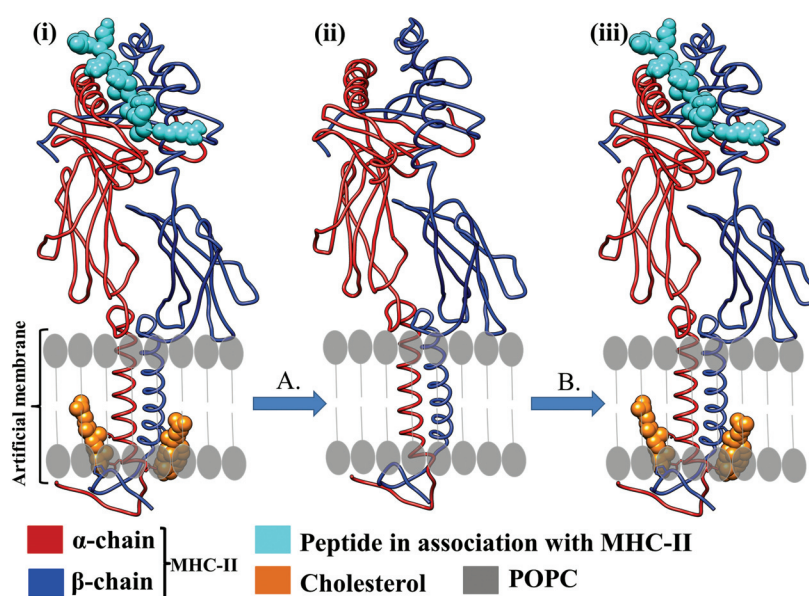


Fig. 2: PALM-IST server output options and there applications. PALM-IST performs literature and data mining task to extract bio-entity terms (like genes, proteins, diseases, drugs, processes etc.) for the user search keyword. PALM-IST output (middle circle) and there applications/features (outer most circle) ranges from multiple keyword based search, protein-protein interaction identification, bio-entity relationship building, pathway assembly and authorship network construction.



A. Parasite mediated cholesterol depletion

B. Restoration of membrane cholesterol by liposomal cholesterol treatment

Fig. 3: Structure of antigen presenting MHC-II complex. The figure shows formation of peptide MHC-II complex on the surface of antigen presenting cells, where peptide is sitting in the peptide binding groove (i). The infection of antigen presenting cells with *L. donovani* causes depletion of membrane cholesterol leading to defective peptide MHC-II stability presumably due to change in the conformation of membrane bound MHC-II protein in absence of cholesterol (ii), which is corrected upon restoring membrane cholesterol by liposomal delivery in infected antigen presenting cells (iii). Arrow A and B represent parasite mediated cholesterol depletion and restoration of membrane cholesterol by liposomal cholesterol treatment.

PUBLICATIONS

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Khan, M.W., Biswas, D., Ghosh, M., Mandloi, S., Chakrabarti, S., and Chakrabarti, P. (2015) mTORC2 Controls Cancer Cell Survival by Modulating Gluconeogenesis. *Cell Death Discovery* doi:10.1038/cddiscovery.2015.16

Banerjee, A., Chakraborty, S., Chakraborty, A., Chakrabarti, S., and Ray, K. (2016) Functional and Structural Analyses of CYP1B1 Variants Linked to Congenital and Adult-Onset Glaucoma to Investigate the Molecular Basis of These Diseases. *PLoS One* **11**, e0156252

Bhattacharyya, D., Hazra, S., Banerjee, A., Datta, R., Kumar, D., Chakrabarti, S., and Chattopadhyay, S. (2016) Transcriptome-wide identification and characterization of CAD isoforms specific for podophyllotoxin biosynthesis from *Podophyllum hexandrum*. *Plant Mol Biol*

Alam, S. K., Yadav, V. K., Bajaj, S., Datta, A., Dutta, S. K., Bhattacharyya, M., Bhattacharya, S., Debnath, S., Roy, S.,

Boardman, L. A., Smyrk, T. C., Molina, J. R., Chakrabarti, S., Chowdhury, S., Mukhopadhyay, D., and Roychoudhury, S. (2016) DNA damage-induced ephrin-B2 reverse signaling promotes chemoresistance and drives EMT in colorectal carcinoma harboring mutant p53. *Cell Death Differ* **23**, 707-722

Das, M. R., Bag, A. K., Saha, S., Ghosh, A., Dey, S. K., Das, P., Mandal, C., Ray, S., Chakrabarti, S., Ray, M., and Jana, S. S. (2016) Molecular association of glucose-6-phosphate isomerase and pyruvate kinase M2 with glyceraldehyde-3-phosphate dehydrogenase in cancer cells. *BMC Cancer* **16**, 152

Ghosh, R.D., Ghuwalewala, S., Das, P., Mandloi, S., Alam, S.K., Chakraborty, J., Sarkar, S., Chakrabarti, S., Panda, C.K., and Roychoudhury, S. (2016) MicroRNA profiling of cisplatin-resistant oral squamous cell carcinoma cell lines enriched with cancer-stem-cell-like and epithelial-mesenchymal transition-type features. *Sci Rep* **6**, 23932

Roy, K., Mandloi, S., Chakrabarti, S., and Roy, S. (2016) Cholesterol Corrects Altered Conformation of MHC-II Protein in *Leishmania donovani* Infected Macrophages: Implication in Therapy. *PLoS Negl Trop Dis* **10**, e0004710

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Structure and functional aspects of disordered human proteome

Participants

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SRF: Swagata Das, Mritunjoy Maity, Supriya Das, Anupam Roy, Sudeshna Sen

SPF: Uttam Pal, Sandip Dolui

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Background

Recent reports suggest the unique presence of intrinsically disordered proteins (IDPs) in eukaryotes and about 30% of amino acid residues in human proteome are in the disordered regions of a protein. The naturally occurring disordered proteins are predominantly present in the cell nucleus. The presence of such large content of disorder regions in a protein is believed to confer suitable plasticity to interact efficiently with several targets, as compared with a globular protein with limited conformational flexibility. The disorderedness thus became an intense field of investigation to know its composition, genomic distribution, cellular localization and energetic aspects linked to function and binding to a targeted partner-molecule.

Aims and Objectives

- (i) Understanding the human disorder proteome
- (ii) Structural and functional aspects of intrinsically disordered proteins
- (iii) Role of protein disordered in amyloid diseases

Work Achieved

We focused our research on disordered proteins in human proteome and investigated intrinsic behavior, such as their stability and role in amyloid formation. Engaging bioinformatics, computational and statistical approaches were able to provide statistical parameters of binding regions (BRs) found in disordered human proteome. These parameters helped us to measure the probability of finding a BR in a group of disordered protein. The content of BRs fitted a Poisson distribution pattern and suggested that the occurrence of BRs in a protein was a stochastic process. The length of the BRs also followed Poisson distribution with a mean of 6 residues in the region. However, the percentage of residues in BR showed a normal distribution pattern. The statistical analysis also revealed that the theoretical isoelectric points (pIs) for both IDPs and the BRs within them followed a bimodal distribution; the BRs were either more

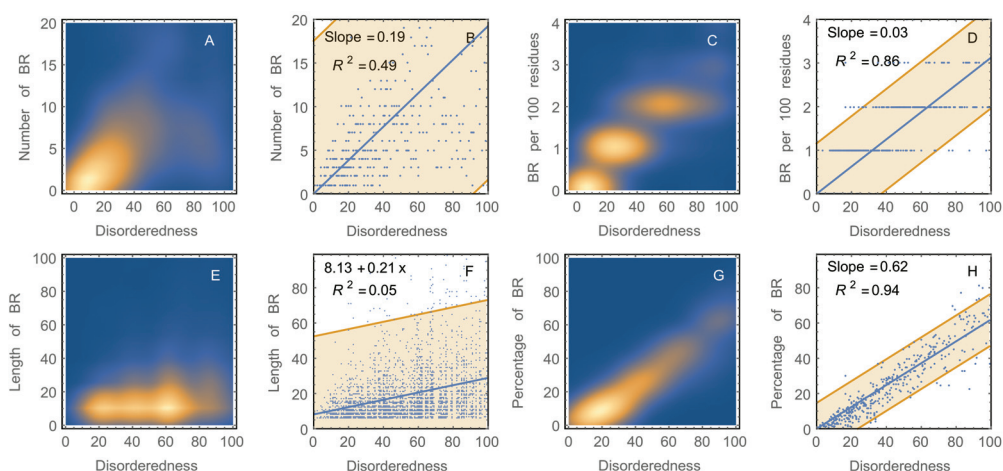


Fig. 1: Correlation of BR frequency/occupancy with protein disorderedness. Distribution of BR frequency with protein disorderedness (A) and the fitted linear model (B). Distribution of BR frequency per 100 residues of protein with the protein disorderedness (C) and the fitted linear model (D). Distribution of BR lengths with protein disorderedness (E) and the fitted linear model (F). Distribution of BR occupancy in a protein with the protein disorderedness (G) and the fitted linear model (H). Confidence level bands at 95% are shown

acidic or basic than the pIs of the proteins. Combining and comparing these statistical information of BRs with other methods could be very useful for high-throughput functional annotation of proteins, drug target identification and drug discovery linking protein disorder that is present in many human proteins.

Future Research Plans

- (i) Conformation of several amyloidogenic proteins when they form neurotoxic aggregates
- (ii) How oligomers interact with membrane bilayers

PUBLICATIONS

Maity, M., Dolui, S., and Maiti, N. C. (2015) Hydrogen bonding plays a significant role in the binding of coomassie brilliant blue-R to hemoglobin: FT-IR, fluorescence and molecular dynamics studies. *Phys Chem Chem Phys* **17**, 31216

Pal, U., Pramanik, S., Bhattacharya, B., Banerji, B. and Maiti, N. C. (2015) Binding interaction of a novel fluorophore with serum albumins: steady state fluorescence perturbation and molecular modeling analysis. *Springer Plus* **4**, 548

Chakraborty, B., Dutta, D., Mukherjee, S., Das, S., Maiti, N.C., Das, P. and Chowdhury, C. (2015) Synthesis and biological

evaluation of a novel betulinic acid derivative as an inducer of apoptosis in human colon carcinoma cells (HT-29). *Eur J Med Chem* **102**, 93-105

Banerji, B., Chatterjee, M., Paul, U. and Maiti, N. C. (2016) Molecular Details of Acetate Binding to a New Diamine Receptor by NMR and FT-IR Analyses. *J Phy Chem A* **120**, 2330-2341

Pal, U., Maity, M., Khot, N., Das, S., Das, S., Dolui, S. and Maiti, N. C. (2016) Statistical insight of binding regions in disordered human proteome. *J Proteins and Proteomics* **7**, 47-60

EXTRAMURAL FUNDING

DBT grant in basic biology 2012- Dec, 2015

CONFERENCES / WORKSHOPS

Number of abstract India: 6 International: 1

CONFERENCES / EVENTS ORGANIZED BY CSIR-IICB

Chaired a Session in 17th All India Congress of Cytology and Genetics and Symposium on "Exploring Genomes: The New Frontier", 22 -24 December 2015 Kolkata, India.

INVITED TALKS

Studying Protein Disordered by Raman Microscopy (Roy A, Dolui S and Maiti N. C.), Invited Talk, OWLS 2016, 16 -19 March 2016. Tata Institute of Fundamental Research, Mumbai, India.

Deuterium isotope effect on chemical shift of carbon in D-Ribose (Maiti N. C), Invited Talk, 22nd Conference of National Magnetic Resonance Society (NMRS 2016), 18 -21 February 2016. IIT Kharagpur, India.

Dr. Sujoy Mukherjee



Role of protein's structure and dynamics in function and disease propagation

Participants

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Project Fellow: Shraboni Dutta

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Background

Proteins exist in multiple states and detailed information of how they interconvert between its various conformations can be helpful in understanding their physiological functions. This knowledge can be helpful in understanding how their malfunction cause diseases and help develop therapies to overcome them. It has been shown that inter-conversion between protein's conformers occur via sparsely populated intermediate states. But their short-lived nature and low population makes them difficult to study by standard biophysical methods. Moreover, in case of certain amyloid-forming diseases, these intermediate are considered to be the main cytotoxic agents responsible for the disease.

Aims and Objectives

To clone, over-express, purify and reconstitute the protein of interest in appropriate medium suitable for biophysical studies.

To characterize the multi-timescale conformational flexibility of proteins using NMR and molecular dynamics simulations.

To characterize the thermodynamic and kinetic properties of the inter-converting states of proteins

Work Achieved

NMR spectroscopy is an emerging technique that can be used to study these transient states of protein that are present in very low fraction of the population (up to 0.5%). We have verified the existence of non-native conformers of an amyloid forming protein (Transthyretin) that is originally a thyroxine transporter protein but implicated in a number of senile and familial forms of amyloidosis. We have used solution NMR and MD simulations to characterize the residue specific conformational flexibility of Transthyretin ranging from picoseconds to milliseconds regime and highlighted its dynamic hot-spots. Subsequently, we performed these experiments in the various clinically relevant and



widespread mutants and upon comparison to the wild type found unique differences in pathogenic and benign forms of the protein. Our research provides a biophysical explanation on the higher pathogenicity of the mutant forms of the protein than the wild type.

Future Research Plans

The future plan of our laboratory is to expand the scope of these studies into other biomolecules that are known to be relevant in diseases ranging from tuberculosis to mental health and cancer. We are undertaking the cloning, over-expression and purification to obtain sufficient quantities of the target protein for biophysical studies in vitro.

PUBLICATIONS

Mishra, P., Choudhary, S., Mukherjee, S., Sengupta, D., Sharma, S., and Hosur, R. V. (2015) Molten globule nature of Plasmodium falciparum P2 homo-tetramer. *Biochem Biophys Res* **1**, 97 - 107

AWARDS / HONOURS / MEMBERSHIPS

Memberships

Elected as member of Executive Committee of NMR Society of India

Membership taken for Indian Peptide Society

EXTRAMURAL FUNDING

Ramanujan Fellowship 2011 - 2016. (Department of Science & Technology, India)

Investigating the dynamic interactions of a toxin-antitoxin module of Mycobacterium tuberculosis by NMR spectroscopy, 2015– 2018. (Department of Science & Technology, India)

CONFERENCES / WORKSHOPS

Number of abstract India: 1

International: 1

INVITED TALKS

A direct correlation between backbone dynamics and disease severity in transthyretin: a protein responsible for amyloidosis; JNCASR / Indian Peptide Society meeting; September 2015. Bengaluru, India,

Investigating the early-misfolding events in transthyretin amyloidosis Vasundhara Sarovar Premiere / “ NMR meets Biology” Conference; January 2016. Cochin, India,

Reshaping of the free energy landscape in an amyloid forming pathway by transiently populated non-native protein conformers; IIT Kharagpur / NMR society conference; February 2016. Kharagpur, India,

Dr. Sucheta Tripathy

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Exploiting cyanobacteria for Bioremediation and Biofuel production using genomics as a tool

Participants

JRF: Mayuri Mukherjee, Samrat Ghosh

SRF: Lubna Sheikh, Subhadeep Das, Abhishek Das, Mathu Malar C., Arijit Panda, Deeksha Singh

RA: Deeya Sen, Rajib Majumdar

Project Assistant: Vinneta Verma

Collaborator(s):

Name of collaborator outside CSIR-IICB

Prof. Sanjoy Guha Roy

West Bengal State University, West Bengal

Prof. Anindita Seal

Calcutta University, West Bengal

Prof. Siba Prasad Adhikary

VC, Fakir Mohan University, Orissa

Dr. Shubho Choudhury

Bose Institute, West Bengal

Dr. Swasthi Tiwari

PGI, Lucknow, UP

Prof. Brett Tyler

Oregon State University, USA

Dr. Takao Kasuga

University of California Davies, USA

Dr. Sophien Kamoun

Sainbury laboratories, UK

Name of collaborator within CSIR-IICB

Dr. Suman Khowala

Drug Development Diagnostics & Biotechnology Division

Dr. Chitra Mandal

Cancer Biology and Inflammatory Disorder Division

Dr. Nahid Ali

Infectious Disease Division

Background

Cyanobacteria are the most ancient organisms that possibly made the earth habitable. In the last few years, they have garnered significant interest due to their adaptability and their ability to synthesize a range of metabolites of commercial significance. Cyanobacteria growing in extreme conditions have acquired a large chunk of their genomes from other prokaryotes to carry out specialized functions. Fatty acid production in these organisms can be tweaked easily if the genome sequences are deciphered.

Aims and Objectives

To decipher the genomes and transcriptomes of extremophilic Cyanobacteria.

Profile metabolites and fatty acids from the extremophiles under various conditions.

To re-engineer strain 6803 in over production of fatty acids and metabolites of commercial importance.

Work Achieved

We have collected Cyanobacteria growing in terrestrial habitats and explored their whole genome sequences by de novo sequencing using Illumina HiSeq. We optimized assembly protocols for these organisms and predicted 6000 - 8000 genes and their genome size ranged between 6 MB to 12 MB. Genomes of these organisms, their annotations are reported for the first time from our lab and ever since, we have attracted significant attention internationally. Currently, we are working on profiling their metabolites so that they can be used for large scale production of bio-metabolites.

Some of the Cyanobacterial species we are working on have tremendous potential in terms of bioremediation. We have observed that they have the ability to convert extreme acidic environments into alkaline within a couple of days. Some of the species of Cyanobacteria also have the ability to absorb heavy metals. We are studying the



genomics and transcriptomics of these organisms to understand the underlying mechanism better.

Future Research Plans

We will identify the pathways responsible for production of fatty acids and biometabolites under several different conditions and will metabolically re-engineer a single celled strain for making it a cell factory.

PUBLICATIONS

Mukherjee S, Chandrababunaidu MM, Panda A, Khowala S, Tripathy S. Tricking *Arthrinium malaysianum* into Producing Industrially Important Enzymes Under 2-Deoxy D-Glucose Treatment. *Front Microbiol.* 2016 May 13;7:596. doi: 10.3389/fmicb.2016.00596. eCollection 2016. PubMed PMID: 27242677; PubMed Central PMCID: PMC4865484

Mohan A, Singh RS, Kumari M, Garg D, Upadhyay A, Ecelbarger CM, Tripathy S, Tiwari S. Urinary Exosomal microRNA-451-5p Is a Potential Early Biomarker of Diabetic Nephropathy in Rats. *PLoS One.* 2016 Apr 21;11(4):e0154055. doi: 10.1371/journal.pone.0154055. eCollection 2016. PubMed PMID: 27101382; PubMed Central PMCID: PMC4839711.

Das A, Panda A, Singh D, Chandrababunaidu MM, Mishra GP, Bhan S, Adhikary SP, Tripathy S. Deciphering the Genome Sequences of the Hydrophobic Cyanobacterium *Scytonema tolypothrichoides* VB-61278. *Genome Announc.* 2015 Apr 2;3(2). pii: e00228-15. doi: 10.1128/genomeA.00228-15. PubMed PMID: 25838486; PubMed Central PMCID: PMC4384490.

Das S, Singh D, Madduluri M, Chandrababunaidu MM, Gupta A, Adhikary SP, Tripathy S. Draft Genome Sequence of Bioactive-Compound-Producing Cyanobacterium *Tolypothrix campylonemoides* Strain VB511288. *Genome Announc.* 2015 Apr 2;3(2). pii: e00226-15. doi: 10.1128/genomeA.00226-15. PubMed PMID: 25838485; PubMed Central PMCID: PMC4384489.

Book Chapters / Invited Reviews

Verma S, Tripathy S., Raychaudhuri S, Swarnakar S. Chapter: Insights into Metalloproteinases Regulation in Gastrointestinal Cancers: Epigenetic Influences in the Book: *Gastrointestinal Cancers: Prevention, Detection and Treatment*. Editor, A Tyagi. Nova Publication (2016) (in press)

AWARDS / HONOURS / MEMBERSHIPS

Award

NSF grant for attending High Throughput Computing at Madison, Wisconsin

Membership

Life membership of BRSI.

EXTRAMURAL FUNDING

Whole genome and Transcription sequencing of selected Indian cyanobacterial species for candidate gene discovery for biometabolites. ICAR (Govt. of India) 2014-2017

DBT Ramalingaswamy (2012-2017)

CONFERENCES / WORKSHOPS

Number of abstract India: 4

Chaired Session: 2

CONFERENCES / EVENTS ORGANIZED BY CSIR-IICB

In the organizing committee of The New Frontier organized by IICB.

Dr. Siddhartha Roy

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Structural and functional characterization of a chromatin reader, ZMYND8 implicated in cancer metastasis

Participants

JRF: Sambit Dalui

SRF: Dushyant Kr. Srivastava, Anirban Dasgupta

Project Assistant: Shantanu Adhikary

Collaborator(s)

Name of collaborator outside CSIR-IICB

Dr. Chandrima Das

Saha Institute of Nuclear Physics, Kolkata

Name of collaborator within CSIR-IICB

Dr. Amitava Sengupta

Cancer Biology and Inflammatory Disorder Division

Dr. Ramalingam Natarajan

Organic and Medicinal Chemistry Division

Background

Chromatin reader/effector proteins specifically recognize histone posttranslational modifications (PTMs) and translate such recognition(s) into meaningful biological outcomes by virtue of either their intrinsic activities or those of their interacting partners. Zinc finger MYND-type containing 8 (ZMYND8) is a putative chromatin reader/effector harbouring a PWWP domain, bromodomain and a PHD type zinc finger. ZMYND8 plays a significant role in embryonic neural differentiation. ZMYND8 is also involved in T-cell lymphoma, breast and cervical cancer. But how ZMYND8 regulates gene expression in the context of chromatin is not known. Presently there is no structural information available on ZMYND8. The endeavor of the present project is to understand the structural aspects of the protein which could elucidate its physiological function in cell.

Aims and Objectives

To uncover the potential binding partners of ZMYND8, a putative chromatin reader/effector protein.

To characterize the modified histone binding preference through biophysical technique. Elucidation of atomic resolution structure of ZMYND8 using X-ray crystallography.

Work Achieved

Zinc finger MYND-type containing 8 (ZMYND8) is a component of coregulator complex network having an extensive interaction with transcription machinery. ZMYND8 has a MYND domain (protein / protein interaction module) and three chromatin-binding domains PHD, Bromo and PWWP (PBP module in combination). We have shown that through its specific key residues present in its conserved chromatin-binding modules, ZMYND8 interacts with selective epigenetic marks H3.1K36Me2/H4K16Ac (**Fig. 1**). Further, ZMYND8 shows a clear preference for canonical histone H3.1 over variant H3.3 (**Fig. 1**). Further, we have quantified the binding affinity H3.1K36 methylated and H4K16 acetylated peptides by fluorescence spectroscopy. While ZMYND8-PBP showed a strong



affinity for H3.1K36Me2 (0.2 μ M) and H4K16Ac (0.7 μ M) peptides, its preference for H3.1K36Me0 and H3.1K36Me1 was rather weak (**Fig. 1**). Thus our study identifies that ZMYND8 is involved in regulating gene expression through its modified histone binding ability. These findings have been published in J. Biol Chem., 2015, 291, 2664. Further, we have crystallized the ZMYND8-PBP

module. The 3 dimensional structure would elucidate the preferential peptide-binding ability and the critical residues mediating such interaction. Interestingly, we have deciphered the physiological consequence of this selective epigenetic recognition and show for the first time that ZMYND8 is a novel regulator of Epithelial Mesenchymal Transition (EMT).

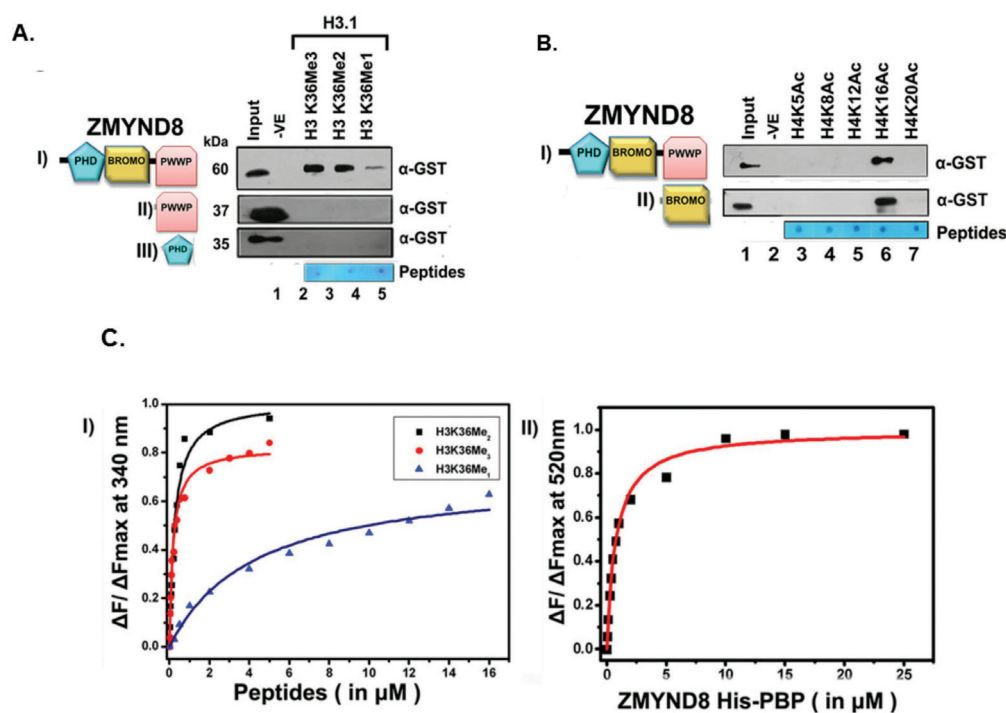


Fig. 1: ZMYND8 interacts preferentially with histone H3.1K36Me2/Me3 and H4K16Ac through its PBP module in vitro (A) Interaction of GST-PBP (panel I), GST-PWWP (panel II) and GST-PHD (panel III) with biotinylated-mono/di/tri-methylated H3.1K36. Similar interaction of GST-PBP with H3.3K36 methylated peptides (panel IV). GST-PBP interaction with biotinylated-mono/di/tri-methylated H3K27 and H4K20 peptides (panel V). (B) Interaction of GST-PBP (panel I), GST-Bromo (panel II) with biotinylated H4-K5/K8/K12/K16/K20 acetylated peptides. (C) Binding isotherms for the interaction of His-PBP (of ZMYND8) with indicated histone peptides as obtained from steady state fluorescence spectroscopy. Data points for H3K36Me₃, H3K36Me₂, and H3K36Me₁ are indicated by circle (red), square (black), and triangle (blue) respectively (Panel I). Binding isotherm for the interaction of His-PBP and H4K16Ac (FAM conjugated) peptide as obtained from steady state fluorescence spectroscopy (Panel II).

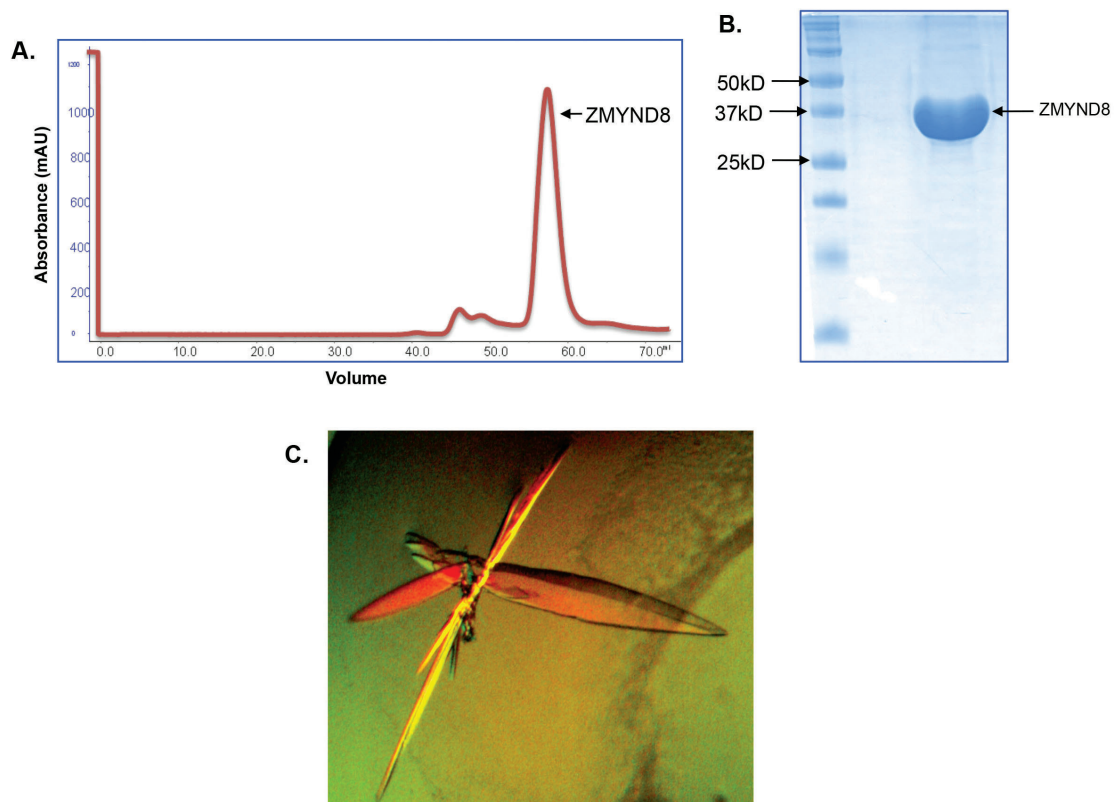


Fig. 2: ZMYND8 purification and crystallization (A) Gel filtration profile of ZMYND8. (B) SDS PAGE profile of ZMYND8. (C) ZMYND8 Co-crystal with acetylated histone H4 peptide

Future Research Plans

Structural characterization of the peptide-binding pocket of ZMYND8.

Structure-based designing of novel inhibitors to occlude the peptide-binding pocket of ZMYND8, as a therapeutic strategy against cancer.

PUBLICATIONS

Sarkar, S., Siddiqui, A.A., Mazumder, S., De, R., Saha, S.J., Banerjee, C., Iqbal, M.S., Adhikari, S., Alam, A., Roy, S. and Bandyopadhyay, U. (2015) *J Agric Food Chem* **63**, 4988-4998

Adhikary, S., Sanyal, S., Basu, M., Sengupta, I., Sen, S., Srivastava, D.K., Roy, S., and Das, C. (2016) Selective Recognition of H3.1K36 Dimethylation/H4K16 Acetylation Facilitates the Regulation of All-trans-retinoic Acid (ATRA)-responsive Genes by Putative Chromatin Reader ZMYND8. *J Biol Chem* **291**, 2664-2681

12th Five year Plan Projects

CSIR-IICB NODAL

1) Project Title (with Acronym) : Understanding and Designing the Supra Molecular Ensembles and Machines (UNSEEN) Sanc. Ltr No. 9/1/BS/IICB(1)/2012-13-PPD

Project Code: BSC 0113

Nodal Scientist: Prof. Siddhartha Roy, Co-Nodal Scientist: Dr. Jayati Sengupta

Participating Institutes : CCMB, IGIB, CDRI and IMTECH

Participating Scientists from IICB: Dr. Samit Adhya, Dr. Krishnananda Chattopadhyay, Dr. Saumen Dutta, Dr. Surajit Ghosh, Dr. Nakul Maiti, Dr. Sujoy Mukherjee and Dr. Siddhartha Roy

Project co-ordinator from PPD, CSIR: Dr. Vandana Bisht

2) Project Title (with Acronym) : Therapeutics of Chronic Obstructive Pulmonary Disease (COPD) and Related Respiratory Disorders (TREAT) Sanc. Letter No: 9/1/BS/IICB (5)2012-13-PPD

Project Code: BSC 0116

Nodal Scientist: Dr. Arun Bandyopadhyay, Co-Nodal Scientist: Dr. Santu Bandyopadhyay NCL

Participating Scientists from IICB : Dr. Subrata Adak, Dr. Subhajit Biswas Dr. Krishnananda Chattopadhyay, Dr. Saikat Chakrabarti, Dr. Tripti De, Dr. Dipyaman Ganguly, Dr. Syamal Roy, Dr. Malini Sen and Dr. Subhajit Biswas

Project co-ordinator from PPD, CSIR: Dr. R.P Singh
Participating Institutes: IGIB, IICT, IIIM, IITR and NEIST

Participating Scientists from IICB: Dr. Nahid Ali, Dr. Padma Das, Dr. Saumen Dutta, Dr. P Jaisankar, Dr. Aditya Konar, Prof. Siddhartha Roy, Dr. Sib Sankar Roy, Dr. Malini Sen and Dr. Snehasikta Swarnakar

Project co-ordinator from PPD, CSIR: Dr. Viswajanani Sattigeri

3) Project Title (with Acronym) : Neurodegenerative Diseases: Causes and Corrections (miND), Sanc. Ltr No. 9/1/BS/IICB(4)/2012-13-PPD

Project Code: BSC 0115

Nodal Scientist : Dr. K.P Mohanakumar, Co-Nodal Scientist: Dr. Subhas Biswas

Participating Institutes: CCMB, IITR, CDRI, NCL and IICT.

Participating Scientists from IICB:

Dr. Kunal Ray, Dr. Nanda Ghoshal, Dr. Debasish Bhattacharyya, Dr. Biswadip Banerji, Dr. Suvendra Nath Bhattacharyya, Dr. Subhash Biswas, Dr. Krishnananda Chattopadhyay, Dr. Sumantra Das, Dr. Mrinal Ghosh, Dr. Ranjan Jana, Dr. Nakul Maiti. Dr. R. Natarajan, Dr. P. Jaisankar and Dr. Debabrata Biswas

Project co-ordinator from PPD, CSIR: Dr. Viswajanani Sattigeri

4) Project Title (with Acronym) : Host Interactome Analysis: Understanding the Role of Host Molecules in Parasitic Infection (HOPE) Sanc. Ltr No. 9/1/BS/IICB(2)/2012-13-PPD

Project Code: BSC 0114

Nodal Scientist: Dr. Nahid Ali

Co-Nodal Scientist: Dr. Suvendra Nath Bhattacharyya

Participating Institutes : CDRI, IMTECH, CCMB and NCL

Participating Scientists from IICB : Dr. Subrata Adak, Dr. Subhajit Biswas, Dr. Krishnananda Chattopadhyay, Dr. Saikat Chakrabarti, Dr. Tripti De, Dr. Dipyaman Ganguly, Dr. Syamal Roy, Dr. Malini Sen and Dr. Subhajit Biswas

Project co-ordinator from PPD, CSIR: Dr. R.P Singh

5) Project Title (with Acronym) : Bio-energetic Disorders: A Multi-model Approach to Monitoring and Management (BEnD). Sanc. Ltr No. 9/1/BS/IICB(3)/2012-13-PPD

Project Code: BSC 0206

Nodal Scientist: Dr. Uday Bandyopadhyay, Co-Nodal Scientist: Dr. Sib Sankar Roy

Participating Institutes: Nil

Participating Scientists : Dr. Samit Adhya, Dr. Rupashri Ain, Dr. Arun Bandyopadhyay, Dr. Biswadip Banerji, Dr. Suvendra Nath Bhattacharyya, Dr. Subhas Biswas, Dr. Partha Chakrabarti, Dr. Pijush K. Das, Dr. K.P. Mohanakumar, Dr. Arindam Talukdar and Dr. Indu Bhushan Deb

Project co-ordinator from PPD, CSIR: Dr. R.P Singh



Nodal Network Projects Details

1) TITLE: Understanding and Designing the Supra Molecular Ensembles and Machines (UNSEEN)

Participating Laboratories: CSIR-IGIB, CSIR-CCMB, CSIR-CDRI, CSIR- IMT

Core Objectives:

In living systems most proteins exist in large dynamic macro-molecular ensembles. To solve the structure and intrinsically complex dynamics of large bio-macromolecular complexes and machines (which are difficult to crystallize as such) using a 'Hybrid Approach'

Uniqueness and importance of core objective:

The proposed study is expected to greatly enhance our understanding of the structure and dynamics of several important biological assemblies and molecular motors involved in key cellular processes. To our knowledge, a structural biology project of this kind does not exist nationally. Additionally, many of the proposed studies have far reaching implications in human diseases. The proposed project would provide scientific information which would be useful to design therapeutic strategies.

Most significant milestones achieved towards attainment of core objective:

Following installation of the high resolution cryo-TEM POLARA, standardization of cryo-grid preparation for several macromolecular complexes has been done.

- 3D cryo-EM reconstructions (preliminary 3D data) of following complexes have been done:
 - i. Complexes of CREB binding protein (p300) with p53 and DNA
 - ii. Initial oligomers (supposed to be toxic intermediates) of PD-related proteins
 - iii. Ribosome biogenesis related GTPase HflX-bound 50S and 30S subunit complexes
 - iv. Macromolecular complexes related to type three secretion system
- Publication (Paul SS, Sil P, Halder S, Mitra S, Chattopadhyay K, J. Biol. Chem. 2015:14476-90) was selected in 'research highlights', Nature Chemical Biology (Vol 11; June 2015)
- Interaction of new proteins (AdhE and OmpC, which may have some role in ribosome biogenesis and/or translation) with the ribosome has been identified

- Publications cited on the Journals cover (cover images)

Publications emanating from the project: 9

Patents: 1

Trainees: Project Fellows: 7

2) TITLE: Therapeutics of Chronic Obstructive Pulmonary Disease (COPD) and Related Respiratory Disorders (TREAT)

Participating Laboratories: CSIR-IGIB, CSIR-IITR, CSIR-IICT, CSIR-IIIM, CSIR-NEIST

Core Objective:

To explore New Targets for the treatment of Chronic Obstructive Pulmonary Disease (COPD) and Related Respiratory Disorders

Most significant milestones achieved towards attainment of core objective:

Scientific Knowledge Creation about overlapping pathways between asthma and COPD which might lead to development of molecular medicine. In effort to develop therapeutics of COPD, synthetic route for amenable for diverse library of compounds generation is optimized in the participating laboratory for the synthesis of elastase 2 inhibitor.

- Screening of 57 compounds against Elastase 2 activity is completed.
- Identified 5 compounds against Elastase 2. IC50 value is determined in the nanomolar range which is better than with existing molecules. Further activity was examined in cell culture system in which PD005 show significant inhibition of elastase 2 activity. In vivo evaluation of this molecule will be conducted in participating laboratory, IGIB. To understand the molecular mechanism of COPD, the animal model of COPD is developed.

Publications: 7

Trainee: 2

3) TITLE: Neurodegenerative Diseases: Causes and Corrections (miND)

Participating Laboratories: CSIR-CCMB, CSIR- IITR, CSIR-CDRI, CSIR-NCL, CSIR-IICT

Core Objective:

To address disease pathology by uncovering the non-canonical, emerging mechanism that govern



neuro-degeneration, and apply the knowledge for development of new treatment.

Most significant milestones achieved towards attainment of core objective:

- Transcriptional regulation of pro-apoptotic proteins Bim and Puma by JNK/c-Jun and its role on neuron death in models of Alzheimer's disease.
- Cell division cycle 25A (Cdc25A) phosphatase is elevated in transgenic AD models and mediates neuron death in various neuron death paradigms.
- Fluorescence correlation microscopy (FCS) can be used to detect the early oligomers in aqueous buffer.
- FoxO3a-Bim-Caspase3 apoptotic pathway operates in β -amyloid induced astrocyte death
- Mitochondrial deficits accompany cognitive decline following single bilateral intra-cerebroventricular streptozotocin.
- Vitamin D3 stimulates GDNF to protect against MPP⁺-induced neurodegeneration.
- RNA processing body components by reducing miRNA binding to Ago2 reduces miRNA activity to induce differentiation of neuronal precursor cells.
- RNA processing body components by affecting miRNA activity prevent neuronal death.
- Thrombin and thrombin derived peptides destabilize β -amyloid aggregation.
- Novel hexapeptide interacts with tubulin and microtubules, inhibits A β fibrillation, and shows significant neuroprotection.
- Melatonin is found to synergize with L-DOPA & help to reduce L-DOPA dose.
- Transplantation recovery in terms of number of differentiated neurons into discrete brain regions to get optimal behavioral recovery.
- Garcinol is identified to scavenge \cdot OH in a Fenton-like reaction in test tubes, to reduce MPP⁺-induced ROS generation, and to enhance complex-1 activity in mitochondrial P2 fraction.
- Garcinol attenuates the striatal dopamine depletion caused by MPTP.
- Garcinol shows neuroprotective activity due to antioxidant and anti-inflammatory activity.

- Using proteomics tools relevant molecules have been identified that show association with disease biogenesis and progression in Parkinson's disease.

Publications emanating from the project: 10

PhD's: 3

Trainees: Project Fellows :5

4) TITLE: Host Interactome Analysis: Understanding the Role of Host molecules in Parasitic Infection (HOPE)

Participating Laboratories: CSIR-CDRI, CSIR-IMTECH, CSIR-CCMB, CSIR-NCL

Core Objective:

To understand the inter-molecular host parasite interactions in the infection process of Leishmania for the development of new generation drugs.

Uniqueness and Importance of Core Objective:

To address the mode of host-parasite interaction an interdisciplinary strategy involving both molecular and bio-informatic tools will be used the for development of new generation drugs.

Most significant milestones achieved towards attainment of core objective:

- PC:SA: AmB formulation has shown satisfactory results against several fungal strains in-vitro. Its in vivo activity against C. albicans has provided promising results.
- L. donovani strain AG83 genome was sequenced and the parasite was submitted to the ATCC with a repository number PRA413. A comparative genomics analysis was done to identify genetic changes leading to loss of virulence observed in the late passage parasites. The data generated will be valuable for targeting the disease specific genes in the parasite and will be an asset for leishmaniasis research.
- Simultaneous transcriptional profiling through Next Generation Sequencing (NGS) of murine peritoneal macrophage infected with virulent and non-virulent L. donovani promastigotes has revealed $\geq 12,000$ genes to be differentially expressed between the control and infected macrophages, as well as between virulent and non-virulent parasites.



- Based on the network analysis, pathway analysis and other parameters, important interacting protein node as probable drug targets for each species was identified. These are-
Leishmania donovani: ATP-dependent Clp protease subunit, heat shock protein;
Leishmania infantum: ABC1 transporter, putative;
Leishmania major: Putative NADP-dependent alcohol dehydrogenase
Publications emanating from the project: 5
PhD's: 5
Trainees: 10

- TxNIP was identified as a factor responsible for ROS-induced Insulin resistance
- Identified special roles of hypoxia and of micro RNAs in activation of satellite stem cells during muscle regeneration. In skeletal muscle, adipose triglyceride lipase(ATGL) constitute a regulatory pathway in aging muscle as a mitochondrial metabolic reserve.

5) Title: Bio-energetic Disorder: A Multi-model Approach to Monitoring and Management (BEnD)

Participating Laboratories:

INTRA - INSTITUTIONAL

Core Objective and Uniqueness:

To understand the reduced bio-energy production and mitochondrial free radical generation through an array of disease models for the development of new generation drugs against mitochondrial diseases.

Most significant milestones achieved towards attainment of core objective:

- Identified a technology to correct mitochondrial dysfunction by protein- coding RNA (US patent: Grant date: September 8, 2015; Patent No: US 9,127080B2).
- Synthesized tryptamine derivative (SEGA) to prevent gastric ulcer (US patent: Grant date: December 2, 2014; Patent no: US 8,901317B2.; European Patent: Grant date: December 16, 2015; Patent No: 2616439; Japanese Patent: Grant date January15, 2016; Patent No: 5868980).
- Carnitine palmitoyl transferase (CPT)-isoforms' ratio plays a major role diabetes type2, we showed. We have identified LRAT enzyme causing hepatic insulin resistance/steatosis and could be both biomarker as well as target for steatosis. Lastly



INDIAN INSTITUTE OF CHEMICAL BIOLOGY 12th Five-Year Plan Projects (IICB PARTICIPATING)

Sl. No.	Project Title (with Acronym)	Project Code	Nodal Institute	Nodal Scientists	Participating Scientists from IICB
1.	Competent gamete production and reproductive dysfunction (PROGRAM)	BSC 0101	CDRI	Dr. Rajender Singh	Dr. R. Ain, Dr. S.R. Dungdung, Dr. S.N. Kabir and Dr. S. S. Roy
2.	Centre for biotherapeutic Molecule discovery (BIODISCOVERY)	BSC 0120	IMT	Dr. Girish Sahni	Dr. N. Ali, Dr. S. Dutta, Dr. S. Roy, Prof. S. Roy, Dr. S. Roychoudhury, Dr. M. Sen and Dr. A. Sengupta
3.	Genomics and informatics solutions for integrating biology (Genesis)	BSC 0121	IMTECH	Dr. GPS Raghava	Dr. S. Chakraborty, Dr. C. Dutta, Dr. N. Maiti and Dr. S. Tripathy
4.	Man as a superorganism: Understanding the human microbiome (HUM)	BSC 0119	IMTECH	Dr. S. Raychaudhuri	Dr. R. Chowdhury, Dr. K. Chaudhury, Dr. S. Chakraborty, Dr. C. Dutta and Dr. S. Swarnakar
5.	Medicinal chemistry for stem cell biology and regenerative medicine (MEDCHEM)	BSC 0108	IIIM	Dr. S.D. Sawant	Dr. M. K. Ghosh
6.	Plant-Microbe and Soil Interactions (PMSI)	BSC 0117	CCMB	Dr. Ramesh Sonti	Dr. S. Chattopadhyay and Dr. S. Dutta
7.	Integrated nextgen approaches in health, disease and environmental toxicity (Indepth)	BSC 0111	IITR	Dr. Devendra Parmar	Dr. A. Bandyopadhyay, Dr. T.K. Dhar and Dr. S. Swarnakar
8.	Genomics of medicinal plants & agronomically important traits (PlaGen)	BSC 0107	NBRI	Dr. Prabodh Trivedi	Dr. S. Chattopadhyay and Dr. S. Dutta



INDIAN INSTITUTE OF CHEMICAL BIOLOGY 12th Five-Year Plan Projects (IICB PARTICIPATING)

Sl. No.	Project Title (with Acronym)	Project Code	Nodal Institute	Nodal Scientists	Participating Scientists from IICB
9.	Development of novel CSIR technology for manufacturing tailored and patent- specific bioceramic implants and biomedical devices at affordable cost (BIOCERAM) Sanc Letter No: 9/1/ES/CGCRI(1)/2012-13-PPD	ESC 0103	CGCRI	Dr. V. B. Krishna	Dr. C. Mandal, Dr. G. Suresh Kumar, Dr. A. Konar and Dr. A. Sengupta
10.	Emerging and re-emerging challenges in infectious diseases: Systems based drug design for infectious diseases (SPlenDID) Sanc. Letter no: 31-2(230)/CDRI(5)/BSC 0104/2012-13/BUDGET	BSC 0104	CDRI	Dr. R. Ravisankar	Dr. U. Bandyopadhyay
11.	Organic reactions in generating innovative and natural scaffolds (ORIGIN)	CSC 0108	IICT	Dr. S. Chandrasekhar	Dr. B. Banerji, Dr. A.K. Banerjee, Dr. P. Chattopadhyay, Dr. C. Chowdhury, Dr. I. Das, Dr. P. Jaisankar, Dr. G. Suresh Kumar and Dr. N.B. Mandal
12.	Genome Dynamics in cellular organization, differentiation and enatiostatis (GenCODE)	BSC 0123	IGIB	Dr. Souvik Maiti	Dr. G. Suresh Kumar
13.	CSIR Knowledge gateway and open source private cloud infrastructure (KNOWGATE)	ISC 0102	NISCAR	Dr. Mukesh Pund	Dr. N.C. Ghosh
14.	Epigenetic in health and disease (EpiHeD)	BSC 0118	CCMB	Dr. Rakesh Mishra	Dr. A. Bandyopadhyay and Dr. D. Biswas

Publication & Information and Planning, Monitoring & Evaluation Division

Dr. K. P. Mohanakumar (Head till September 2015), Dr. G. Suresh Kumar (Head from October 2015), Dr. Neeta V M Khalkho, Mr. Anil Kumar, Mr. Binayak Pal, Mr. Arupesh Majumder, Mrs. Purnima Chatterjee, Mr. Dipak Kumar Guin, Mr. Sankar Bhakta, Mr. Nishikanta Naskar, Mr. Pallab Mukherjee, Mr. Soumalya Sinha, Mr. Samir Thami and Mr. Bhaskar Basu

The scientific administration, supervision and thus management of different R&D activities of the institute are the primary foci of this division. The activities of this division are carried out by three major sections, e.g. [a] **Publication & Information;** [b] **Business Development Group and Patent Cell** [c] **Planning, Monitoring & Evaluation.** Therefore the success of this division mostly depends upon strong interrelation among these sections and excellent communication with R&D departments. Thorough interactions and proper attention in execution of the time-bound tasks facilitated successful management of this division. The details of the scientific management activities of the individual sections are given below separately for the reporting year.



IAS Officers Trainees at CSIR-IICB on 22nd January, 2016 for Winter Study Tour



Publication and Information Section

Dr. G. Suresh Kumar (Head), Dr. Neeta V. M. Khalkho (Incharge) Mr. Binayal Pal, Mr. Sankar Bhakta, Mr. Nishikant Naskar and Mr. Pallab Mukherjee

This section deals with diverse informational activities, publication and monitoring of reports and dissemination of information in electronic and printed forms. 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 was involved in the following wide spectrum of programmes during the report year.

- Preparation of CSIR-IICB Annual Report.
- Preparation of documents released during events.
- Preparation of Annual Plan and Budget.
- Dissemination of information to scientific milieu on relevant subjects.
- Documentation of CSIR-IICB inputs for "CSIR Annual Report 2015-16" and "CSIR Research".
- Assistance to scientists, fellows and staff members for participation in seminars, symposia and conferences.
- Maintenance of database for testing and calibration.
- Assistance for record of the proceedings of Research Council meeting.
- Preparation of a new up-to-date brochure for CSIR-IICB.
- Updated information's regarding P&I section for CSIR-IICB website.
- Public relations, advertisement and news and views forum.
- Organization display of exhibition and science news dissemination.
- Advice and comments for management of parliament queries whenever required.
- Organization of 'OPEN HOUSE' and active help for 'LAB-VISIT' programmes.

- Reply to Audit report regarding publication matters of the Institute.
- Monthly Report of CSIR-IICB for PPD, CSIR.
- Compilation of CSIR-IICB News for CSIR News Letter.
- Preparation of Performance Indicator data for CSIR-IICB.
- CSIR-IICB inputs for National survey of Biomedical laboratories and inventories sorting with.
- Polio Virus material for Ministry of Health & family Welfare, GOI.
- CSIR-IICB achievements for " CSIR Science Communication Forum".
- CSIR-IICB inputs for CSIR Plan Projects through Slides.

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 CSIR-IICB faculties. About 41 numbers of Scientist visitors delivered their lecture during 2015-16. A total list of 'Scientific Seminars' 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.

Management of Laboratory Visit for Students

On the occasion of CSIR Foundation Day celebration-2015, the members of this section have actively helped for the arrangement of 'OPEN HOUSE' programme where one hundred thirty three students eight schools/colleges/universities within and around Kolkata visited CSIR-IICB. A large number of students from seven /schools and one 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 colleges and universities from



outside Kolkata particularly from North East States. A total of (7) numbers of visits were organized throughout the year (2015-16). Lal Bahadur Shastri National Academy of Administrative (LBSNA), the pioneer training institute for civil servants has chosen CSIR-IICB, Kolkata for a Winter Study Visit organized for Officers Trainees 2015 batch. CSIR-IICB is welcomed a batch of 18 IAS Officers Trainees on Friday, January 22, 2016 for Winter Study Tour “ Bharat Darshan” .

Art & Photography

Art Section 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's achievement. The section also participated in preparing artwork and cover design for Hindi Day and Hindi Report. This section has also carried out work for decoration of floor & institute during various scientific and official programmes. The achievement of this section is the total design & e-publication of CSIR-IICB Annual Report for the year 2014-15. Photography Section has been successfully covering every event taking place in the institute. The section is continuously supplying all the photos for publications, Annual Reports, Journals and other related documents. Besides these they are also assisting the scientists of the institute. Apart from that they also handled photographs of scientific activities and experiment slides for publication in different international journals.



B.Sc. Environmental Biotechnology & Biochemistry,
St. Anthony's College, Shillong, 4.12.15



CSIR-IICB Scientist Explaining Experiment to
Visiting Students



M.Sc. Biotechnology, St. Anthony's College,
Shillong, 13.4.15



M.Sc. Biotechnology, Sambalpur University, 14.1.16



M.Sc. Zoology, Gauhati University, 22.3.16



M.Sc. Environmental Science,
Calcutta University, 4.11.15



PhD. Scholar Demonstrating Experiment to
Visiting Students



B.Sc. Environmental Biotechnology & Biochemistry,
St. Anthony's College, Shillong, 4.12.15

Business Development Group and Patent Cell (BDG)

Dr. G. Suresh Kumar (Head), Mr. Anil Kumar, Mr. Arupesh Majumdar, Mr. Deepak Kumar Guin and Mr. Bhaskar Basu

CSIR-IICB has excelled in both basic and applied aspects of chemical biology. Today, by its mandate, CSIR-IICB is engaged in research on diseases and certain biological problems of global interest. It is conducting basic research on infectious diseases, specifically leishmaniasis and cholera, along with the development of technologies for the diagnosis, immune-prophylaxis, and chemotherapy of various diseases. Over the past years, CSIR-IICB has generated various successful products.

CSIR-IICB is putting emphasis on quality basic research having applied potential and is looking forward to a successful Industry-Institute liaison towards closer partnership. The Intellectual Property Management and Business Development Group is the technology transfer arm of CSIR-IICB facilitating protection of institute's intellectual property and marketing inventions/know-how's generated. It plays a major role in Human Resource Development by training PG and Ph.D. students.

The group facilitates to maintain strong relationships with the Industries in India and abroad with an aim to utilize the technologies and opportunities coming out of the state of art research and development activities.

Vision

We are dedicated to support and encourage the researchers, with an aim to turn science into commercial products for societal gain.

Goals & Objectives

- To protect, promote and market commercially promising inventions and know-how developed at CSIR-IICB.
- To scout for the "right fit" for each intellectual property available.
- To deliver, manage, and optimize knowledge transfer to domestic and global market through multiplicity of business development activities and services.

Major Activities of Business Development Group:

- Liaison with industries and R&D institutions
- Licensing / Transfer of in house Technologies
- Utilization of Knowledge base / expertise developed in house
- Business and Partnership Negotiations
- Assistance for Technical Services
- Negotiation of Collaborative/Interdisciplinary Research, Agreements and MoUs



MoU with the NRDC to promote entrepreneurship



Intellectual Property Management Cell

Dr. G. Suresh Kumar (Head), Mr. Anil Kumar, Mr. Arupesh Majumdar, Mr. Deepak Kumar Guin and Mr. Bhaskar Basu

CSIR-Indian Institute of Chemical Biology is continuously developing its knowledgebase through world class science and innovation. Those having potential for commercialization are protected through patents and copyrights by its Intellectual Property Management (IPM) cell. The IPM cell of CSIR-IICB, in co-ordination with Innovation Protection 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 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 the prescribed time-limit. During the reporting period, a large number of correspondences were made with IPU, CSIR, a significant number of responses were conveyed on patent applications in India and abroad interacting with CSIR-IICB scientists and inventors regarding patent queries to provide necessary information to obtain productive results. The IPM Cell always extended co-operation to the inventors, 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 and Project Monitoring &

Evaluation Division of CSIR-IICB for technologies developed; patents filed and granted; sent information on patent and technology to IPU, CSIR regarding Audit and Parliamentary Question; prepared year wise documents on total Patents of CSIR-IICB filed and granted.

Some of the significant work done are as follows:

1. Reviewing renewal and lapse of Indian and Foreign patents in force and recommendations prepared for each patent sent to IPU, CSIR.
2. Commercial Working Report for 13 Indian Patents of CSIR-IICB prepared and sent to IPU, CSIR.
3. Response to IPU, CSIR regarding IPER, IPRP, OA, Designated Countries and other queries relating to patent application and filing.
4. Year wise documents prepared on total Patents of CSIR-IICB filed and granted.
5. Information on patent and technology transfer to IPU, CSIR regarding Audit and Parliamentary Questions.
6. Maintenance of CSIR-IICB Patent Database to keep it up-to-date.

During reporting period, the performance at a glance of IPM Cell is as follows:

Patents Filed:

International Patents Filed	...	3
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Patents Granted:

Indian Patents Granted	...	1
International Patents Granted	...	8

Copyright Application Filed:

Indian Copyright Application	...	1
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PATENTS FILED ABROAD

Sl.No.	Title	Inventors	Country	Comp. Filing Date
1.	A DNA VACCINE FORMULATION IN CATIONIC LIPOSOME VEHICLE USEFUL FOR MAXIMIZING VACCINE POTENCY FOR LEISHMANIASIS	NAHID ALI, AMRITA DAS	WORLD	28/Apr/2015
2.	A KIT USEFUL FOR MEASURING A NON-RECOMBINANT MEMBRANE ANTIGEN (LAG) IN THE URINE SAMPLE	NAHID ALI, SARFARAZ AHMAD EJAZI	WORLD	29/Jun/2015
3.	A HEXAPEPTIDE INTERACTS WITH TUBULIN/MICROTUBULE AND EXHIBITS SIGNIFICANT NEUROPROTECTION AGAINST A β TOXICITY THEREOF	SURAJIT GHOSH, ATANU BISWAS, BATAKRISHNA JANA, SASWAT MOHAPATRA, SUBHAS CHANDRA BISWAS, SURAIYA SALEEM, PRASENJIT MONDAL, ANINDYASUNDAR ADAK, SUBHAJIT GHOSH, ABHIJIT SAHA, DEBMALYA BHUNIA	USA	07/Mar/2016

PATENTS GRANTED IN INDIA

Sl.No.	Title	Inventors	Grant Date	Patent No.
1.	COMPLETE SOLUBLE PROTEIN ANTIGEN AS VACCINE AND THERAPEUTICS AGAINST KALA-AZAR	DE TRIPTI, BHAUMIK SIDDHARTHA KUMAR	27/Jul/2015	267639



PATENTS GRANTED ABROAD

Sl. No.	Title	Inventors	Country	Grant Date	Patent No.
1.	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	USA	21/Jul/ 2015	9085559
2.	BIOMARKER FOR VALVULAR HEART DISEASE	ARUN BANDYOPADHYAY, TANIMA BANERJEE, SOMADITYA MUKHERJEE, SANTANU DUTTA	SOUTH AFRICA	26/Aug/ 2015	2013/02538
3.	COMPOSITIONS AND METHODS FOR DELIVERY OF PROTEIN-CODING RNAS TO CORRECT MITOCHONDRIAL DYSFUNCTION	ADHYA SAMIT	USA	08/Sep/ 2015	9127080
4.	TRIAZINE-ARYL-BIS-INDOLES AND TRYPTAMINE DERIVATIVES, THEIR PREPARATION AND THEIR USE IN GASTROPATHY	BANDYOPADHYAY UDAY, PAL CHINMAY, BINDU SAMIK, ADHIKARI SUSANTA SEKHAR	EUROPE	16/Dec/ 2015	2616439
5.	TRYPTAMINE DERIVATIVES, THEIR PREPARATION AND THEIR USE IN GASTROPATHY	BANDYOPADHYAY UDAY, PAL CHINMAY, BINDU SAMIK, ADHIKARI SUSANTA SEKHAR	JAPAN	15/Jan/ 2016	5868980



PATENTS GRANTED ABROAD

Sl. No.	Title	Inventors	Country	Grant Date	Patent No.
6.	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	CHINA	20/Jan/ 2016	CN 102666529 B
7.	INHIBITORS OF NUCLEAR FACTOR - KAPPA B (NF- B) AND INFLAMMATORY CYTOKINES	SANTU BANDYOPADHYAY, BIKAS CHANDRA PAL, PARASURAMAN JAISANKAR, SIDDHARTHA ROY, JAYASHREE BAGCHI CHAKRABORTY, INDRANI CHOUDHURY MUKHERJEE, SANJIT KUMAR MAHATO, ADITYA KONAR, SRABANTI RAKSHIT, LABANYA MANDAL, DIPYAMAN GANGULY, KAUSIK PAUL, ANIRBAN MANNA, JAYARAMAN VINAYAGAM, CHURALA PAL	USA	22/Mar/ 2016	9,290,473
8.	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	EUROPE	23/Mar/ 2016	2417129

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Sl. No.	Title	Inventors	Filing Date
1.	ABPGA-BACTERIAL PAN GENOME ANALYSIS PIPELINE	NARENDRAKUMAR M. CHAUDHARI, VINOD KUMAR GUPTA, CHITRA DUTTA	09/Feb/ 2016



Project Monitoring & Evaluation Section

Dr. G. Suresh Kumar (Head), Mr. Soumalya Sinha, Mr. Samir Thami and Mrs. Purnima Chatterjee

PME set up in August, 2009 effectively manages the Institute's plan and non-plan projects, grant-inaid, sponsored and collaborative R&D projects. The Division maintain liaison with Principal Investigators-Finance section-Purchase Section and the Grant Giving Agency. PME provides proper logistic support for the management, maintenance and monitoring of Institute's plan and non-plan projects and externally funded projects. PME will help in effective, timely and successful implementation of the institute's commitments. PME is also entrusted with appropriate dissemination of information regarding ongoing and completed projects. PME of CSIR-IICB like other CSIR laboratories is actively involved in the preparation and timely maintenance of databases for all intramural and extramural research projects, project expenditure monitoring of all projects, monitoring ECF of the Institute, preparation of responses to Parliamentary questions in relation to the activities of the Institute, dissemination of information on all relevant National & International Research Program requests for applications, including fellowships and maintenance of mandatory registration with such agencies, and liaison with all grant giving agencies, make awareness among scientists regarding terms & conditions of relevant funding agencies, responding to various audit queries in relation to both ongoing and completed projects, participation in Institute's annual plan, budget preparation expenditure status, monitoring the receipts of cheques as well as online transfer of fund by the sponsors against the project granted, and request for such fund, and proper record keeping of the projects, regular interactions with finance division regarding the expenditure carried out against the projects in each and every month and recorded in the concerned project, and obtaining approval of projects for submission to external funding agencies from competent authorities (RC, Director, MC, etc.) Twelve projects have been newly sanctioned during the financial year 2014 - 15. Details of extramural project activities (completed, sanctioned and currently progressing) are provided in a separate page as 'External Funding',



COMPLETED PROJECTS DURING 2015-16

Sl. No.	Principal Investigator	Project Title	Project Code	Funding Agency
1.	Dr. Suman Khowala	Lignocellulolytic enzymes production by the filamentous fungus <i>Termitomyces clypeatus</i> using low cost agro wastes	GAP - 289	DBT
2.	Dr. Asish K Sen (Jr.)	Synthesis and Characterization of Receptor Specific Mannose/Manno-oligosaccharides Linked Miltefosine Derivatives; Biological Evaluation of their Antileishmanial Activity	GAP - 290	DBT
3.	Dr. K. P. Mohanakumar	Effect of hypercholesterolemia on brain function: Effects of indigenous plants components of North-East India	GAP - 293	DBT
4.	Dr. Mrinal K. Ghosh	Crosstalk between Stat3 and Beta-catenin: Understanding the Mechanisms to Counteract Prostate Cancer	GAP - 297	SERB, DST
5.	Dr. Nakul Chandra Maiti	β -Synuclein and Tau Interaction : Implication on Neurodegenerative Diseases	GAP - 299	DBT
6.	Dr. Suman Khowala	Protein stabilization and prevention of Protein aggregation by fugal sucrose from <i>Termitomyces clypeatus</i> an application in biotechnology and biomedical research	GAP - 303	DBT
7.	Dr. Malini Sen	Role of Wnt5a Signaling in the Initiation and Progression of Sepsis	GAP - 304	DBT
8.	Dr. Hemanta K. Majumder	A Joint INDO-BRAZIL Project to decipher biological processes of organisms causing diseases of clinical importance in both the countries	GAP - 298	DST
9.	Dr. Debasish Bhattacharya	Finger-printing and Biochemical Characterization of the Drug Sterodin	SSP - 314	Union Drug Company
10.	Dr. Debasish Bhattacharya	Growth Inhibition and Destabilization of B- Amyloid Aggregate by Protease Derived Peptides	GAP - 295	DST
11.	Dr. Chitra Mandal	Evaluation of a blood-based antigen detection assay by quantitating unique sialoglycoprotein specifically induced on erythrocytes for early diagnosis and monitoring patients with Indian Visceral Leishmaniasis in two referral centers	GAP - 294	ICMR



SANCTIONED AND IMPLEMENTED PROJECTS (2015-16)

Sl. No.	Principal Investigator	Project Title	Sanction Order No.	Project Code No.	Funding Agency
1.	Dr. Snehasikta Swarnakar	Role of matrix metalloproteinases and heat shock proteins in stress induced gastric cell damage: Effect of antioxidants thereon	CC R&D (TM)/81/48222/LS RB-287/EPB/2014	GAP - 329	LSRB-DRDO, Govt. of India
2.	Dr. Sanjay Dutta	Discovery of RNA binding ligands- Targeting Hepatitis C virus RNA	BT/PR6922/BRB/10/1144/2012	GAP - 330	DBT, Govt. of India
3.	Dr. Mita Chatterjee Debnath	In vitro and in vivo evaluation of ^{99m} Tc(CO) ₃ -labeled RGD conjugated bioreductive pharmacophore and nucleoside analogue for potential use as tumor targeted SPECT	SB/SO/HS-009/2014	GAP - 331	SERB, DST, Govt. of India
4.	Dr. Ranjan Jana	Molecular Diversity Through Cascade C-H Activations	SERB/F/3779/2015-16	GAP - 332	SERB, DST, Govt. of India
5.	Dr. Arindam Talukdar	Probing endosomal toll-like receptor biology using novel small molecule antagonists	SERB/F/3747/2015-16	GAP - 333	SERB, DST, Govt. of India
6.	Dr. Pijush K. Das -PI Dr. Uday Bandyopadhyay -Co-PI	An insight into the role and regulation of mitochondrial inner membrane uncoupling protein 2 in manipulating host-conductive oxidant-derived macrophage defense mechanism	SERB/F/3923/2015-16	GAP -334	SERB, DST, Govt. of India
7.	Dr. Biswadip Banerji	Targeting HSP-90 as cancer therapy: Design and synthesis of mathanine-derived Second Generation lead molecules.	EMR/2015/001229	GAP-336	SERB DST, Govt. of India
8.	Dr. Krishna Das Saha	Modulatory role of Quercetin on radiation-induced oxidative stress in human colorectal carcinoma cells: Assessment of possible role of certain trace elements.	UGC-DAE-CSR-KC/CRS/15/IOP/09/0645/0660	GAP-338	UGC-DAE



ONGOING PROJECTS DURING 2015-16

Sl. No.	Principal Investigator	Project Title	Sanction Order No.	Project Code No.	Funding Agency
1.	Dr. Asish K. Sen (Jr.)	Synthesis and Characterization of Receptor Specific Mannose/Manno-oligosaccharides Linked Miltefosine Derivatives; Biological Evaluation of their Antileishmanial Activity	BT/PR4243/MED/29/339/2011	GAP - 290	DBT
2.	Dr. K. P. Mohanakumar	Effect of hypercholesterolemia on brain function: Effects of indigenous plants components of North-East India	BT/230/NE/TBP/2011	GAP - 293	DBT
3.	Dr. Rupasri Ain	Studies on trophoblast and natural killer cell interaction at the maternal-fetal interface	SB/SO/AS-114/2012	GAP - 301	SERB, DST
4.	Dr. Nukul Chandra Maiti	β -Synuclein and Tau Interaction: Implication on Neurodegenerative Diseases	BT/PR14633/BRB/10/872/2010	GAP - 299	DBT
5.	Dr. Malini Sen	Role of Wnt5a Signaling in the Initiation and Progression of Sepsis	BT/PR7106/MED/29/639/2012	GAP - 304	DBT
6.	Dr. Mita Chatterjee Debnath	Evaluation of the therapeutic efficacy of liposomal and nanoparticulated flavonoids in combating oxidative hepatocellular degeneration by nuclear imaging technology using Tc-99m radiopharmaceuticals	2013/35/25/BRNS	GAP - 305	BRNS, DAE
7.	Dr. Subrata Adak	Examine mechanism of electron transfer Leishmania major (LmAPX) by site directed mutagenesis	BT/HRD/NBA/34/01/2012(iv)	GAP - 306	DBT
8.	Dr. Partha Chakrabarti	Octreotide derivative modified lipid nanoparticles: Preparation, Radiolabeling & applications a tumor radiopharmaceuticals	2013/35/44/BRNS	GAP - 307	BRNS, DAE
9.	Dr. Krishnananda Chattopadhyay	Experimental and computational study of the aggregation pathway of alpha synuclein	SB/YS/LS-65/2013	GAP - 308	SERB, DST



ONGOING PROJECTS DURING 2015-16

Sl. No.	Principal Investigator	Project Title	Sanction Order No.	Project Code No.	Funding Agency
10.	Dr. Ramalingam Natarajan	Metal-Organic Frameworks (MOFs) from Bile Acid Derivatives as Carriers for Drug Delivery	SB/S1/IC-26/2013	GAP - 310	SERB, DST
11.	Dr. Indrajit Das	N-Heterocyclic Carbene Catalyzed Diastereoselective Synthesis of Substituted Cyclohexanones from Modified Carbohydrates: Application to the Total Synthesis of Conduramines and Phenanthridone Alkaloids	SB/FT/CS-105/2012	GAP - 310	SERB, DST
12.	Dr. Partha Chakraborty	Insulin and Nutrient Mediated Regulation of Adipocyte Metabolism	SB/SO/HS/0064/2013	GAP - 311	DST
13.	Dr. Amitava Sengupta	Polycomb repressive complex in Myelodysplastic syndromes	SB/SO/HS-053/2013	GAP 313	SERB, DST
14.	Dr. Hemanta K. Majumder	A Joint INDO-BRAZIL Project to decipher biological processes of organisms causing diseases of clinical importance in both the countries	DST/INT/Brazil/RP O 01/2009/2	GAP - 298	DST
15.	Dr. Krishna Das Saha	Studies on anticancer activities of extracts (Bromelain and Peroxidase) of different pineapple (Ananas comosus)	BT/472/NE/TBP/2013	GAP 312	DBT
16.	Dr. Debasish Bhattacharya	Finger-printing and Biochemical Characterization of the Drug Sterodin		SSP - 314	Union Drug Company
17.	Dr. Sucheta Tripathy	Whole Genome and Transcriptome sequencing of selected Indian Cyanobacterial species for candidate gene discovery for bio-metabolites	NBAIM/AMAAS/2014-15	GAP - 315	ICAR
18.	Dr. Rupasri Ain	Transgenic Over-Expression of NOSIP in Mice and Pregnancy - Induced Hypertension	BT/PR9113/MED/97/134/2014	GAP - 316	DBT
19.	Dr. P. Jaisankar	Identification of eight obligately halophilic cyanobacteria of the Sundarbans and molecular characterization of antimicrobial compounds therefrom	MoES-2/DS/6/2007 PC-IV	GAP - 318	Ministry of Earth Sciences, Govt. of India
20.	Dr. Debabrata Biswas	Functional characterization of human DBC1 complex in eukaryotic transcriptional regulation and leukemic transformation	IA/I/14/1/1501287	GAP - 319	Wellcome Trust, London/DBT



ONGOING PROJECTS DURING 2015-16

Sl. No.	Principal Investigator	Project Title	Sanction Order No.	Project Code No.	Funding Agency
21.	Dr. Surajit Ghosh	Bimimetic approach to measure in-situ generated force from nucleated microtubules on 2D micropattern surfaces by atomic force microscopy	SR/SO/BB-0102/2012	GAP - 320	DST
22.	Dr. Indu Bhushan Deb	Iron Catalysed directing group assisted C-H bond functionalization reaction	SB/FT/CS-016/2013	GAP - 321	SERB, DST, Govt. of India
23.	Dr. Aditya Konar	Influence of corneal nerve regeneration on wound healing and its therapeutic modulation	SB/SO/HS-054/2013(B)	GAP - 322	DST, Govt. of India
24.	Dr. Aditya Konar	Delivery of drugs and cells to the cornea using silk protein – A novel therapeutic approach	BT/PR12304/TDS/121/2/2014	GAP - 323	Central Silk Board, Govt. of India
25.	Dr. Sujoy Mukherjee	Investigating the dynamic interactions of a toxin- antitoxin module of Mycobacterium tuberculosis by NMR spectroscopy	SB/SO/BB-106/2013	GAP - 324	SERB, DST
26.	Dr. Malini Sen	Mechanism of metabolic regulation by Wnt-Induced secreted protein - 3 (WISP3)	SB/SO/BB-106/2014	GAP - 325	SERB, DST
27.	Dr. Rupasri Ain	Transgenic Over-Expression of Nostrin in Mice and Pregnancy - Induced Hypertension	5/7/909/15-RCH	GAP - 326	ICMR
28.	Dr. Jayati Sengupta	Processing of the Nascent Polypeptide Chain on Mycobacterium 70S Ribosome: Structural and Functional Studies	SB/SO/BB-0025/2014	GAP - 327	SERB, DST
29.	Dr. Saumen Datta	Structural and Functional Elucidation of T3SS Effectors with or without their Cognate Chaperone/Target Proteins from Pathogenic Bacteria	SB/SO/BB-36/2014	GAP - 328	SERB, DST
30.	Dr. Snehasikta Swarnakar	Role of matrix metalloproteinases and heat shock proteins in stress induced gastric cell damage : Effect of antioxidants thereon	CC R&D (TM)/81/48222/LSRB-287/EPB/2014	GAP - 329	LSRB-DRDO, Govt. of India
31.	Dr. Sanjay Dutta	Discovery of RNA binding ligands- Targeting Hepatitis C virus RNA	BT/PR6922/BRB/10/1144/2012	GAP - 330	DBT, Govt. of India



ONGOING PROJECTS DURING 2015-16

Sl. No.	Principal Investigator	Project Title	Sanction Order No.	Project Code No.	Funding Agency
32.	Dr. Mita Chatterjee Debnath	In vitro and in vivo evaluation of $^{99m}\text{Tc}(\text{CO})_3$ -labeled RGD conjugated bio-reductive pharmacophore and nucleoside analogue for potential use as tumor targeted SPECT	SB/SO/HS-009/2014	GAP - 331	SERB, DST, Govt. of India
33.	Dr. Ranjan Jana	Molecular Diversity Through Cascade C-H Activations	SERB/F/3779/2015-16	GAP - 332	SERB, DST, Govt. of India
34.	Dr. Arindam Talukdar	Probing endosomal toll-like receptor biology using novel small molecule antagonists	SERB/F/3747/2015-16	GAP - 333	SERB, DST, Govt. of India
35.	Dr. Pijush K. Das -PI Dr. Uday Bandyopadhyay -Co-PI	An insight into the role and regulation of mitochondrial inner membrane uncoupling protein 2 in manipulating host-conductive oxidant-derived macrophage defense mechanism	SERB/F/3923/2015-16	GAP - 334	SERB, DST, Govt. of India
36.	Dr. Krishna Das Saha	Mechanistic study of effect of Spargulin-A extracted from <i>Glinus oppositifolius</i> on macrophages to raise anti-leishmanial host defense.	EMR/2015/001674	GAP-335	DST, Govt. of India
37.	Dr. Biswadip Banerji	Targeting HSP-90 as cancer therapy: Design and synthesis of mathanine-derived Second Generation lead molecules.	EMR/2015/001229	GAP-336	SERB DST, Govt. of India
38.	Dr. Krishna Das Saha	Modulatory role of Quercetin on radiation-induced oxidative stress in human colorectal carcinoma cells: Assessment of possible role of certain trace elements.	UGC-DAE-CSR-KC/CRS/15/IOP/09/0645/0660	GAP-338	UGC-DAE
39.	Dr. Chitra Mandal	Evaluation of anti-leukemic and immunogenicity properties of engineered <i>Escherichia coli</i> asparaginase - II for the treatment of acute lymphatic leukemia in preclinical model	SB/SO/HS- 203/2013(B)	GAP-339	SERB, GOVT. of India
40.	Dr. Chinmoy Chowdhury	Study of Anti-leukemic and Anti-oxidant potential of some wild Edible Mushrooms of West Bengal: Leading to chemical identification of the lead Molecules	162/BT/RD-2/2013	GAP- 340	DBT, Govt. of West Bengal

ISTAD SECTION

Activities of this section were supervised by Dr. K P. Mohanakumar, Chief Scientist, with the active help Mrs. Shapoo Sengupta. The foreign visit of CSIR-IICB scientists during the reporting year is listed as 'Deputation Abroad'.

Sl. No.	Year	Name of official & Designation	Purpose of visit	Duration of foreign visit	Amount (in Rupees) of Tour Advance (TA) drawn	Total expenditure incurred on foreign visits along with source of funding (amount in Rupee)			Dt. of submission of TA bill	Whether any bond etc. obtained from official before going abroad?	Whether Official Returned to India and joined duty in time after foreign visit?	Whether official is still working in CSIR? If not, provide details.
						Own grant	Other Govt. Deptt	Private Firm (Foreign/Indian)				
1	2	3	4	5	6	7	8	9	10	11	12	13
1	2015	Dr. S. Swarnakar, Principal Sct.	For attending a meeting on collaborative work on advanced materials design of drug at the National Institute for Material Science Tsukuba, Ibaraki, Japan	15.06.2015 to 26.06.2015		NIMS, Network Project Head	BSC 0111			NO	YES	Still working
2	2015	Dr. S. Chattopadhyay, Principal Sct.	For delivering a talk at the '3rd International Symposium on Plant Signaling Behavior' at the Univ. Paris, Diderot-Paris, France	29.06.2015 to 02.07.2015		Organizers, DBT				NO	YES	Still working
3	2015	Dr. P. Jaisankar, Sr. Principal Sct.	To attend 'INSA International Collaboration/ Exchange Programme - 2015', Taiwan	04.07.2015 to 19.07.2015		Network Project (TREAT- BSC 0116)				NO	YES	Still working
4	2015	Dr. K.N. Chattopadhyay, Principal Sct.	To participate in a workshop jointly organized by the Dept. Of Science and Technology, India (DST) and the Academy of Finland	28.10.2015 to 30.10.2015		DST and the Academy of Finland				NO	YES	Still working
5	2015	Dr. Dipyaman Ganguly, Sr. Sct.	To attend the Sun Yat-sen University International Young Scholars Forum	17.12.2015 to 20.12.2015		Organizers and his Ramanujan Fellowship				NO	YES	Still working
6	2016	Dr. Rupak K Bhadra, Sr. Principal Sct.	To attend the US-Japan Cooperative Medical Sciences Programme, USA	11.01.2016 to 15.01.2016		Organizers				NO	YES	Still working
7	2016	Dr. Amitava Sengupta, Sr. Sct.	For a poster presentation in the Keystone Symposium on 'Chromatin and Epigenetics (C2)' at Whistler Conference Centre, Whistler, Canada	20.03.2016 to 24.03.2016		DBT-Ramalingaswamy Fellowship				NO	YES	Still working



COLLOQUIUM FROM APRIL 2015 TO MARCH 2016

1. Speaker Dr. Malini Sen, Senior Scientist, CSIR-Indian Institute of Chemical Biology, Kolkata- 700032.
 Title "The Many Faces of Wnt and Wisp : Evolving Concepts in Relation to Disease."
 Date 23rd April, 2015 at 4.00 P.M., CSIR-IICB Auditorium.
2. Speaker Dr. Chitra Mandal, Acting Director & Outstanding Scientist
 CSIR-IICB, Kolkata- 700 032.
 Title "A journey to decipher the mystery of glycosylation in understanding disease biology."
 Date 25th June, 2015 at 4.00 P.M., CSIR-IICB Auditorium.
3. Speaker Dr. K.P. Mohanakumar, Chief Scientist & Prof. of Biological Sciences, AcSIR, Division
 of Cell Biology & Physiology, CSIR-IICB, Kolkata - 700 032.
 Title "CONTROL YOUR MOTION "
 Date 9th July, 2015 at 4.00 P.M., CSIR-IICB Auditorium.
4. Speaker Dr. Padma Das, Principal Scientist, CSIR-IICB, Kolkata - 700 032.
 Title A journey with Cancer : "The Emperor of all Maladies"
 Date 27th August, 2015 at 4.00 P.M., CSIR-IICB Auditorium.
5. Speaker Prof. Brett Tyler, Director, Center for Genome Research and Bio-computing, Oregon
 Genome Center, Oregon State University, USA.
 Title "Using genomics and bioinformatics to understand how oomycete and fungal
 pathogens suppress host immunity."
 Date 7th September, 2015 at 11.00 A.M., CSIR-IICB Auditorium.
6. Speaker Dr. Samit Chattopadhyay DIRECTOR, CSIR-IICB.
 Title "Dysregulation of Alternative Splicing (AS) of CD44 promotes cancer cell metastasis."
 Date 18th September, 2015 at 4.00 P.M., CSIR-IICB Auditorium.
7. Speaker Prof. Sankar Ghosh, Chair, Silverstein and Hutt Family
 Professor of Microbiology & Immunology, Columbia University, USA.
 Title "Regulation of Inflammation and Immunity."
 Date 17th November, 2015 at 4.00 P.M., CSIR-IICB Auditorium.
8. Speaker Dr Ranjan Sen, Staff Scientist, Centre for DNA Fingerprinting and Diagnostics
 (CDFD), Hyderabad.
 Title " Rho-dependent transcription termination in bacteria: from mechanism to
 physiology."
 Date 3rd March, 2016 at 4pm, Prof. J.C. Ray Auditorium.



SEMINAR FROM APRIL 2015 TO MARCH 2016

1. Speaker Dr. Tanmay Majumdar, Georgia Regents University, Augusta, Georgia, USA.
 Title "Impact of commensal microbial consortium in the diversity of tolerance vs
 immunity in infectious diseases."
 Date 13.04.2015, at 3.30 p.m., 1st floor Seminar Room.
2. Speaker Dr. Sabyasachi Das, Department of Pathology & Laboratory Medicine, Emory
 University, Atlanta, GA 30322.
 Title "Evolution of Immunome composition in adaptive immunity."
 Date 16.04.2015, at 3.30 p.m., 1st floor Seminar Room.
3. Speaker Dr. Sanjoy Samanta, Department of Molecular, Cell & Cancer Biology, University
 of Massachusetts Medical School, Worcester, MA, USA
 Title "Insulin-like Growth Factor-2 mRNA Binding Protein 3 (IMP3) and its Role in Breast
 Cancer Stem Cell Function."
 Date 01.05.2015, at 3.30 p.m., 1st floor Seminar Room.
4. Speaker Dr. Pritha Bhattacharjee, Assistant Professor, Department of Environmental
 Science,
 University of Calcutta.
 Title "Arsenic in Ground Water: Health effects, Susceptibility and Mitigation."
 Date 08.05.2015, at 3.30 p.m., 1st floor Seminar Room.
5. Speaker Dr. Somdeb Bose D, Assistant Professor, School of Biomedical Engg., IIT (BHU),
 Varanasi.
 Title "Journey of a decade on Leishmania parasite biology, Mycobacteria-Macrophage
 inter-actions and role of Coronin 1 in learning and memory related processes."
 Date 09.06.2015, at 3.30 p.m., Prof. B.K. Bacchawat Hall 1st floor Seminar Room.
6. Speaker Dr. Angshumoy Roy, M.D., PH.D., Assistant Professor of Pathology, Immunology
 and Pediatrics, Baylor College of Medicine, Houston, Texas, USA.
 Title "Clinical applications of genomic sequencing in childhood cancers."
 Date 05.08.2015, at 4.00 p.m., Prof. B.K. Bacchawat Hall 1st floor Seminar Room.
7. Speaker INSA LOCAL CHAPTER LECTURE
 Prof Bruce P. Lanphear, MD, Scientist, Faculty of Health Sciences, Simon Fraser
 University, Vancouver, BC, Canada.
 Title "Children's Health, Nutrition and Environment."
 Date 08.09.2015, at 4.00 p.m., Prof. B.K. Bacchawat Hall 1st floor Seminar Room.
8. Speaker Dr. Andrew Peterson, Senior Director Genentech, California.
 Title "Genetics of Human Diseases."
 Date 11.09.2015, at 5.00 p.m., Prof. B.K. Bacchawat Hall 1st floor Seminar Room.



SEMINAR FROM APRIL 2015 TO MARCH 2016

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| 9. | Speaker | Dr. Tanmoy Mondal, Department of Medical Genetics, Institute of Biomedicine, Sahlgrenska Hospital?, Gothenburg University, Sweden. |
| | Title | "Long non-coding RNA mediated epigenetic regulation in disease and development." |
| | Date | 09.10.2015, at 4.00 p.m., Prof. B.K. Bacchawat Hall 1st floor Seminar Room. |
| 10. | Speaker | Dr. Shubhra Majumder, Research Associate, Department of Molecular Genetics, The Ohio State University. |
| | Title | "Identifying novel molecular mechanisms regulating ciliogenesis in mammalian cells and in Naegleria gruberi." |
| | Date | 29.10.2015, at 4.00 p.m., Prof. B.K. Bacchawat Hall 1st floor Seminar Room. |
| 11. | Speaker | Prof. Dieter Bromme, professor, oral and biological sciences, Dept. of Biochemistry and Molecular Biology, Vancouver, BC Canada. |
| | Title | "Ectosteric inhibitors : a novel class of substrate specific protease inhibitors." |
| | Date | 02.11.2015, at 4.00 p.m., Prof. B.K. Bacchawat Hall 1st floor Seminar Room. |
| 12. | Speaker | Dr. Sanjan K. Das, Ph.D., Imperial Colleague, London, |
| | Title | "Translational Molecular Medicine - an engineered platform, Presenting research carried out at The Universities of Oxford and Sheffield, UK." |
| | Date | 03.11.2015, at 4.00 p.m., Prof. B.K. Bacchawat Hall 1st floor Seminar Room. |
| 13. | Speaker | Dr. Abhijit De, Principal Investigator, Molecular Functional Imaging Lab, ACTREC, Tata Memorial Centre, Navi Mumbai. |
| | Title | "In vivo Molecular Imaging at the Chemical biology interface." |
| | Date | 16.11.2015, at 4.00 P.M., J.C. Ray Auditorium. |
| 14. | Speaker | Dr. Arnob Dutta, Stowers Institute for Medical Research, USA. |
| | Title | "Switches within theSwi/Snf chromatin remodeler regulate its functions." |
| | Date | 07.12.2015, at 4.00 P.M., 1st floor Seminar Room . |
| 15. | Speaker | Dr. Pinki Chowdhury, Department of Internal Medicine (Hematology-Oncology), University of Michigan Cancer Center, Ann Arbor, Michigan. |
| | Title | "Target TopBP1: a convergent point of multiple oncogenic pathways, for cancer treatment." |
| 16. | Date | 09.12.2015, at 4.00 P.M., Prof. B.K. Bacchawat Hall (1st Floor). |
| | Speaker | Dr. Debashis Mitra, National Centre for Cell Science, Pune. |
| | Title | "Novel molecules and strategies in the fight against HIV/AIDS." |
| | Date | 18.12.2015, at 4.00 P.M., Prof. J.C. Ray Auditorium. |
| 17. | Speaker | Dr. Hem Chandra Jha, Dept. of Microbiology and Tumor Virology Program, AbramsonCancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA. |
| | Title | "Role of Gammaherpesviruses in cancer progression." |
| | Date | 4th January, 2016, Monday at 4pm, Prof. B.K. Bacchawat Hall (1st Floor). |



SEMINAR FROM APRIL 2015 TO MARCH 2016

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| 18. | Speaker | Dr. Vivek Sharma, Khorana Nirenberg Fellow, National Cancer Institute, NIH, USA. |
| | Title | "Linc'ing' RNA to DNA repair." |
| | Date | 6th January, 2016 at 4pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 19. | Speaker | Dr. Dipankar Bhandari, Department of Biochemistry, Max Planck Institute for Developmental Biology, Tübingen, Germany. |
| | Title | "Nanos family RNA binding proteins recruit the CCR4-NOT complex to repress translation of their target mRNAs." |
| | Date | 18th January, 2016 at 4pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 20. | Speaker | Dr. Shubhasis Halder, University of California, School of Engineering, USA. |
| | Title | "Mechanism of Chaperonin-Assisted Protein Folding: Investigation at Single Molecular Resolution." |
| | Date | 27th January, 2016 at 4pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 21. | Speaker | Dr. Dipanjan Bhattacharya, Singapore-MIT Alliance for Research and Technology Center, Singapore. |
| | Title | "Mechanobiological understanding of tissue patterning during Zebrafish neurulation." |
| | Date | 28th January, 2016 at 4pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 22. | Speaker | Prof. Virinder S Parmar, Institute of Nanoscience and nanomedicine, University of Massachusetts, USA |
| | Title | "Biocatalytic Synthesis of Novel Polymeric Nanoparticles: Applications in Health and Industrial Sectors." |
| | Date | 3rd February, 2016 at 4pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| | Speaker | Dr. Christophe Len, UTC, France. |
| | Title | "Water as green solvent for synthesis of added value chemicals." |
| | Date | 3rd February, 2016 at 4pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 23. | Speaker | Dr. Jayanta Bhattacharyya, Duke University, Durham, USA. |
| | Title | "Genetically Engineered Nano-particles for Drug Delivery." |
| | Date | 11th February, 2016 at 4pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 24. | Speaker | Dr. Dipayan Rudra, Assistant Investigator, Academy of Immunology and Microbiology/POSTECH Campus, Institute for Basic Science (IBS), South Korea. |
| | Title | "Control of Systemic and Organ-specific Inflammation by Foxp3-associated Transcription Factors in Regulatory T cells." |
| | Date | 16th February, 2016 at 5pm, Prof. B.K. Bacchawat Hall (1st Floor). |



SEMINAR FROM APRIL 2015 TO MARCH 2016

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| 25. | Speaker | Dr. Rajarshi Choudhury, Department of Pharmacology and Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, NC 27599, USA. |
| | Title | "Synthetic Biology and Systematic Regulation of RNA-Protein Interactions." |
| | Date | 17th February, 2016 at 4pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 26. | Speaker | Dr. Sourav Sarkar, Department of Chemistry, Lehigh University, Bethlehem, USA. |
| | Title | "Mapping enzymatic interactions of bacterial cell wall biosynthesis with photo-affinity probes." |
| | Date | 18th February, 2016 at 4.00 pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 27. | Speaker | Prof. Florian Hollfelder, Department of Biochemistry, University of Cambridge, Cambridge, UK |
| | Title | "Rules and Tools for Efficient Enzyme Evolution, Recruitment and Discovery." |
| | Date | 19th February, 2016 at 4.00 pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 28. | Speaker | Dr. Biplab Dasgupta, Associate Professor of Pediatrics, Division of Oncology, Cincinnati Children's Hospital Medical Center, Cincinnati OH, USA. |
| | Title | "Understanding Metabolic Vulnerabilities in Human Cancer." |
| | Date | 22nd February, 2016 at 4.00 pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 29. | Speaker | Dr. Arun Kumar Haldar, Duke University Medical Center Department of Molecular Genetics and Microbiology, USA. |
| | Title | The Molecular "Kiss of Death": Finding the Enemy Within—How Cells Recognize and Respond to a Microbial Pathogen Hidden in a Vacuole. |
| | Date | 4th March, 2016 at 4.00 pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 30. | Speaker | Dr. Amit Lahiri, Yale University School of Medicine, USA. |
| | Title | "How genetic polymorphisms contribute to inter-individual variation in immune responses ~ making SNPs make sense!" |
| | Date | 8th March, 2016 at 4.00 pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 31. | Speaker | Dr. Amarnath Mukherjee, USA. |
| | Title | "Targeting Prostate Specific membrane Antigen (PSMA) for cancer theranostics; Development, Application and mechanism of some targeted nanoparticles." |
| | Date | 22nd March, 2016 at 4.00 pm, Prof. B.K. Bacchawat Hall (1st Floor). |
| 32. | Speaker | Prof. Yoshio Aso, ISIR, Osaka University, Japan. |
| | Title | "Highly Electron-Accepting •-Conjugated Compounds for Organic Electronics." |
| | Date | 30th March, 2016 at 4.00 pm, Prof. B.K. Bacchawat Hall (1st Floor). |

Performance at a Glance

THE LAURELS

Awardees	Awards / Recognition
Dr. Samit Chattopadhyay	<ul style="list-style-type: none"> • The World Academy of Science (TWAS)
Dr. Chitra Mandal	<ul style="list-style-type: none"> • Distinguished Biotechnology Research Professor(2015) by Department of Biotechnology (Received on 2nd Nov, 2015) • Extension of Sir J.C. Bose Fellowship (2016-2020) by DST • Sir J C Bose Memorial Award for the year 2015 (received on 19th Jan, 2016) by Indian Science Monitor • Dr. Jan Chandra Ghosh Memorial lectureAward (2015) by The Science Association of Bengal.
Dr. Nahid Ali	<ul style="list-style-type: none"> • Top 10 Innovators Award for dipstick Technology, organized by FICCI jointly with the Department of Science and Technology (Govt. of India), Lockheed Martin Corporation, Indo-US Science and Technology Forum, Stanford Graduate School of Business, IC² Institute, University of Texas at Austin and TiE Silicon Valley, New Delhi, May 2015. • 'National Women Bioscientist Award' under the 'Senior Category' for the year 2014 from the Secretary, Gov. of India, Ministry of Science & Technology, Department of Biotechnology, New Delhi. • 'J.C. Bose Fellowship Award-2015' from the Gov. of India, Ministry of Science & Technology, Department of Science and Technology, New Delhi.
Dr. G. Suresh Kumar	<ul style="list-style-type: none"> • C.R. Krishna Murti Award (2015) of the Society of Biological Chemists (India) • Setaram-ITAS Calorimetry Excellence Award 2016
Dr. Krishnananda Chattopadhyay	<ul style="list-style-type: none"> • American Chemical Society Membership Award
Dr. Mrinal K. Ghosh	<ul style="list-style-type: none"> • FNASc- 2015 (National Academy of Sciences, Allahabad) • FAScT- 2015 (WB Academy of Science & Technology)
Dr. Suvendra Nath Bhattacharyya	<ul style="list-style-type: none"> • NASI Scopus Young Scientist Award in Biological Sciences by Elsevier • SwarnaJayanti Fellowship of The Dept of Science and Technology, Govt. of India • Selected as the Member of Guha Research Conference • Selected as the Member of West Bengal Academy of Science • Awarded with Prof B K Bachhawat Memorial International travel • Award for Young Scientists by the Christian Medical College, Vellore.
Dr. Surojit Ghosh	<ul style="list-style-type: none"> • Associate Editor in RSC Advances
Dr. Ashok K. Giri	<ul style="list-style-type: none"> • Elected as a Fellow of the National Academy of Sciences, India for the year 2015.
Dr. D. Bhowmick, Student of Dr. G. Suresh Kumar	<ul style="list-style-type: none"> • Dr. Gurdip Singh award for best thesis in thermal analysis.

CSIR-IICB in News-Upcoming Technology

Serum and Urine Based DIPSTICK for Diagnosis of Visceral Leishmaniasis and Post Kala-azar Dermal Leishmaniasis

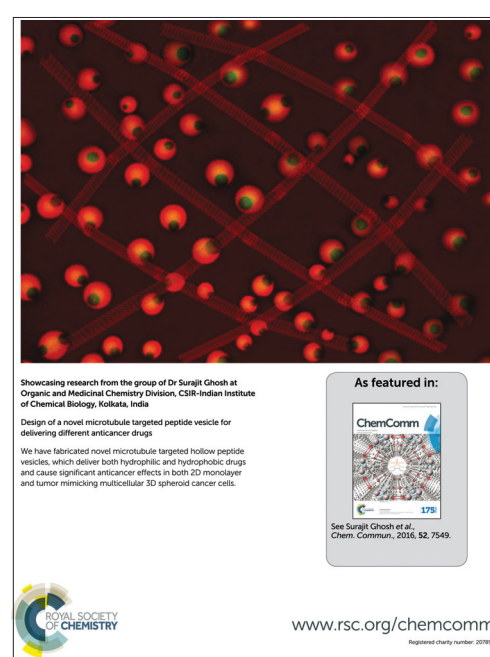
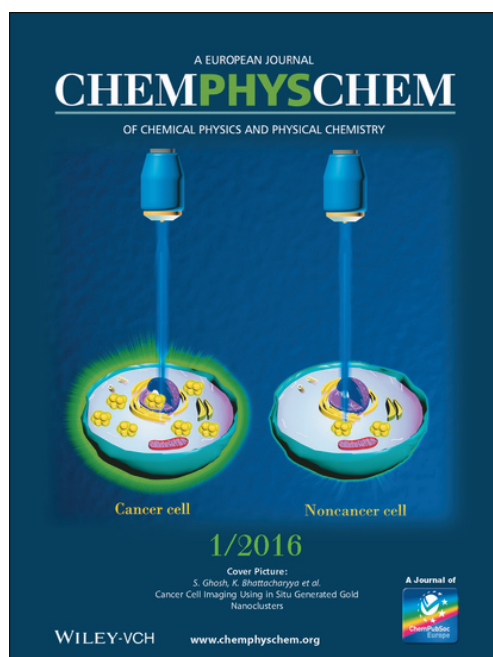
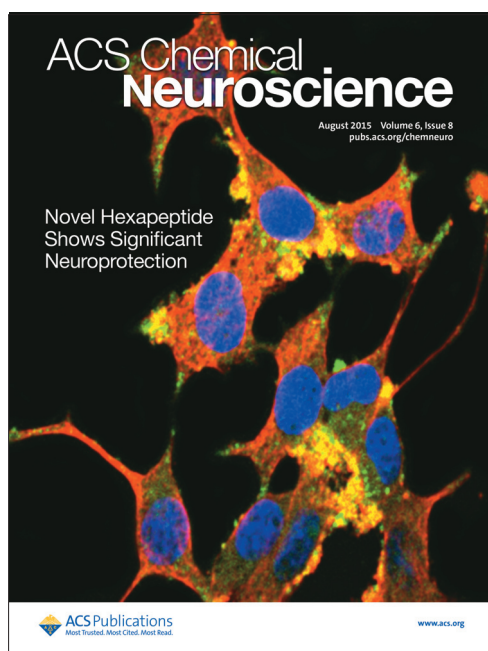
Links of media coverage for dipstick technology

- <http://www.thehealthsite.com/news/india-developed-blood-test-for-kala-azar-to-be-tested-in-africa/>
- <http://www.avenuemail.in/bengal/india-developed-blood-test-for-kala-azar-to-be-tested-in-africa/85049/>
- <http://english.tahikanews.com/archives/21056>
- <http://www.irishsun.com/index.php/sid/239114553>
- <https://in.news.yahoo.com/india-developed-blood-test-kala-azar-tested-africa-092005638.html>
- <http://www.brazilsun.com/index.php/sid/239114553>
- <http://www.brazilnews.net/index.php/sid/239114553>
- <http://www.newkerala.com/news/2015/fullnews-157698.html>
- <http://m.newsnow.in/news/india-developed-blood-test-for-kala-azar-to-be-tested-in-africa>
- <http://www.news9.in/n/Health/755d9y8ip/India-developed-blood-test-for-kala-azar-to-be-tested-in-africa>
- <http://www.nerve.in/news:2535002718260>



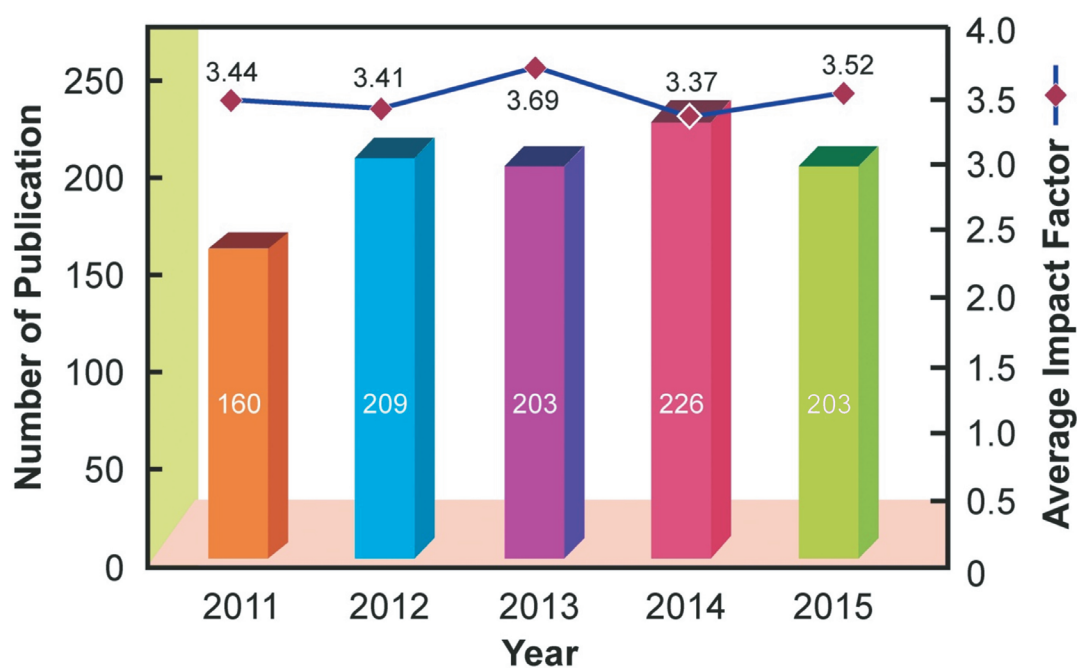
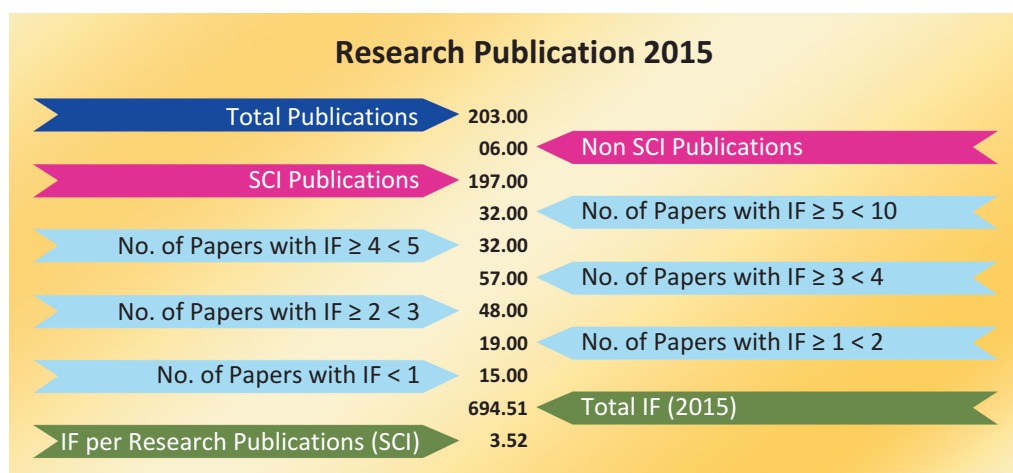


COVER PAGES OF JOURNALS



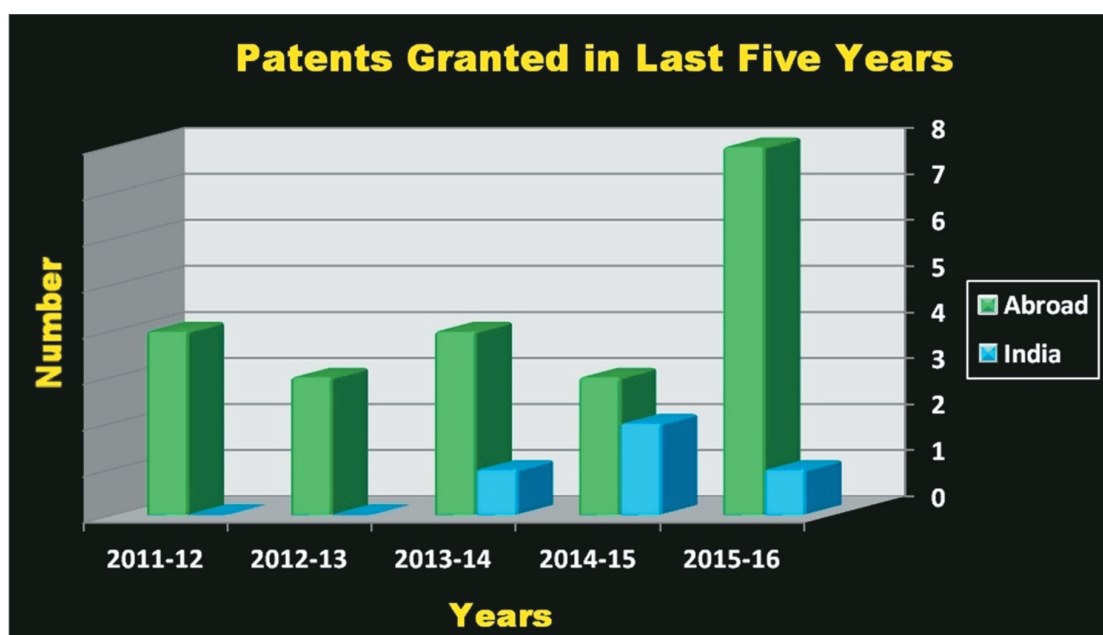
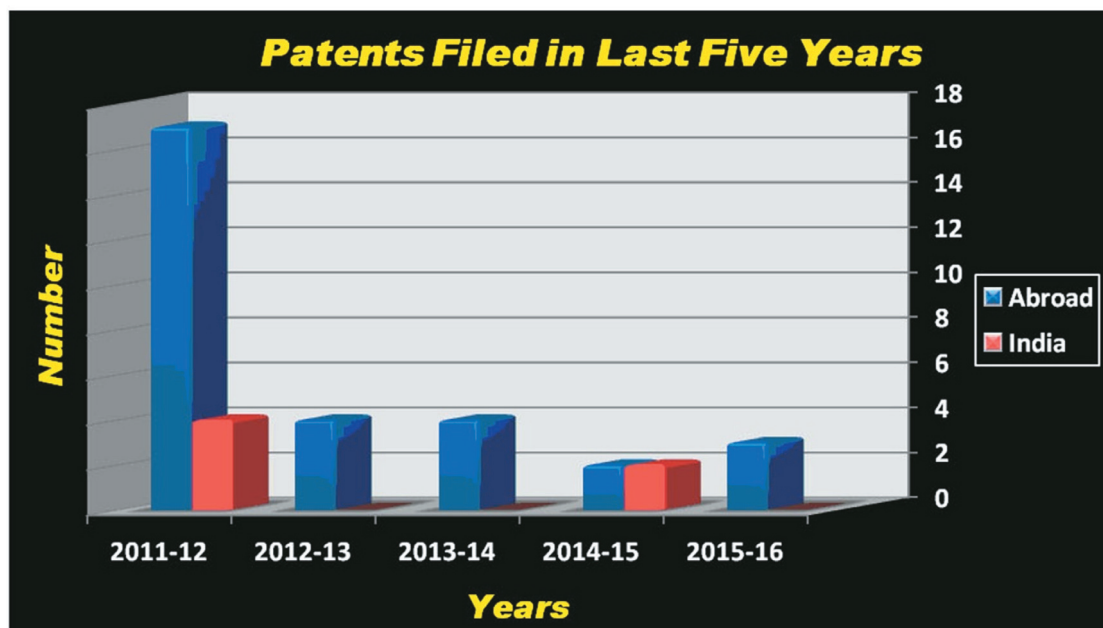


PUBLICATIONS

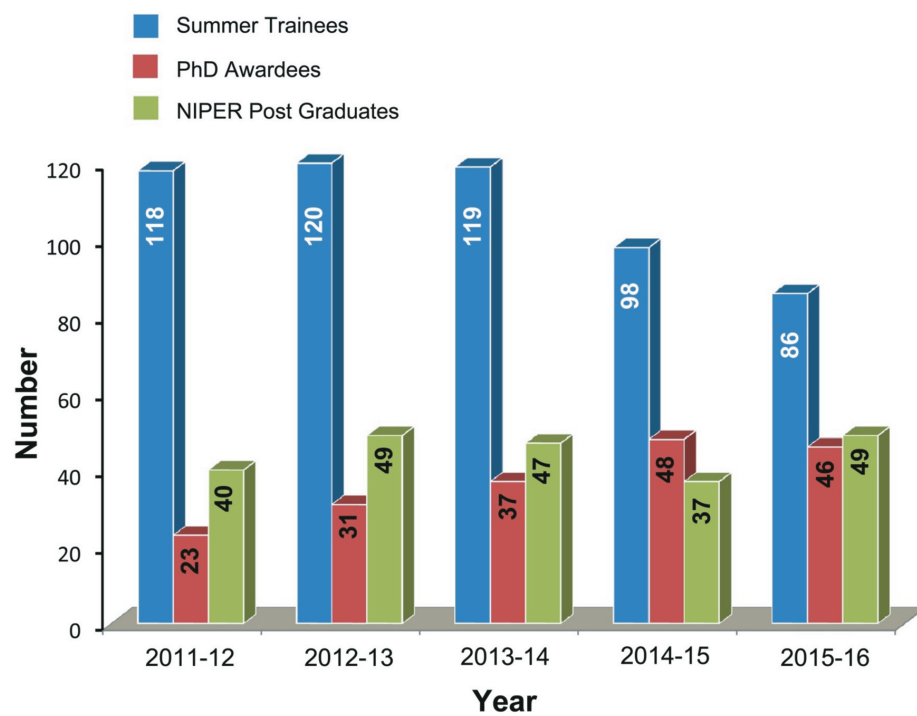




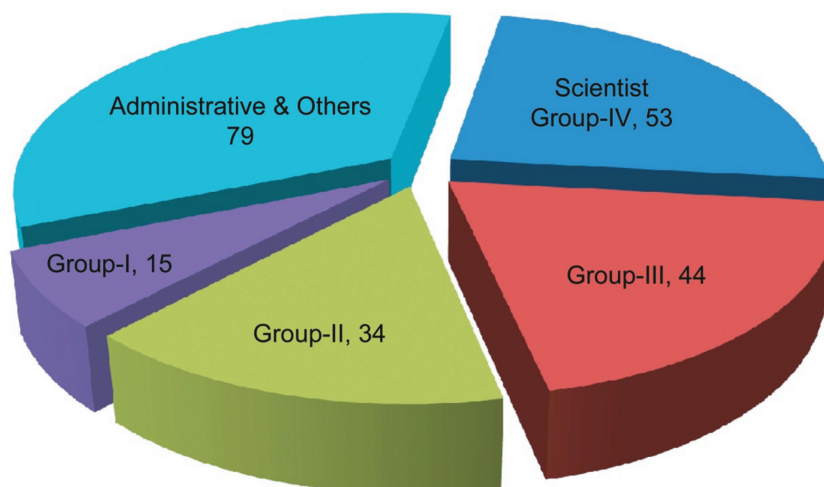
PATENTS



HUMAN RESOURCE DEVELOPMENT



Total manpower- 225

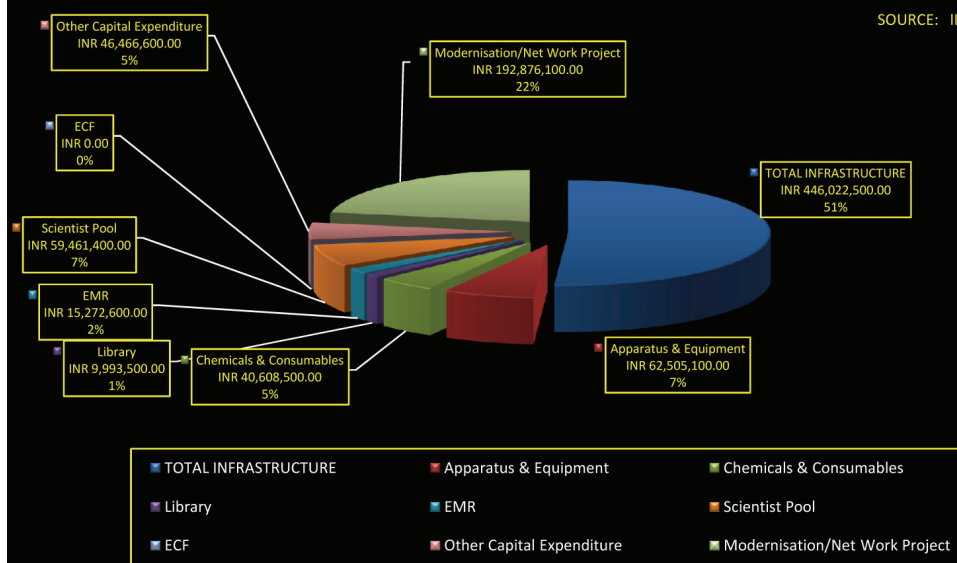


Scientist : Technical Staff : Administrative Staff :: 53 : 93 : 75



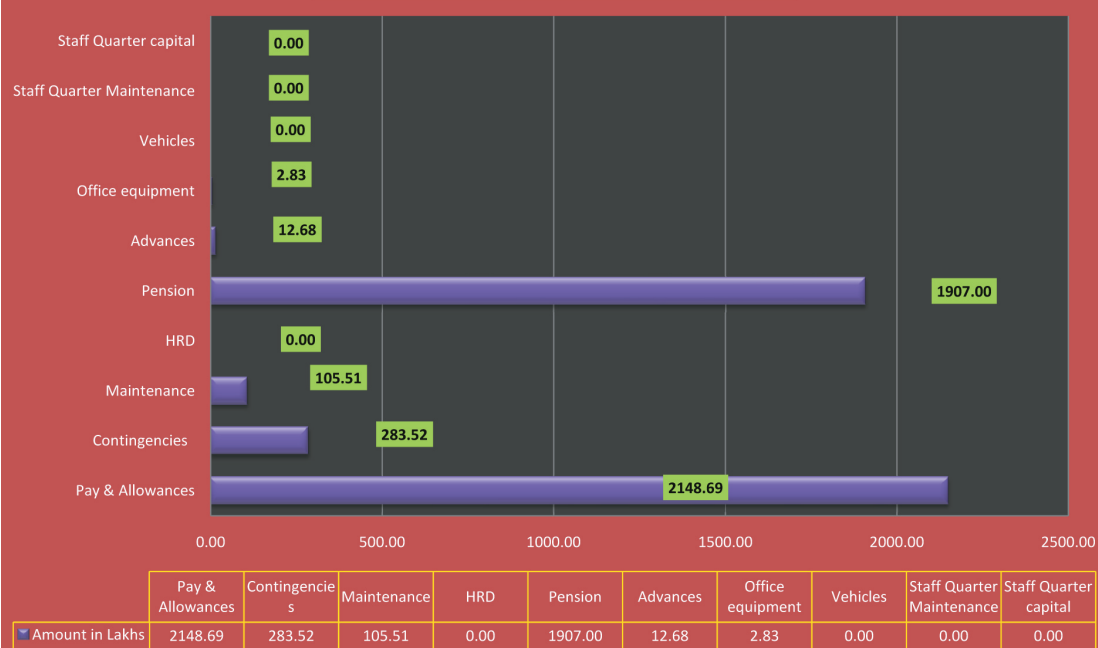
R & D AND TOTAL EXPENDITURE BREAK-UP 2015-16

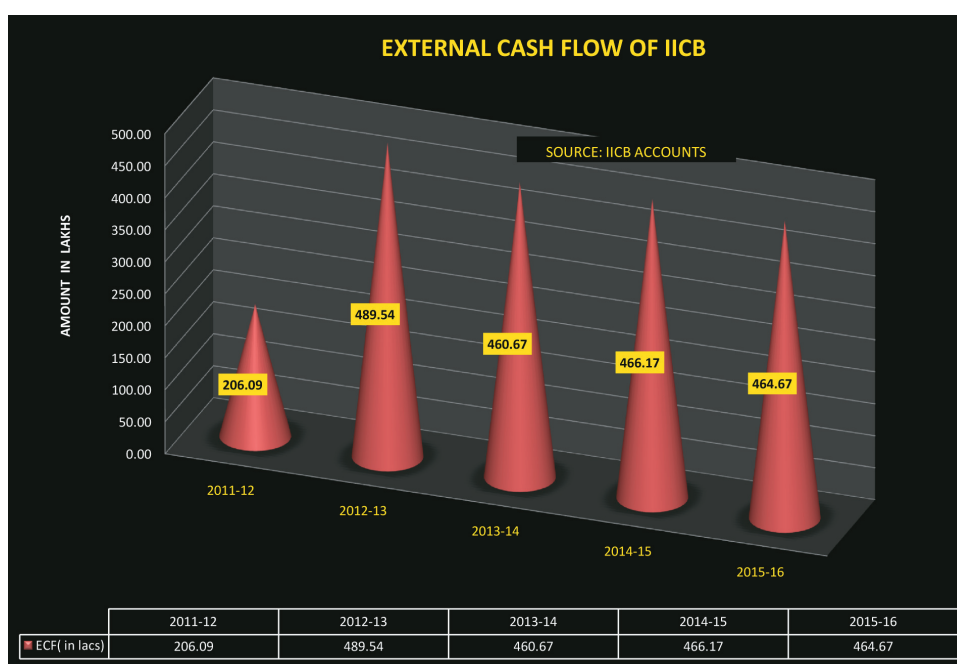
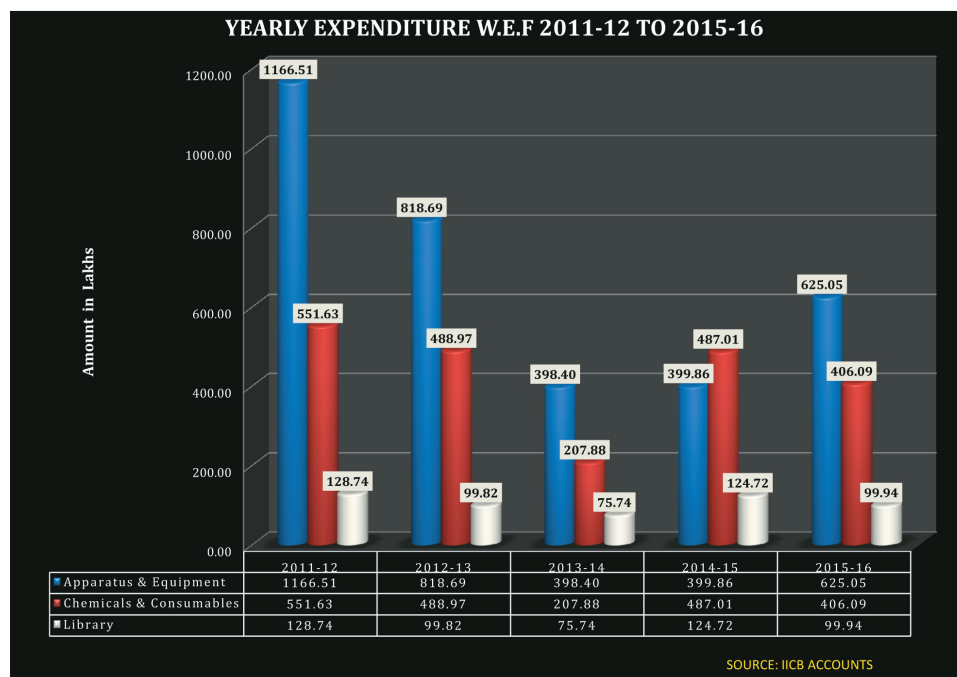
SOURCE: IICB ACCOUNTS



INFRASTRUCTURAL BREAKUP 2015-16

SOURCE: IICB ACCOUNTS

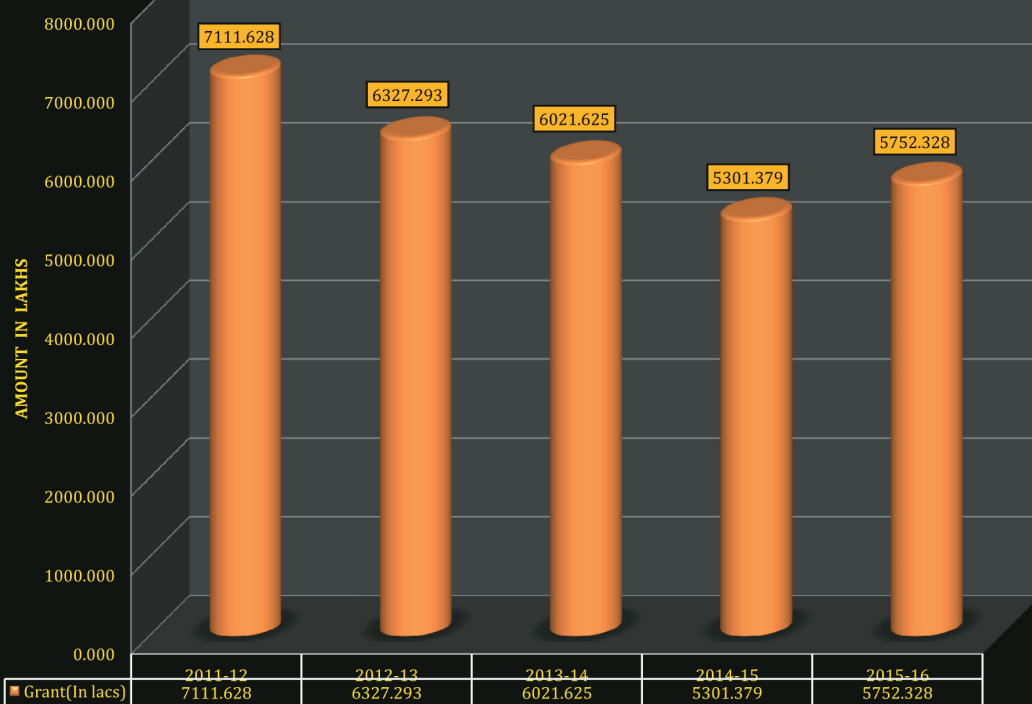






YEARWISE GRANT RECEIVED FROM CSIR

SOURCE : IICB ACCOUNTS





Central Facilities

ACADEMIC AFFAIRS DIVISION

**Dr. Syamal Roy (Head till January 2016),
Dr. Siddhartha Majumdar, Ms. Debasree
Das and Md. Ayub Shah**

The activities related to the overall academic affairs of the institute are the primary focus of this Division. The activities of AAD along with HRG were successfully carried out in functions related to CSIR-IICB PhD Course Work program and also to extend academic-administrative affairs of AcSIR activities in this institute. The CSIR-IICB Academic Affairs Committee, acts as an Advisory Committee to the Academic Affairs Division in connection with CSIR-IICB PhD program including AcSIR programme.

CSIR-IICB PhD Course Work (CW): 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 framing of the course content & guidelines is designed in the line of AcSIR courses as well as per UGC requirement.

The existing CSIR-IICB PhD Course Work programme constitutes basic and advanced level courses. The basic course is for bridging the gap between M.Sc. and PhD. The advanced level course comprises of frontline areas of research and covers research methodology and review of current literature.

2014-15 courses continued till August 2015 (spring semester). Further PhD course work 2016 scheduled in January 2016.

PhD CW in new format (2016) comprises of three level of courses [total 12 credits]:

Level 100 [basic courses] (Total 4 credits, all compulsory): Computation And Bioinformatics, Basic Chemistry, Introduction to Chemical Biology, Research Methodology (Including Ethics), Patent

& Biostatistics & Bio-safety, Chemical Safety & Radioactive Safety & Scientific Communication Skill Development, Research Proposal Writing.

Level 200 [mid level courses] (Total 4 credits): Biology of Macromolecules, Molecular & Cellular Immunology, Cell Biology & Cell Signaling, Techniques of Chemical Biology & Hands-on Training, Advanced Analytical Chemistry, Advanced Organic Chemistry, Green Chemistry.

Level 300 [advanced level Course] (Total 4 credits): Cancer Biology, Cell & Tissue Biology, Eukaryotic Gene Regulatory Mechanism, Natural Products and Drug Discovery, Advances in Nanoscience and Nanotechnology, Total Synthesis and Supramolecular Chemistry.



HUMAN RESOURCE GROUP (HRG)

Dr. Siddhartha Majumdar, Ms. Debasree Das and Md. Ayub shah

Human Resource Group (HRG) of CSIR-IICB promotes professional Human Resources Management in this institute by evolving and implementing HR development plan.

The major area where HR group contributes: Activities related to Academic–Administration concerning PhD program, student affairs, post graduate (PG) Training Programme, and different training programs.

The functions include: oversight, guidance and co-ordination of different HR development program & talent-management activities.

Activities, Guidance and Initiatives:

Student Affairs

- 1) PhD course work and PhD program: Management of academic calendar, attendance and class schedule, Coordination with the teachers, management of semester examinations, evaluation, seminar, and publication of result & issuance of certificates.
- 2) Maintenance of PhD registration databases and PG summer/winter trainees academic records and coordination of Academic Affairs meeting.
- 3) Scrutiny of applications of RFs & RAs related to academic affairs.
- 4) Oversee the NET JRF entrance interview
- 5) Content development for Research fellow's handbook, course catalogue, Teachers Guideline, academic Calendar and different guidelines related to PhD program and PhD course work.
- 6) Organization of science communication and presentation skill development program for the PhD course work students
- 7) Organization of Orientation programme for PhD students.

Human Recourses :

PhD students, post-docs & project assistants (Up to March 2016)

At a Glance:

Number of existing Research Fellows & Associates: 343 (CSIR/UGC/DST/DBT/ICMR/TLP)

Number of Project Assistants: 19

Summer Training / Project Work / Dissertation Work

HRG coordinates Summer Training Programme for the eligible Post Graduate students of different Universities, Institutions and Colleges for partial fulfilment of their degrees. 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 provide them the opportunity to do basic research in top-notch research areas, in a supportive learning environment with plenty of interaction with graduate students and faculty members. Detailed guidelines are made available in CSIR-IICB website.

This year "Biotechnological based -Research Internships programme" (*Biotech-RISE*) for the selected postgraduate students of WB, launched by the Department of biotechnology, Government of West Bengal was conducted at CSIR-IICB.

Number of Summer Trainee/Project Trainee (2015-16): 86

Learning and instructional support: PhD Course Work

HRG function as overall coordinating centre for the *CSIR-IICB PhD course work* for the PhD students. The PhD course work is carried out with the advice of Head, AAD and the Academic Affairs Committee and the Examination committee constituted for this purpose.

Total number of Course work students for 2016: 78 (Chemistry –10, Biology – 68)



Hands-on training / workshop for CSIR-IICB PhD Course work 2014-15 students

FACS :

An extensive training on flow cytometry was carried out for coursework students. 35 students from both biology & chemistry background took the course. 90 mins of theoretical introduction lecture was delivered by Dr. Dipyaman Ganguly, which covered history of different physical operating principles of the technology, the anatomy of flow cytometry instruments and potentials of application of the technology for biomedical and drug discovery research. This was followed by a practical training program in three batches, wherein 10-12 students were given first hand demonstration on flow cytometric data acquisition and analysis.

Dr. Dipyaman Ganguly was entrusted to coordinate the FACS training.

Confocal Microscopy:

A hands-on training program on confocal microscopy involving all the course work students of biological sciences for 2014-2015 academic year has been organized. Dr. Suvendra Bhattacharyya was entrusted to coordinate the course. He also delivered the introductory lecture on the principal and development in confocal imaging at the beginning of the course. The students in different groups participated in the hands-on training arranged on the Andor Spinning Disc Confocal System located at IICB. The technical person in charge of the machine was involved in the practical training process where accusation and processing of live cell images were performed and FRAP and TIRF techniques were highlighted.

NMR spectroscopy:

A Five-day workshop on practical aspects of solution NMR spectroscopy was held for students of Chemistry and Biology disciplines. At the onset, a 4 hour theory course, describing the key steps to perform NMR experiments was presented by Dr. Sujoy Mukherjee. Following this, Mr. Tapas Sarkar and Dr. E. Padmanaban demonstrated on 300 and 600 MHz spectrometers, respectively, the procedures to record ^1H and ^{13}C (decoupled) NMR spectra. In addition, Dr. Mukherjee showed the procedure to record multidimensional ^1H - ^{15}N spectrum of proteins to the students.



Batch of Students for FACS



Batch of Students for Confocal Microscopy



Batch of Students for NMR

COMPUTER DIVISION

Dr. Chitra Dutta (Head), Dr. Aparna Laskar, Mr. Pradeep Sypureddi, Mr. Akash Gupta, Mr. Shiv Kumar Gupta and Mr. Prahlad Das

Introduction

Computer Division is a key component of CSIR-IICB infrastructure, which continuously strives to cater the need of computer and IT related services of users in research, administration, learning and personal communications.

The Division helps in providing support to Desktop, Laptop, Printers, Scanners, Software's, Video Conferencing, Biometric System and Network infrastructure services from time to time along with setup and maintenance.

The Division also provides secured network services including the design of campus wide LAN/WAN

solutions and internet /intranet solutions besides providing computing services to ongoing R&D projects and conducting periodical training programs. The IT group has been in the forefront of deploying information technologies to help our Faculty members, students & other staff members.

The Division has extended its services to CSIR-IICB TRUE, Salt Lake campus along with P to P link upgradation of 10 Mbps. The present CSIR-IICB Network facility management system has been upgraded with latest technologies like MAC Authentication for Wi-Fi Users, Webmail, VPN etc. The ILL connection from NKN has been upgraded to 1G.

Technical Activities:

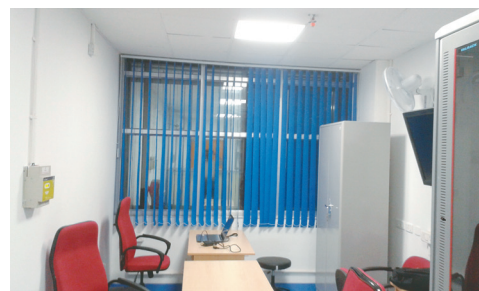
- Wired and Wireless Networking Solutions & Services.
- Internet Connectivity to all Scientists, Staff and Students of IICB.
- Cyber Security Solutions.
- Infrastructure Procurement, Installation and Maintenance.
- Biometric System and Video Conferencing Facility Support and Maintenance.
- ERP Storage Solutions and Backups.
- Web Services include Website / Bulletin board / E-Resource Access.
- Electronic Display System Services for various types of Official instant notices.
- User Support Services including Software and Hardware installations, printers, scanners and all other computer related devices.



CSIR-IICB Server Room, Jadavpur Campus



Work Area Server Room, CSIR-IICB



CSIR-IICB TRUE Server Room, Salt Lake Campus



CSIR-IICB Website

- E-mail Service for IICB Staff members including Scientists, Technical & Administrative Staffs and Students.
- Technical support in Video Conferencing and Biometric System
- Design and Maintenance of Intranet and IICB Websites (www.iicb.res.in and www.csiriicb.in)

Facilities:

- High performance Servers managing services like Web, DHCP, DNS and Proxy
- Email services for Staff and Students
- Video Conferencing System
- Biometric System
- Wi-Fi Internet Management System
- VPN Network Service Management System

- SAN and ERP application Servers Management System
- Network Management System with high speed Routers and Switches
- Network Security Management System with Firewall and Radius Servers

New Initiatives:

- Upgradation of NKN ILL connection to 1G
- Upgradation of Point to Point connectivity with 10 Mbps between CSIR-IICB TRUE, Salt Lake Campus and CSIR-IICB Jadavpur campus
- Procurement of New servers for facilitating new services along with upgradation
- Upgradation of LAN System to 10G at Jadavpur Campus, CSIR-IICB
- Setup of Data centers in both the campuses of CSIR-IICB with Infrastructure facilities like Cooling, UPS and Humidity controlling systems
- Extension of Services like LAN, Wi-Fi, Biometric and Internet Services to Salt Lake Campus CSIR-IICB TRUE
- New alternative website www.csiriicb.in has been introduced
- Display System introduced for various types of Official works



CSIR - IICB Intranet

LIBRARY & DOCUMENTATION DIVISION Knowledge Resource Centre (KRC)

Dr. N. C. Ghosh, Mr. S. K. Naskar, Mrs. S Ganguly, Mr. M. Halder, Mr. S. Nath and Mr. Asoke Ram

Knowledge Resource Centre (Library) has been playing a pivotal role as one of the important infrastructure division by providing tireless supports to its users. During the period under review, the Division has marked growth in collection, systems, facilities and services.

Collections	Up to 31.03.2016
Books (including Hindi)	14376
Journals (online only)	109
Bound volumes	33860
Science-Direct (Back files) (http://www.iicb.res.in/bkfiles_library.html)	202 journals full text up to 1994
Annual Reports	3944
Thesis (CDs)/online	279
Newspapers (English, Bengali & Hindi)	3

CSIR-IICB has been accessing in full text of about more than 1000 (thousand) STM journals in addition to the subscribed content by IICB, through *National Knowledge Resource Consortium (NKRC)*, (<http://nkrc.niscair.res.in/indexpage.php>) which is a CSIR Network Project implemented by NISCAIR.

Science Citation Indexing Database – *Web of Science (WOS)* has been subscribing and various tailor-made services are being rendered by the division to the researchers.

iThenticate – plagiarism detection service is available in the Library & Documentation Division for reviewing the manuscripts by the researchers.

Various other services have been provided by the division during the period. Some of such services presented here in quantities.



Reading Room



Services

Reading Room & E-journals section accessed

Photocopy services rendered

Circulation services (Issue/Return including NIPER)

Resource Sharing (Electronic Document Delivery Service)

Walk in users

Up to 31.03.2016

6280 users

1087 pages during the year

903 documents during the year

255 Articles during the year

36

Open Access Repository (IR) maintaining in E-prints for archiving peer reviewed journals articles, Conference papers, Theses and other research documents produced by IICB researchers. This can be viewed in at: <http://www.eprints.iicb.res.in>. So far 1774 documents have been uploaded in the repository.

We have been developing *NIPER- Knowledge Resource Centre* in the library premises since its inception. We are catering services to the NIPER-Kolkata students and faculty members. Presently a total of 1092 text & reference books are available in its holdings till date. Subscription to '*SciFinder Scholar*' has been continuing for the period under review and login id & password has been provided to all the NIPER students and faculty members for accessing the same.

Online Public Access Catalogue (OPAC)

is available at

<http://14.139.223.107:8080/webopac/html/SearchForm>

which has been utilized as a very useful tool for searching library holdings.



E-journals access corner with thirty desktop computers



CENTRAL INSTRUMENTATION DIVISION

Dr. Debashish Bhattacharyya (Head), Mr. Shekhar Ghosh, Dr. (Mrs) Shila Elizabeth Besra, Dr. Tapas Sarkar, Dr. Ramdhan Maji, Mr. R. N. Mandi, Dr. E. Padmanaban, Miss. Banasri Das, Mr. Diptendu Bhattacharya, Mr. Sandip Chowdhury, Mrs. Arti Grover, Mr. Sandip Chakraborty, Mr. Jishu Mandal, Mr. T. Muruganandan, Mr. Soumik Laha, Mr. Sadip kundu, Mr. K. Suresh Kumar, Mr. Santu Paul, Mr. M. Vigneshwaran, Mr. Tapas Chowdhury, Mr. Tarak Prasad Nandi and Mr. Hari Shankar Beni.

Central Instrumentation Facilities (CIF) Division provides major analytical support to researchers at IICB as well as other researchers from India, who would like to use the facilities for their research work. In a major step the facilities were open to researchers outside IICB, to fill the gap of lack of availability of sophisticated and dedicated instruments in several small/big institutions. Presently there are about 30-40 big and small instruments under CIF with several of them having dedicated operators for smooth and high quality data acquisitions. Few new equipments like Beta counter (Tri-Carb2810TR) from Perkin Elmer (**Pic. 1**) and Chemidoc-Geldoc system (C400) from Azure Biosystem (**Pic. 2**) have been added to the facilities.



Pic. 1: The newly acquired Beta Counter (Tri-Carb2810TR from Perkin Elmer) at CIF being used by operator Tapas Chowdhury (Jun 2015).

CIF also organized special hands on training sessions for students as well as staff members to acquaint them with the capability of the machine as well give them hands on experience of using the machine themselves. One such training session was organized on 22nd March, 2016 for training the students with Confocal Microscopy. It was attended by about 19 students from different labs of IICB. Similar training sessions were also organized for FACS facility.

CIF also entertains students from different colleges within as well as outside West Bengal (WB). **Pic. 3** shows Students of Srirampore college (WB) and **Pic. 4** shows visit of students and faculties of Kirti College-Mumbai. Several officers of Indian Administrative Services (IAS) undergoing their probationary training also visited CIF as part of their training to get acquainted with scientific activities (**Pic. 5**).

Presently the entire list of instruments of central instrumentation is available on the IICB webpage with their physical location and the name and phone no of operators, the working status of instruments and the process of booking the time slot for using instruments. The data collection charges for each instruments as well as the process of booking the time slot for people outside CSIR-IICB is also made available through IICB webpage which allows easy official contact and access of these instruments to all. Earlier the payment for



Pic. 2: Newly acquired Chemidoc-Geldoc system (C400-Azure Biosystems) being used by an IICB student.



data collection charges for outside users was a major problem as they needed to visit the institute for making the payments. The payment process is now streamlined. Now the data collection charges can either be paid by depositing cash at cash-counter, writing a check in the name of Director IICB or making the payment online payment. The payment whole process is explained on the website for simplicity.

Presently CIF plans to make separation unit

(comprising HPLCs, FPLCs, GCs etc. to separate both types of chemical viz. small-molecules as well as macromolecules) under one roof to help both chemists as well as Biology researchers. Similar plans are being made for making imaging unit under one roof (comprising simple Confocal microscopes, Live cell confocal microscopes, inverted microscopes and high resolution confocal microscopes etc.), which shall help solve growing need of different types of sample imaging.



Pic. 3: Visiting Students of Srirampore College (West Bengal) being introduced About Atomic Force Microscope at CIF by operator Mr. Murugananda (extreme right), Aug 2016.



Pic. 4: The students and faculties of Kirti College-Mumbai on a scientific visit to the CIF seen in a group photograph along with Dr. Umesh Prasad Singh-Principal Scientist (extreme right), Jan 2016.



Pic. 5: Visiting probationary IAS officers (from left 1st, 5th and 6th) being introduced about Cryo-Electron Microscope at CIF along with Dr. Umesh Prasad Singh-Principal Scientist (2nd from left), Operator Mr. Chiranjit Biswas (3rd from left) and Dr. Jayati Sengupta-Sr. Scientist (4th from left), Aug 2016.



ANIMAL HOUSE

Dr. A. Konar, Mr. S. S. Verma, Mr. A. Das, Mr. R. Sarkar, Mr. A. Sardar, Mr. J. Midya, Mr. P. Midya, Mr. T. Sarkar, Mr. Lalu Sardar, Mr. G. Sardar and Mr. S. Midya

The animal facility of IICB provides a very important support to biomedical research programs of the Institute. The facility is registered to CPCSEA and strictly adheres to the regulations laid down by CPCSEA. Animal house produces different species and strains of animals in its breeding colony as per requirement. However, some special strains are procured. Apart from fulfilling its own requirements, IICB Animal House also supports other research institutes registered to CPCSEA.

The animals are maintained in an uniform environmental condition (Room Temp.24,20C; relative humidity 55 – 60%; light and dark schedule 12:12hrs; illumination 400 lux at 1 mt above the

floor). This year Individually Ventilated Caging System has been adopted for rearing animals.

They are raised under strict hygienic condition. The house keeping of the facility acclaimed high appreciation not only from the associated scientists but also the representatives of CPCSEA, representative of different NGOs and private entrepreneurs, visiting guests and scientists.

Institutional Animal Ethics Committee (IAEC) is committed to ensure rational and humane use of animals for experiments and always ensures that 3R's are followed for any animal experiment protocol.

The species and strains of animals, routinely maintained in the facility are as follows:

Mice - Balb/C, C57BL/6J, Rat - Sprague Dwalley, Hamster - Golden, Guinea Pig - English, Rabbit- New Zealand White.

A brief account of animal produced/supplied from the animal house in during this period is given in the following table:

Species	Stock on 1 st April 2015	No. of animals		Total (A)	No. of animals issued		No. of animals		Total (B)	Stock on 31.3. 2016
		Produce d	Purchased		Produced	Purchased	died in- stock	Supplied to other R&D organization		
Mouse	1206	2965	1220	5391	2659	1030	0	0	3689	1702
Rat	679	329	651	1659	656	501	0	0	1157	502
Hamster	323	413	0	736	400	0	0	0	400	336
Rabbit	68	75	0	143	14	0	0	20	34	109
Guinea pig	05	0	0	05	0	0	0	0	0	05

Engineering Services Unit (ESU)

Dr. S. N. Kabir (Head till April 2015), Dr. P. Jaisankar (Head from May 2015), Dr. Rupak K. Bhadra (Head from Jan 2016 onwards), Mr. U. K. Barua, Mr. C. Debdas, Mr. Sandip Saha, Mr. S. Ray, Mrs. N. Bage, Mr. D. Banik, Mr. S. K. Ghosal, Mr. R. Das, Mr. A. Das, Mr. A. Paul, Mr. P. K. Chanda, Mr. S. Biswas, Mr. S. R. Tudu, Mr. S. Nath, Mr. S. Majumder, Mr. U. Roy, Mr. A. Karmakar and Mr. A. Pal

Electrical Engineering Section under Engineering Services Unit (ESU) of CSIR- Indian Institute of Chemical Biology Kolkata Electrical Engineering Section plays a vital role to provide various Electrical and associated services for different R&D and other activities at the Institute campuses at Jadavpur & Salt Lake. Following are some important activities, involvements and achievements of ESU- Electrical Section.

- Providing Electrical Power throughout the Institute for round the clock use.
- Arrangement is there to provide Emergency
- Electrical Power instantly from the installed D.G Sets in case of failure in Power supply.
- Service & Maintenance of Electrical & associated systems.
- Adopted the method for Optimization of utilization of Electrical Power to keep the installed systems Energy Efficient.
- Estimation, Planning, Execution and Monitoring of Engineering Works related to Electrical systems.
- Maintained the Power Factor (PF) Level of Electrical System at above desired level and gained rebate in the range of ₹ **12.60 Lacs** in Electricity consumption Bill in the financial year 2015-16. (Please Ref. Table – 1)
- Provided all Technical Assistance to effective functioning AV Projection of Video Conferencing System.

1. Carried out Modernization works for Electrical systems of different Laboratories and other Working areas have been carried out at IICB Jadavpur and Salt Lake Campus.
2. Carried out Electrification Works including installation of new Power Panel for setting up of new Data Centre at both the Institute Campuses of IICB Computer Division.
3. Installed Electrical power Panel for BSL- 3 Lab at new location and done modernization works inside Lab.
4. Process initiated for procurement of Energy Efficient LED Lighting systems to minimize the consumption of Electrical Energy by the Institute.

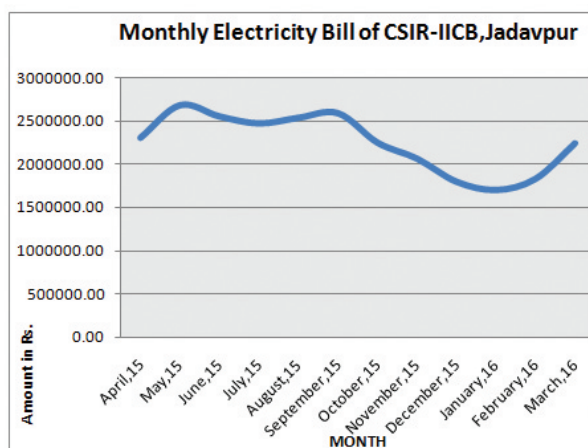
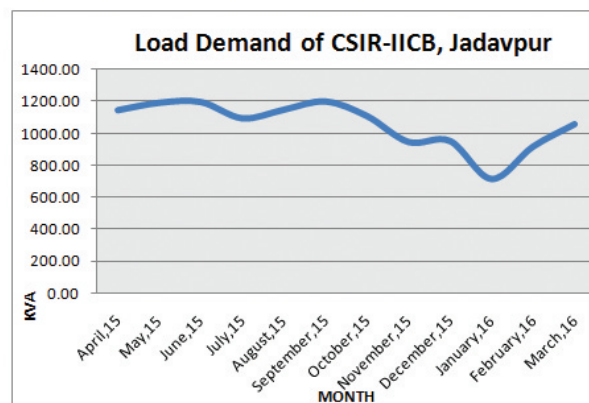
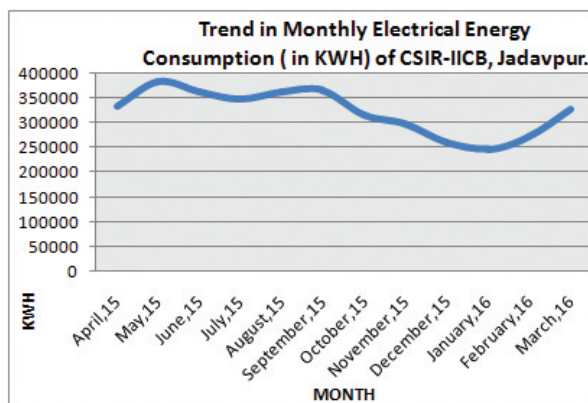
Remote Operated Curtain Opening Device was designed and developed by the Electrical Engineering Section. Dr. Harsh Vardhan, Minister of Science and Technology, Govt. of India, was inaugurated the CSIR-IICB, TRUE Campus using this device.
5. Power supply Management was efficiently done during the Inaugural function of CSIR-IICB, TRUE Campus in the month of February, 2016.
6. Different Electrical & Electro-economic parameters related to Electrical Energy utilization at CSIR-IICB Jadavpur campus are indicated here.





Table - 1

Month of the Bill	Max.Demand (KW)	Monthly Demand (KVA)	Unit Consumed (KWH)	Rebate for Maintaining Power Factor	Bill Amount
April,15	1137.60	1150.40	333564	118916	2301882
May,15	1168.00	1196.80	383244	136626	2678471
June,15	1171.20	1201.60	363672	129649	2548554
July,15	1067.20	1099.20	349416	99234	2468473
August,15	1118.40	1153.60	362876	128821	2533135
September,15	1161.60	1204.80	367068	104247	2586383
October,15	1089.60	1113.60	316092	89770	2245881
November,15	924.80	950.40	298688	84469	2062177
December,15	916.80	956.80	261220	92341	1794862
January,16	697.60	718.40	246684	87203	1699173
February,16	889.60	921.60	272280	96251	1827039
March,16	1038.40	1062.40	328492	93686	2238335
Total				1261214	26984365



Electro - Economic parameters at a Glance CSIR-IICB, Jadavpur	
Monthly Average Unit Consumption	3, 24,000 Units / KWH
Monthly Average Load Demand	1061 KVA
Monthly Average Electricity Bill	₹ 22.5 Lacs.
Monthly Average Power Factor Rebate	₹ 1.05 Lacs.

A background image showing various laboratory glassware including Erlenmeyer flasks, graduated cylinders, and beakers containing liquids of different colors (blue, orange, green).

Administration

General Administration

Finance & Accounts Stores & Purchase Official Language Activities of the Institute . 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.

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 & nonplan expenditure, which is about ₹ 80 crores per annum. Keeping track of progressive expenditure of budget for every month, keeping financial records for Networked Projects, externally funded projects, disbursement of pension to pensioners, accounting and auditing files routed through Establishment, Purchase and other scientific divisions. 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 administrative software. Through this entry, our Annual Accounts and Balance Sheet is generated for onward transmission to CSIR,HQ.

Stores & Purchase

The Stores & Purchase Division caters to the research and other requirement of CSIR-IICB. The annual procurement budget of CSIR-IICB is about ₹28 crore 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 CSIR-IICB that are either purchased by CSIR-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.

OFFICIAL LANGUAGE (HINDI)

Many Rajbhasha activities throughout 2015-16 marked an eventful year in Hindi implementation in the Institute with Hindi workshops, Hindi week celebration, Sanjivani publication etc.

On 30th June, 2015 there was a workshop in the Institute. The technical officers & employees were trained in Rajbhasha in the workshop. The senior Hindi Officer of CGCRI Sri Priyanka Paliwal conducted the workshop and explained the 'unicode' (Hindi software) and its uses in the computers to the participants. Mr. Paliwal invited each of the participants and made them practice typing words and, use of email in unicode on the computers.

14 September saw the Hindi workshop where Sri Paliwal Hindi officer from CGCRI conducted a workshop in unicode. He conducted the workshop for scientists. There were 30 scientists present in the workshop.

A workshop was held for the administrative staff on 21st December in the Institute. Sri Rishikesh Ray (Deputy Director Rajbhasha, Tea board) conducted the workshop. He conducted an workshop on 'Globalization of Rajbhasha'. He explained to all the administrative staffs how Hindi was accepted and understood all over the world and how by hindi language we can reach science to the common man.

Hindi week was observed in the Institute from 10-15 September, 2016. Hindi noting drafting and essay competition was held on 11 September and essays on general topics were very interestingly penned by the participants concerned. 14 September saw the workshop in Globalization of

Hindi. Hindi day and closing of Hindi week was held on 15th September when recitation and extempore competition in Hindi were held in the Institute. Senior Prof of Hindi Calcutta University was the chief guest of the day. Sri Satish Kumar Pandey Asst Director of Central Translation Bureau was the special guest of the day. Dr Chitra Mandal presided on the occasion and requested all the members of the Institute to work in Hindi.

This week-old celebration ended with a cultural programme and the members of the Institute staged a drama in Hindi. The Hindi officer Smt Nag moved the vote of thanks.

On 19th January, 2016 Dr. Puran Pal Senior Hindi Officer, CSIR from headquarters Delhi visited IICB for an inspection of Hindi work in the Institute. A workshop was arranged on this occasion. All the departmental heads and chief scientists were invited to this workshop. Sri Pal reminded the officers to work in Rajbhasha and use Hindi in day to day work without any hesitation.

'Sanjivani' Hindi patrika was published this year. Many articles in science, literature, poetry were published in Hindi. All the write-ups were written by the employees of the Institute.

Two Hindi words with English meaning are displayed everyday in the electronic board near the reception. There are library books in Hindi purchased every year where selected renowned books are selected by a committee constituted for this purpose. Hindi implementation is also monitored in the Institute by a four member committee consisting of Hindi Officer & three scientists.



30th June 2015, Hindi Training on Unicode for Technical Officers

HINDI WORKSHOP 2015-16



14th September 2015, Hindi Training on Unicode for Scientists



21st December 2015, Hindi Training on 'Globalization of Rajbhasha' for Administrative Staff



19th January 2016, Hindi Workshop on Rajbhasha Rules Implementation for Department Heads & Scientists

NATIONAL INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH (NIPER - KOLKATA)



No. G-15/12/1/2015/NIPER-Kolkata
8th June, 2016

1. Chairman of Board of Governor/Steering Committee (with period): Secretary, Department of Pharmaceuticals, Ministry of Chemicals & Fertilizers, Govt. of India from 2007.

2. Director/Project Director (with period):

i) Director- in charge, from August, 2007 to September, 2014: Prof. Siddhartha Roy (Ex. Director, CSIR-IICB)

ii) Project Director, from August, 2007 to November, 2014: Dr. Asish Kr. Banerjee (Ex. Scientist, CSIR-IICB)

iii) Director in charge cum Project Director, from October, 2014 to 5th July, 2015: Prof. Chitra Mandal (Ex. Director, CSIR-IICB)

iv) Regular Director, from 6th July, 2015: Dr. V. Ravichandiran



Dr. Ravichandiran, V welcomed by CSIR-IICB's acting director Dr. Chitra Mandal on his joining as NIPER Director on 8.7.15

3. Historical Milestones (incl. Inauguration date): The National Institute of Pharmaceutical Education & Research-Kolkata (NIPER-Kolkata) was established as an Institute of National Importance by the Government of India through Act of Parliament (NIPER Act 1998 & NIPER amendment Act 2007). The main objectives of NIPER-Kolkata are:

(a) To tone up the level of pharmaceutical education and research.

(b) To produce leaders in the field industry and Academic Institutes etc.

4. Mentor Institute if any: CSIR-Indian Institute of Chemical Biology, Kolkata

5. Achievements till date: Two hundred and eighty three students have graduated. Among them, 190 are engaged in companies and academic institutions. Out of the seven batches, 66 students are carrying out Ph.D. in various Institutes including 12 in abroad and out of them 12 have been awarded the degrees. The students of NIPER-Kolkata have been exposed to different types of conference, workshop and events, for example, Swachh Bharat, Rashtriya Ekta Diwas, and NIPER-Kolkata Foundation Day etc. NIPER-Kolkata convocation was conducted on 21 August 2015. Dr. V. K. Subburaj, IAS, Chairman Steering Committee of NIPERs and Secretary to the Govt. of India, presided over the convocation and Dr. Ashok Rakhit from St. John's University, Queens, New York, USA was the Chief Guest. Director of NIPER-Kolkata attended Steering Committee meeting of NIPERs and DoP on 17.09.2015.

6. Manpower-Academic and Non-Academic staff-Sanction/In-position/Vacancy: No permanent sanctioned posts till date. All the administrative works are managed by the retired Govt. employees and outsourcing with the help of the Mentor Institute. Regular Director of NIPER-Kolkata joined on 6th July, 2015.



7. Finances: Government- Allocations, releases, utilization, balance during the last 5 years.

Year	Allocation BE	Allocation RE	Total Release	Rupees in Lakh	
				Expenditure	Exp.% to RE
2010-11	350.00	160.00	160.00	281.89	176.18%
2011-12	300.00 (general) 1875.00 (Capital) Total: 2175	300.00 50.00 (capital) Total: 350.00	269.00 40.00(capital) Total: 309.00	228.88 17.06 (capital) Total: 245.94	70.27%
2012-13	400.00 50.00 (capital) Total: 450.00	450.00	175.00	251.86 26.30 Total: 278.16	61.81%
2013-14	450.00	400.00 40.50 (capital) Total: 450.00	400.00 40.50 Total: 440.50	298.59 24.48 Total: 323.07	73.34%
2014-15	450.00 50.00 (capital) Total: 500.00	400.00 50.00 Total: 450.00	400.00 37.34 Total: 437.34	348.74 32.28 (capital) Total: 381.02	84.67%
2015-16	500 300 (capital)	-	500.00 130.00 (capital) Total: 630.00	522.078 2.03 (capital) Total: 524.308	63.03%

8. Learning Environment/Academics:

A. Number and Names Departments/ Disciplines
(with opening year)

No.	Names Departments/Disciplines	Opening Year
1	Medicinal Chemistry	2007
2	Natural Products	-DO-
3	Pharmacoinformatics	-DO-

B. Students

i. Degrees/programmes offered and Subjects offered (with year) with admission status:

Level Masters/ Doctoral	Degree MS/MBA/ M.Tech/Ph.D	Discipline	No. of students admitted	
			2014-15	2015-16
Masters	M.S. (Pharm.)	Medicinal Chemistry	16	17
		Natural Products	12	13
		Pharmacoinformatics	14	09



ii. *Completion rates: Students pass out year wise against capacity and admission at PG, Ph.D, PDF since the beginning*

Year	Masters level		Doctoral level	
	Admission	Completion	Admission	Completion
2007-2009	29	29	NIL	NIL
2008-2010	32	32	NIL	NIL
2009-2011	40	40	NIL	NIL
2010-2012	49	49	NIL	NIL
2011-2013	47	47	NIL	NIL
2012-2014	37	37	NIL	NIL
2013-2015	49	49	NIL	NIL
2014-2016	42	Pursuing 3 rd & 4 th Semester	NIL	NIL
2015-2017	39	Pursuing 1 st Semester	NIL	NIL

C. Employability/Placements Status:

(i) *Year wise companies participated in campus selection/placements:* Since the inception, fourteen pharma companies came to NIPER-Kolkata to recruit students.

(ii) *Last 2 years placements status:* in campus/off campus: Placement was achieved for NIPER Kolkata students according to their options. Most of the students have been absorbed in the Industries, colleges and research Institutes. Many numbers of students are pursuing their higher studies within the country as well as in abroad.

(iii) *A draft placement calendar has been prepared by NIPER Kolkata and the same has been circulated to DoP and all NIPERs.*

(iv) *Ranking by Subject, if any:* Yet to be received.

D. Teachers

i. *Recognition to Faculty:* All the guest faculties invited from the mentor Institute and other Institutes of Kolkata, such as Calcutta University, Jadavpur University, Indian Association for the Cultivation of Science, Bose Institute, Saha Institute of Nuclear Science, SSKM Hospital, and TCG Life Sciences. Scientists from these Institutes are well recognized in their own areas of research and scientific activities.

ii. Two contractual faculties one in each discipline of MC and NP has joined. One is from NIPER Mohali and one is from NICED, Kolkata. Scientists from these Institutes are well recognized in their own areas of research and scientific activities. Three adjunct faculties have also joined two from CSIR-CGCRI and one from Industry.

iii. *Peer review system:* Yet to be introduced.



9. Land and Civil Works if any:

No land has been received and possession taken over from the State Government till date. However, matter is under active persuasion.

Progress till date: Thirty acres of land was allocated in Nadia District by the Govt. of West Bengal for NIPER-Kolkata. This site was visited by NIPER officials along with DM and ADM of Nadia District and found that the land was inadequate and requested DM to provide more land to NIPER-Kolkata at least of 100 acres. Another Meeting was held with the Commissioner of land and land reform and Chief Secretary of the State urging allotment of more suitable land around similar academic and research institutions at Kalyani of Nadia District. Several visits were made to the office of the land commissioner by Director NIPER-Kolkata and recently Dr. V.K. Subburaj and Director NIPER-Kolkata. In Nadia District close to Krishnanagar land has been located and it is under active consideration.

10. Academia-Industry partnership:

- a. Capacity utilization of Common facilities viz., Technology Development Centre/ SMPIC/National Bio-availability Centre etc.: NIL
- b. Consultancy projects/Knowledge Process Outsourcing (KPO)/Contract Research Organisation (CRO)/ Contract Research & Manufacturing Services(CRAM)/ IPRs etc.: NIL
- c. Entrepreneurship / Incubators: NIL
- d. During the year under report the following initiatives have been taken:
 - i) Director, NIPER-Kolkata visited BCPL Corporate Office facility at Maniktala, 6, Ganesh Chunder Avenue and Panihati factory and also visited Bengal Immunity Centre on 04/09/2015. On 09/10/2015, a team consisting of Dr. Ravichandiran V., Director, NIPER-Kolkata; Dr. Samit Chattopadhyay, Director, CSIR-IICB; Dr. Arun Bandopadhyay; Dr. Rupak Bhadra and Dr. P. Jaisankar; Dr. Asish Kumar Banerjee and Dr. K. K.

Datta visited BCPL for the collaborative partnership with NIPER.

- ii) NIPER-Kolkata has signed a MoU with Bengal Chemical and Pharmaceuticals Ltd. (BCPL), Kolkata to develop a new product of detox agent to clean various organs and other systems of the body and to develop a new anti-snake venom adjuvant which is least toxic to the animal and best immunogenic for snake bite.

i. Collaboration:

With National and International Institutions:

Rare Diseases Initiative

NIPER-Kolkata took up a novel programme of establishing a rare disease initiative at NIPER-Kolkata. Towards that end a concept paper on the subject was made and shared with experts of DoP, National Institute of Health (NIH), and Minnesota University, USA. This initiative was appreciated by DoP and also advised to NIPER-Kolkata to develop a Course Curriculum for students of all the NIPERs and to implement by the end of this year. A discussion is on with NIH, USA, to assist in rare diseases initiative through skill development in rare diseases, teaching and diagnosis through the use of 2nd generation genome sequencing. A draft syllabus on the course regarding rare diseases has been prepared and circulated to all NIPERs.

Strengthening Academia and academia relationship:

- Conducted Industry-academia meeting at NIPER, Kolkata.
- Attended academia and regulatory meeting in Regulatory dept at Kolkata drugs controller office, Kolkata.
- On Sept 14, 2015, visited the school of Tropical Medicine, Kolkata and discussed in details with Prof. Dr Santanu Tripathi, Head, Department of Experimental medicine and pharmacology to set up a joint centre for poison information cell.



- MoU made with School of Tropical Medicine to set up the poison information cell and action has been initiated accordingly.
- Director visited Jadavpur University to initiate a collaborative research and to avail additional resource centre.
- Director and NIPER officials visited Bose Institute, Saltlake, Kolkata and discussed with Dr. Siddhartha Roy, Dean of academic studies for collaborative research.
- Director and NIPER officials visited All India Institute of Hygiene and Public Health on 10.09.2015 to initiate collaborative research on public health care.
- Director visited National Institute of Cholera and Enteric Diseases, Kolkata to initiate a collaborative study in antibacterial resistance and its molecular characterisation and faculty exchange program.
- Director visited CSIR-Central Glass and Ceramic Research Institute, Kolkata, to initiate future collaboration in technology development in medical devices.
- a. NIPER-Kolkata has signed a MoU with BMS (R&D), Bangalore on Nanotechnology application and development activity.
- b. Proposed collaborative venture between KIPMR (King Institute of Preventive Medicine and Research, Guindy and NIPER-Kolkata.
- c. Discussion is on to establish an Extension Centre of NIPER at KIPMR to execute a range of functions and the rich medical and clinical expertise of KIPMR will further strengthen the activities of the joint venture useful for the society. The Centre of Excellence resulting from collaboration between the institutes will bring in more innovations and products that further augment research activities.
- d. Collaborative efforts are on with KIPMR on developing synthetic, phytochemical and herbal-based antiviral and anticancer formulations (NIPER will provide standards, analytical chemistry expertise, expertise in medicinal chemistry, purity details, validation details), formulations developed according to AYUSH guidelines.
- e. KIPMR will successfully validate the antiviral herbal formulation against hepatitis B.
- f. Participated in GMP SEMINAR and GST Seminar conducted by IDMA and DoP.
- g. Participated and delivered a lecture on pharmacovigilance held at KPC Medical College at Kolkata.
- h. Participated and delivered a lecture on antibiotic resistance at Jadavpur University, Kolkata.
- i. Delivered Valedictory address during the 2nd Convention, 2015, Society for Ethnopharmacology, India on 6th December 2015.
- j. NIPER-Kolkata organised a International Symposium during 1st – 3rd March, 2016 on Chemical Biology and Drug Discovery and
- k. Also a programme on diabetes individualized care to precision medicine on 21st March, 2016.

Publication Highlights

Sl. No.	PUBLICATIONS	IF 2014
1.	Park S., Okamura I., Sakashita S., Hye Yum J., Acharya C, Gao L and Sugiyama H. (2015) Development of DNA Metalloenzymes Using a Rational Design Approach and Application in the Asymmetric Diels-Alder Reaction. <i>ACS Catalysis</i> 5 , 4708-4712	9.312
2.	Jaiswal, P., Mohanakumar, K. P., and Rajamma, U. (2015) Serotonin mediated immunoregulation and neural functions: Complicity in the aetiology of autism spectrum disorders. <i>Neurosci Biobehav Rev</i> 55 , 413-	8.802
3.	Sarkar, M., Khare, V., Guturi, K. K., Das, N., and Ghosh, M. K. (2015) The DEAD box protein p68: a crucial regulator of AKT/FOXO3a signaling axis in oncogenesis. <i>Oncogene</i> 34 , 5843-5856	8.459
4.	Naskar, A., Prabhakar, V., Singh, R., Dutta, D., and Mohanakumar, K. P. (2015) Melatonin enhances L-DOPA therapeutic effects, helps to reduce its dose, and protects dopaminergic neurons in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced Parkinsonism in mice. <i>J Pineal Res</i> 58 , 262-274	7.812
5.	Datta, R., Kumar, D., Sultana, A., Hazra, S., Bhattacharyya, D., and Chattopadhyay, S. (2015) Glutathione Regulates 1-Aminocyclopropane-1-Carboxylate Synthase Transcription via WRKY33 and 1-Aminocyclopropane-1-Carboxylate Oxidase by Modulating Messenger RNA Stability to Induce Ethylene Synthesis during Stress <i>Plant Physiol</i> 169 , 2963-2981	6.841
6.	Jana, B., Sarkar, J., Mondal, P., Barman, S., Mohapatra, S., Bhunia, D., Pradhan, K., Saha, A., Adak, A., and Ghosh, S. (2015) A short GC rich DNA derived from microbial origin targets tubulin/microtubules and induces apoptotic death of cancer cells. <i>Chem Commun (Camb)</i> 51 , 12024-12027	6.834
7.	Roy, S., Baral, A., Bhattacharjee, R., Jana, B., Datta, A., Ghosh, S., and Banerjee, A. (2015) Preparation of multi-coloured different sized fluorescent gold clusters from blue to NIR, structural analysis of the blue emitting Au7 cluster, and cell-imaging by the NIR gold cluster. <i>Nanoscale</i> 7 , 1912-1920	6.739
8.	Saha, A., Mohapatra, S., Kurkute, P., Jana, B., Mondal, P., Bhunia, D., and Ghosh, S. (2015) Interaction of Abeta peptide with tubulin causes an inhibition of tubulin polymerization and the apoptotic death of cancer cells. <i>Chem Commun (Camb)</i> 51 , 2249-2252	6.718
9.	Nair, J. B., Mohapatra, S., Ghosh, S., and Maiti, K. K. (2015) Novel lysosome targeted molecular transporter built on a guanidinium-poly-(propylene imine) hybrid dendron for efficient delivery of doxorubicin into cancer cells. <i>Chem Commun (Camb)</i> 51 , 2403-2406	6.718
10.	Ahmed, S. F., Das, N., Sarkar, M., Chatterjee, U., Chatterjee, S., and Ghosh, M. K. (2015) Exosome-mediated delivery of the intrinsic C-terminus domain of PTEN protects it from proteasomal degradation and ablates tumorigenesis. <i>Mol Ther</i> 23 , 255-269	6.425
11.	Bharitkar, Y. P., Das, M., Kumari, N., Kumari, M. P., Hazra, A., Bhayye, S. S., Natarajan, R., Shah, S., Chatterjee, S., and Mondal, N. B. (2015) Synthesis of Bis-pyrrolizidine-Fused Dispiro-oxindole Analogues of Curcumin via One-Pot Azomethine Ylide Cycloaddition: Experimental and Computational Approach toward Regio- and Diastereoselection. <i>Org Lett</i> 17 , 4440-4443	6.364
12.	Manna, M. K., Hossian, A., and Jana, R. (2015) Merging C-H activation and alkene difunctionalization at room temperature: a palladium-catalyzed divergent synthesis of indoles and indolines. <i>Org Lett</i> 17 , 672-675	6.324
13.	Chakraborty, A., and Chakrabarti, S. (2015) A survey on prediction of specificity-determining sites in proteins. <i>Brief Bioinform</i> 16 , 71-88	5.919
14.	Baidya, A. K., Bhattacharya, S., and Chowdhury, R. (2015) Role of the Flagellar Hook-Length Control Protein FliK and sigma28 in cagA Expression in Gastric Cell-Adhered Helicobacter pylori. <i>J Infect Dis</i> 211 , 1779-1789	5.778
15.	Pal, C., Bindu, S., Dey, S., Alam, A., Goyal, M., Shameel Iqbal, M., Maity, P., Adhikari, S. S., and Bandyopadhyay, U. (2015) Corrigendum to "Gallic acid prevents nonsteroidal anti-inflammatory drug-induced gastropathy in rat by blocking oxidative stress and apoptosis" [Free Radic. Biol. Med. 49 (2010) 258-267]. <i>Free Radic Biol Med</i> 86 , 65-66	5.736



Sl. No.	PUBLICATIONS	IF 2014
16.	Bhunias, S. K., Polley, A., Natarajan, R., and Jana, R. (2015) Through-Space 1,4-Palladium Migration and 1,2-Aryl Shift: Direct Access to Dibenzo[a,c]carbazoles through a Triple C-H Functionalization Cascade. <i>Chemistry</i> 21 , 16786-16791	5.731
17.	Roy, M., Giri, A. K., Dutta, S., and Mukherjee, P. (2015) Integrated phytobial remediation for sustainable management of arsenic in soil and water. <i>Environ Int</i> 75 , 180-198	5.664
18.	Paul, S., and Giri, A. K. (2015) Epimutagenesis: A prospective mechanism to remediate arsenic-induced toxicity. <i>Environ Int</i> 81 , 8-17	5.664
19.	Kundu, P., Mondal, A., Das, B., and Chowdhury, C. (2015) A Straightforward Approach for the Stereo selective Synthesis of (E)-2-Aryl/vinylmethylenes-1, 4-benzodiazepines and-1,4-benzodiazepin-5-ones through Palladium/Charcoal-Catalyzed Reactions. <i>Adv Syn Catal</i> 357 , 3737-3752	5.663
20.	Jain, C. K., Pradhan, B. S., Banerjee, S., Mondal, N. B., Majumder, S. S., Bhattacharyya, M., Chakrabarti, S., Roychoudhury, S., and Majumder, H. K. (2015) Sulfonylquinovosyl diacylglyceride selectively targets acute lymphoblastic leukemia cells and exerts potent anti-leukemic effects in vivo. <i>Sci Rep</i> 5 , 12082	5.578
21.	Ghosh, A. K., Sardar, A. H., Mandal, A., Saini, S., Abhishek, K., Kumar, A., Purkait, B., Singh, R., Das, S., Mukhopadhyay, R., Roy, S., and Das, P. (2015) Metabolic reconfiguration of the central glucose metabolism: a crucial strategy of Leishmania donovani for its survival during oxidative stress. <i>FASEB J</i> 29 , 2081-2098	5.48
22.	Bhattacharjya, S., Roy, K. S., Ganguly, A., Sarkar, S., Panda, C. K., Bhattacharyya, D., Bhattacharyya, N. P., and Roychoudhury, S. (2015) Inhibition of nucleoporin member Nup214 expression by miR-133b perturbs mitotic timing and leads to cell death. <i>Mol Cancer</i> 14 , 42	5.397
23.	Jain, C. K., Roychoudhury, S., and Majumder, H. K. (2015) Selective killing of G2 decatenation checkpoint defective colon cancer cells by catalytic topoisomerase II inhibitor. <i>Biochim Biophys Acta</i> 1853 , 1195-1204	5.297
24.	Pradhan, N., Guha, R., Chowdhury, S., Nandi, S., Konar, A., and Hazra, S. (2015) Curcumin nanoparticles inhibit corneal neovascularization. <i>J Mol Med (Berl)</i> 93 , 1095-1106	5.107
25.	Maiti, G. P., Ghosh, A., Mondal, P., Baral, A., Datta, S., Samadder, S., Nayak, S. P., Chakrabarti, J., Biswas, J., Sikdar, N., Chowdhury, S., Roy, B., Roychowdhury, S., and Panda, C. K. (2015) SNP rs1049430 in the 3'-UTR of SH3GL2 regulates its expression: Clinical and prognostic implications in head and neck squamous cell carcinoma. <i>Biochim Biophys Acta</i> 1852 , 1059-1067	5.089
26.	Saha S., Ghosh M., Dutta S.K., 2015. A potent tumoricidal co-drug 'Bet-CA' - an ester derivative of betulinic acid and dichloroacetate selectively and synergistically kills cancer cells. <i>Scientific Reports</i> , 5 Article Number:7762	5.078
27.	Mandloi, S., and Chakrabarti, S. (2015) PALM-IST: Pathway Assembly from Literature Mining--an Information Search Tool. <i>Sci Rep</i> 5 , 10021	5.078
28.	Mahata, B., Banerjee, A., Kundu, M., Bandyopadhyay, U., and Biswas, K. (2015) TALEN mediated targeted editing of GM2/GD2-synthase gene modulates anchorage independent growth by reducing anoikis resistance in mouse tumor cells. <i>Sci Rep</i> 5 , 9048	5.078
29.	Anshu, A., Mannan, M. A., Chakraborty, A., Chakrabarti, S., and Dey, M. (2015) A novel role for protein kinase Kin2 in regulating HAC1 mRNA translocation, splicing, and translation. <i>Mol Cell Biol</i> 35 , 199-210	5.036
30.	Nath, S., Chowdhury, A., Dey, S., Roychoudhury, A., Ganguly, A., Bhattacharyya, D., and Roychoudhury, S. (2015) Deregulation of Rb-E2F1 axis causes chromosomal instability by engaging the transactivation function of Cdc20-anaphase-promoting complex/cyclosome. <i>Mol Cell Biol</i> 35 , 356-369	5.036
31.	Banerjee, P., Chander, V., and Bandyopadhyay, A. (2015) Balancing functions of annexin A6 maintain equilibrium between hypertrophy and apoptosis in cardiomyocytes. <i>Cell Death Dis</i> 6 , e1873	5.014
32.	Khan, M. W., and Chakrabarti, P. (2015) Gluconeogenesis combats cancer: opening new doors in cancer biology. <i>Cell Death Dis</i> 6 , e1872	5.014



Sl. No.	PUBLICATIONS	IF 2014
33.	Mukherjee, B., Paul, J., Mukherjee, S., Mukhopadhyay, R., Das, S., Naskar, K., Sundar, S., Dujardin, J. C., Saha, B., and Roy, S. (2015) Antimony-Resistant <i>Leishmania donovani</i> Exploits miR-466i To Deactivate Host MyD88 for Regulating IL-10/IL-12 Levels during Early Hours of Infection. <i>J Immunol</i> 195 , 2731-2742	4.922
34.	Chatterjee, D., Bhattacharjee, P., Sau, T. J., Das, J. K., Sarma, N., Bandyopadhyay, A. K., Roy, S. S., and Giri, A. K. (2015) Arsenic exposure through drinking water leads to senescence and alteration of telomere length in humans: A case-control study in West Bengal, India. <i>Mol Carcinog</i> 54 , 800-80	4.808
35.	Das, S. N., Chowdhury, A., Tripathi, N., Jana, P. K., and Mandal, S. B. (2015) Exploitation of in situ generated sugar-based olefin keto-nitrones: synthesis of carbocycles, heterocycles, and nucleoside derivatives. <i>J Org Chem</i> 80 , 1136-1148	4.638
36.	Mal, K., Das, S., Maiti, N. C., Natarajan, R., and Das, I. (2015) ZnI2-Catalyzed Diastereoselective [4 + 2] Cycloadditions of beta,gamma-Unsaturated alpha-Ketothioesters with Olefins. <i>J Org Chem</i> 80 , 2972-2988	4.638
37.	Mal, K., Kaur, A., Haque, F., and Das, I. (2015) PPh3.HBr-DMSO: A Reagent System for Diverse Chemoselective Transformations. <i>J Org Chem</i> 80 , 6400-6410	4.638
38.	Kesh, K., Subramanian, L., Ghosh, N., Gupta, V., Gupta, A., Bhattacharya, S., Mahapatra, N. R., and Swarnakar, S. (2015) Association of MMP7 -181A-->G Promoter Polymorphism with Gastric Cancer Risk: INFLUENCE OF NICOTINE IN DIFFERENTIAL ALLELE-SPECIFIC TRANSCRIPTION VIA INCREASED PHOSPHORYLATION OF CAMP-RESPONSE ELEMENT-BINDING PROTEIN (CREB). <i>J Biol Chem</i> 290 , 14391-14406	4.6
39.	Paul, S. S., Sil, P., Halder, S., Mitra, S., and Chattopadhyay, K. (2015) Subtle Change in the Charge Distribution of Surface Residues May Affect the Secondary Functions of Cytochrome c. <i>J Biol Chem</i> 290 , 14476-14490	4.6
40.	Barman, B., and Bhattacharyya, S. N. (2015) mRNA Targeting to Endoplasmic Reticulum Precedes Ago Protein Interaction and MicroRNA (miRNA)-mediated Translation Repression in Mammalian Cells. <i>J Biol Chem</i> 290 , 24650-24656	4.573
41.	Ghosh, S., Bose, M., Ray, A., and Bhattacharyya, S. N. (2015) Polysome arrest restricts miRNA turnover by preventing exosomal export of miRNA in growth-retarded mammalian cells. <i>Mol Biol Cell</i> 26 , 1072-1083	4.548
42.	Lande, R., Chamilos, G., Ganguly, D., Demaria, O., Frasca, L., Durr, S., Conrad, C., Schroder, J., and Gilliet, M. (2015) Cationic antimicrobial peptides in psoriatic skin cooperate to break innate tolerance to self-DNA. <i>Eur J Immunol</i> 45 , 203-213	4.518
43.	Bhunia, D., Chowdhury, R., Bhattacharyya, K., and Ghosh, S. (2015) Fluorescence fluctuation of an antigen-antibody complex: circular dichroism, FCS and smFRET of enhanced GFP and its antibody. <i>Phys Chem Chem Phys</i> 17 , 25250-25259	4.493
44.	Maity, M., Dolui, S., and Maiti, N. C. (2015) Hydrogen bonding plays a significant role in the binding of coomassie brilliant blue-R to hemoglobin: FT-IR, fluorescence and molecular dynamics studies. <i>Phys Chem Chem Phys</i> 17 , 31216-31227	4.493
45.	Sinha, R., Roychoudhury, J., Palit, P., and Ali, N. (2015) Cationic liposomal sodium stibogluconate (SSG), a potent therapeutic tool for treatment of infection by SSG-sensitive and -resistant <i>Leishmania donovani</i> . <i>Antimicrob Agents Chemother</i> 59 , 344-355	4.451
46.	Gupta, P., Das, P. K., and Ukil, A. (2015) Antileishmanial effect of 18beta-glycyrrhetic acid is mediated by Toll-like receptor-dependent canonical and noncanonical p38 activation. <i>Antimicrob Agents Chemother</i> 59 , 2531-2539	4.451
47.	Saha, S., Choudhury, J., and Ain, R. (2015) MicroRNA-141-3p and miR-200a-3p regulate insulin-like growth factor 2 during mouse placental development. <i>Mol Cell Endocrinol</i> 414 , 186-193	4.405
48.	Halder, S., Sil, P., Thangamuniyandi, M., and Chattopadhyay, K. (2015) Conversion of amyloid fibrils of cytochrome c to mature nanorods through a honeycomb morphology. <i>Langmuir</i> 31 , 4213-4223	4.384
49.	Das, P. J., Paul, P., Mukherjee, B., Mazumder, B., Mondal, L., Baishya, R., Debnath, M. C., and Dey, K. S. (2015) Pulmonary Delivery of Voriconazole Loaded Nanoparticles Providing a Prolonged Drug Level in Lungs: A Promise for Treating Fungal Infection. <i>Mol Pharm</i> 12 , 2651-2664	4.384



Sl. No.	PUBLICATIONS	IF 2014
50.	Joshi, N., Basak, S., Kundu, S., De, G., Mukhopadhyay, A., and Chattopadhyay, K. (2015) Attenuation of the Early Events of a-Synuclein Aggregation: A Fluorescence Correlation Spectroscopy and Laser Scanning Microscopy Study in the Presence of Surface-Coated Fe ₃ O ₄ Nanoparticles. <i>Langmuir</i> 31 , 1469-1478	4.384
51.	Biswas, A., Kurkute, P., Saleem, S., Jana, B., Mohapatra, S., Mondal, P., Adak, A., Ghosh, S., Saha, A., Bhunia, D., and Biswas, S. C. (2015) Novel hexapeptide interacts with tubulin and microtubules, inhibits Abeta fibrillation, and shows significant neuroprotection. <i>ACS Chem Neurosci</i> 6 , 1309-1316	4.362
52.	Basu, A., and Kumar, G. S. (2015) Interaction of toxic azo dyes with heme protein: biophysical insights into the binding aspect of the food additive amaranth with human hemoglobin. <i>J Hazard Mater</i> 289 , 204-209	4.331
53.	Akhter, R., Sanphui, P., Das, H., Saha, P., and Biswas, S. C. (2015) The regulation of p53 up-regulated modulator of apoptosis by JNK/c-Jun pathway in beta-amyloid-induced neuron death. <i>J Neurochem</i> 134 , 1091-1103	4.281
54.	Bhattacharjee, A., Majumder, S., Majumdar, S. B., Choudhuri, S. K., Roy, S., and Majumdar, S. (2015) Co-administration of glycyrrhizic acid with the antileishmanial drug sodium antimony gluconate (SAG) cures SAG-resistant visceral leishmaniasis. <i>Int J Antimicrob Agents</i> 45 , 268-277	4.259
55.	Basu, M., Bhattacharya, R., Ray, U., Mukhopadhyay, S., Chatterjee, U., and Roy, S. S. (2015) Invasion of ovarian cancer cells is induced by PITX2-mediated activation of TGF-beta and Activin-A. <i>Mol Cancer</i> 14 , 162	4.257
56.	Mondal, P., Chatteraj, S., Chowdhury, R., Bhunia, D., Ghosh, S., and Bhattacharyya, K. (2015) Direct observation of the growth and shrinkage of microtubules by single molecule Forster resonance energy transfer. <i>Phys Chem Chem Phys</i> 17 , 6687-6690	4.198
57.	Jash, C., Basu, P., Payghan, P. V., Ghoshal, N., and Kumar, G. S. (2015) Chelerythrine-lysozyme interaction: spectroscopic studies, thermodynamics and molecular modeling exploration. <i>Phys Chem Chem Phys</i> 17 , 16630-16645	4.198
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Sl. No.	PUBLICATIONS	IF 2014
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Sl. No.	PUBLICATIONS	IF 2014
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Sl. No.	PUBLICATIONS	IF 2014
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148.	Bharitkar, Y.P., Kanha,R.S., Suneel N., Mondal, S.K., Hazra, A., and Mondal, N.B. (2015) Chemistry of withaferin-A: chemo, regio, and stereoselective synthesis of novel spiro-pyrrolizidino-oxindole adducts of withaferin-A via one-pot three-component [3+2] azomethine ylide cycloaddition and their cytotoxicity evaluation. <i>Mol Divers</i> 19 , 251-261	2.544
149.	Baishya, R., Nayak, D.K., Karmakar, S., Chattopadhyay, S., Sachdeva, S.S., Sarkar, B.R., Ganguly, S., and Debnath, M.C. (2015) Synthesis and Evaluation of Technetium-99m-Labeled Bioreductive Pharmacophores Conjugated with Amino Acids and Peptides for Tumor Imaging. <i>Chem Biol Drug Des</i> 85 , 504-517	2.507
150.	Naiya, G., Kaypee, S., Kundu, T.K., and Roy, S. (2015) A Constrained Helical Peptide Against S100A4 Inhibits Cell Motility in Tumor Cells. <i>Chem Biol Drug Des</i> 86 , 945-950	2.485
151.	Datta De, D., and Roychoudhury, S. (2015) To be or not to be: The host genetic factor and beyond in Helicobacter pylori mediated gastro-duodenal diseases. <i>World J Gastroenterol</i> 21 , 2883-2895	2.433
152.	Basu, P., and Kumar, G.S. (2015) Entropy driven binding of the alkaloid chelerythrine to polyadenylic acid leads to spontaneous self-assembled structure formation. <i>J Chem Thermodyn</i> 81 , 116-123	2.423
153.	Basu, A., and Kumar, G.S. (2015) Thermodynamic characterization of proflavine-DNA binding through microcalorimetric studies. <i>J Chem Thermodyn</i> 87 , 1-7	2.423
154.	Dinda, M., Dasgupta, U., Singh, N., Bhattacharyya, D., and Karmakar, P. (2015) PI3K-mediated proliferation of fibroblasts by Calendula officinalis tincture: implication in wound healing. <i>Phytother Res</i> 29 , 607-616	2.397
155.	Sanyal, I., Barman, P. D., and Banerjee, A. K. (2015) Stereoselective synthesis of higher homologues of pantolactone from (R)-glyceraldehyde acetonide. <i>Tetrahedron Lett</i> 56 ,789-792	2.391
156.	Sarkar, S., Pal, R., Roy, M., Chatterjee, N., Sarkar, S., and Sen, A. K . (2015) Nanodomain cubic copper (II) oxide as reusable catalyst for the synthesis of amides by amidation of aryl halides with isocyanides. <i>Tetrahedron Lett</i> 56 , 623-626	2.391
157.	Chatterjee, N., Pal, R., and Sarkar, S. (2015) Synthesis of triazole-fused tetracyclic glycosides in aqueous medium: application of nanodomain cubic cuprous oxide as reusable catalyst in one-pot domino Sonogashira-cyclization. . <i>Tetrahedron Lett</i> 56 , 3886-3889	2.391
158.	Ghosh, J., Biswas, P., Sarkar, T., and Bandyopadhyay, C. (2015) Iodine-induced efficient construction of a chromone-linked furo-[3,2-c]chromene scaffold by a one-pot 3-component cascade reaction. <i>Tetrahedron Lett</i> 56 , 7193-7196	2.379
159.	Majumder, R., Banik, S., P., Ramrakhiani, L., and Khowala, S. (2015) .Bioremediation by alkaline protease (AkP) from edible mushroom Termitomyces clypeatus: optimization approach based on statistical design and characterization for diverse applications. <i>J Chem Technol Biot</i> 90 ,1886-1896	2.349
160.	Banerjee, S., Chattopadhyay, A., Banerjee, A., Haridas, M., Saini, P., Das, M., Majik, M.S., and Maurya, Y.K. (2015) Synthesis and photophysical characterization of quasi push-pull dicyanodibenzodioxins and their anti-tumor activity against glioma cell line C6. <i>Bioorg Med Chem Lett</i> 25 ,753-757	2.331
161.	Padmanaban, E., Boccaletti, S., and Dana, S. K. (2015) Emergent hybrid synchronization in coupled chaotic systems. <i>Phys Rev E Stat Nonlin Soft Matter Phys</i> 91 , 022920	2.326
162.	Hens, C., Pal, P., and Dana, S. K. (2015) Bursting dynamics in a population of oscillatory and excitable Josephson junctions. <i>Phys Rev E Stat Nonlin Soft Matter Phys</i> 92 , 022915	2.288



Sl. No.	PUBLICATIONS	IF 2014
163.	Mishra, A., Hens, C., Bose, M., Roy, P. K., and Dana, S. K. (2015) Chimeralike states in a network of oscillators under attractive and repulsive global coupling. <i>Phys Rev E Stat Nonlin Soft Matter Phys</i> 92 , 062920	2.326
164.	Padmanaban, E., Saha, S., Vigneshwaran, M., and Dana, S. K. (2015) Amplified response in coupled chaotic oscillators by induced heterogeneity. <i>Phys Rev E Stat Nonlin Soft Matter Phys</i> 92 , 062916	2.288
165.	Katarkar, A., Haldar, Pallab K., and Chaudhuri, K. (2015) De novo design based pharmacophore query generation and virtual screening for the discovery of Hsp-47 inhibitors. <i>Biochem Mol Biol Edu</i> 456 , 707-713	2.288
166.	Samanta, T., Munda, R. N., Roymahapatra, G., Nand, y A., Das Saha, K., Al-Deyab, S. S., and Dinda, J. (2015) Silver(I), Gold(I) and Gold(III)-N-Heterocyclic carbene complexes of naphthyl substituted annelated ligand: Synthesis, structure and cytotoxicity. <i>J Organomet Che</i> , 791 . 183-191	2.288
167.	Bhowmik, D., Fiorillo, G., Lombardi, P., and Kumar, G. S. (2015) Recognition of human telomeric G-quadruplex DNA by berberine analogs: effect of substitution at the 9 and 13 positions of the isoquinoline moiety. <i>J Mol Recognit</i> 28 , 722-730	2.281
168.	Pradhan, A. B., Mandal, S. K., Banerjee, S., Mukherjee, A., Das S., Bukhsh, A. R. K., and Saha, A. (2015) A highly selective fluorescent sensor for zinc ion based on quinoline platform with potential applications for cell imaging studies, <i>Polyhedron</i> 94 , 75-82	2.173
169.	Chatterjee, D., Jaiswa, I N., Bose, J.C., Bose, K., Mahato, R.B., and Bhattacharyya, D. (2015) Interaction of Ru-III(EDTA) with cellular thiols and O-2: biological implications thereof. <i>J Coord Chem</i> 68 , 3229-3235	2.151
170.	Mukherjee, A., and Swarnakar, S. (2015) Implication of matrix metalloproteinases in regulating neuronal disorder. <i>Mol Biol Rep</i> 42 , 1-11	2.047
171.	Hongray, T., Balakrishnan, J., and Dana, S. K. (2015) Bursting behaviour in coupled Josephson junctions. <i>Chaos</i> 25 , 123104	2.012
172.	Molla ,H.A., Bhowmick, R., Katarkar, A., Chaudhuri, K., Gangopadhyay, S., and Ali, M. (2015) A novel rhodamine-3, 4-dihydro-2H-1, 3-benzoxazine conjugate as a highly sensitive and selective chemosensor for Fe ³⁺ ions with cytoplasmic cell imaging possibilities. <i>Anal Methods-UK</i> 7 , 5149-5156	1.958
173.	Kundu, S., Banerjee, A., De, A., Khan, A. Y., Kumar, G. S., Bhadra, R., and Ghosh, P. (2015) Synthesis, Fluorescence Spectra, Redox Property and the DNA Binding Studies of 7-phenylacenaphtho[1,2-b]quinoxalin-7-ium chloride: Evidences of the Formation of Neutral Radical Analogue. <i>J Fluoresc</i> 25 , 1645-1654	1.954
174.	Bhattachary, A P., Ghosh, S., Swarnakar, S., and Mukhopadhyay, A. (2015) Tannery Effluent Treatment by Microfiltration through Ceramic Membrane for Water Reuse: Assessment of Environmental Impacts. <i>Clean-Soil Air Water</i> 43 , 633-644	1.938
175.	Hens, C., Dana, S. K., and Feudel, U. (2015) Extreme multistability: Attractor manipulation and robustness. <i>Chaos</i> 25 , 053112	1.927
176.	Banik, S. P., Mukherjee, S., Pal, S., Ghorai, S., Majumder, R., and Khowala, S. (2015) Enhancement of extracellular cellobiase activity by reducing agents in the filamentous fungus <i>Termitomyces clypeatus</i> . <i>Biotechnol Lett</i> 37 , 175-181	1.838
177.	Ghosh, S., Chaudhuri, T., Padmanaban, E., and Mukhopadhyay, C. (2015) The idiosyncrasies of (BBIM-alkane)DB30C10 MIMs. <i>J Mol Struct</i> , 1097 , 6-14	1.761
178.	Sharma, K., and Bhattacharyya, D. (2015) Immunoglobulin isotype isolated from human placental extract does not interfere in complement-mediated bacterial opsonization within the wound milieu. <i>Febs Open Bio</i> 5 , 369-377	1.736



Sl. No.	PUBLICATIONS	IF 2014
179.	Ghosh, S., Schmiedekamp, Ann Marie, Padmanaban, E. Ray, b J. Butcher, Chaudhuri, T, Rao, N., and Mukhopadhyay, C. (2015) Anomalous behaviour of the bis(benzimidazolium)butane [2]pseudorotaxanes of dibenzo-24-crown-8: a comparative study of methane, ethane, propane and butane bis(benzimidazolium)alkane]dibenzo-24-crown-8 systems with variable spacers. <i>J Incl Phenom Macro</i> 81 , 321-340	1.515
180.	Behera, A., De, K., Chattopadhyay, S., and Misra, M. (2015) Metabolic stability and biological evaluation of Tc-99m-HYNIC-Tyr(3)-Octreotide as somatostatin receptor positive tumor imaging agent. <i>J Radioanal Nucl Ch</i> 304 , 595-602	1.426
181.	Banerjee, I., Behera, A., De, K. Chattopadhyay, S., Sachdev, S. S., Sarkar, B., Ganguly, S., and Misra, M. (2015) Synthesis, characterization, biodistribution and scintigraphy of Tc-99m-paclitaxel: a potential tracer of paclitaxel. <i>J Radioanal Nucl Ch</i> 304 , 633-643	1.415
182.	Mondal, A., Guria, T., and Maity, T. K. (2015) A new ester of fatty acid from a methanol extract of the whole plant of <i>Amaranthus spinosus</i> and its alpha-glucosidase inhibitory activity. <i>Pharm Biol</i> 53 , 600-604	1.415
183.	Singh, N., and Bhattacharyya, D. (2015) Evaluation of the presence of reduced nicotinamide adenine dinucleotide phosphate in bacterial metabolites used as immunostimulators and its role in nitric oxide induction. <i>Microbiol Immunol</i> , 59 , 311-321	1.337
184.	Maiti, G.P., Ghosh, A., Monda, I P., Ghosh, S., Chakraborty, J., Roy, A., Roychowdhury, S., and Panda, C.K. (2015) Frequent inactivation of SLIT2 and ROBO1 signaling in head and neck lesions: clinical and prognostic implications. <i>Or Surg Or Med Or Pa</i> 119 , 202-212	1.306
185.	Bharitkar, Y. P., Hazra, A., Apoorva Poduri, N. S., Ash, A., Maulik, P. R., and Mondal, N. B. (2015) Isolation, structural elucidation and cytotoxicity evaluation of a new pentahydroxy-pimarane diterpenoid along with other chemical constituents from <i>Aerva lanata</i> . <i>Nat Prod Res</i> 29 , 253-261	1.265
186.	Singh, M. K., Paul, J., De, T., and Chakraborti, T. (2015) Bioactivity guided fractionation of <i>Moringa oleifera</i> Lam. flower targeting <i>Leishmania donovani</i> . <i>Indian J Exp Biol</i> 53 , 747-752	1.225
187.	Datta, S., Roy, S., and Manna, M. (2015) Therapy with radio-attenuated vaccine in experimental murine visceral leishmaniasis showed enhanced T cell and inducible nitric oxide synthase levels, suppressed tumor growth factor-beta production with higher expression of some signaling molecules. <i>Braz J Infect Dis</i> 19 , 36-42	1.165
188.	Bhar, K., Maity, A., Ghosh, A., Das, T., Dastidar, S. G., and Siddhanta, A. (2015) Phosphorylation of Leghemoglobin at S45 is Most Effective to Disrupt the Molecular Environment of Its Oxygen Binding Pocket. <i>Protein J</i> 34 , 158-167	1.096
189.	Kumar, A., Chowdhury, S. R., Jatte, K. K., Chakrabarti, T., Majumder, H. K., Jha, T., and Mukhopadhyay, S. (2015) Anthocephaline, a new indole alkaloid and cadambine, a potent inhibitor of DNA topoisomerase IB of <i>Leishmania donovani</i> (LdTOP1LS), isolated from <i>Anthocephalus cadamba</i> . <i>Nat Prod Commun</i> 10 , 297-299	1.039
190.	Kumar, D., Tejaswi, C., Rasamalla, S., Mallick, S., and Pala, B. C. (2015) Bio-assay Guided Isolation of Anti-cancer Compounds from <i>Anthocephalus cadamba</i> Bark. <i>Nat Prod Commun</i> 10 , 1349-1350	0.924
191.	Ghosh, P., Mukherjee, N., Ghosh, K., Mallick, S., Pal, C., Laskar, A., and Ghosh, A. (2015) Prospective microglia and brain macrophage distribution pattern in normal rat brain shows age sensitive dispersal and stabilization with development. <i>Indian J Exp Biol</i> 53 , 561-567	0.906
192.	Mitra, J., Sharma, K., and Bhattacharyya, D. (2015) Molecular modelling approaches for designing inhibitors of L-amino acid oxidase from <i>Crotalus adamanteus</i> venom. <i>Curr Sci India</i> 108 , 1086-1096	0.835



Sl. No.	PUBLICATIONS	IF 2014
193.	Islam, A. S., Alam, R., Katarkar, A., Chaudhuri, K., and Ali, M. (2015) Di-oxime based selective fluorescent probe for arsenate and arsenite ions in a purely aqueous medium with living cell imaging applications and H-bonding induced microstructure formation. <i>Analyst</i> 140 , 2979-2983	0.833
194.	Banerjee, R., Padmanaban, E., and Dana, S. K. (2015) Control of partial synchronization in chaotic oscillators <i>Pramana-J Phys</i> 84 , 203-215	0.833
195.	Hens, C. R. Mishra, A., Roy, P.K., Sen, A., and Dana, S.K. (2015) Chimera states in a population of identical oscillators under planar cross-coupling. <i>Pramana-J Phys</i> 84 , 229-235	0.72
196.	Ahmed, S. M., Mukherjee, P. K., Bahadur, S., Kar, A., Mukherjee, K., Karmakar, S., and Bandyopadhyay, A. (2015) Interaction potential of <i>Trigonella foenum graecum</i> through cytochrome P450 mediated inhibition. <i>Indian J Pharmacol</i> 47 , 530-534	0.72
197.	Biswas, P., Ghosh, J., Sarkar, T., and Bandyopadhyay, C. (2015) Amine-controlled reduction of 2-aminochromone-3-carbaldehyde with Zn and acetic acid. <i>J Chem Res</i> 12 , 734-737.	0.691
198.	Bhowmik, A., Khan, R., and Ghosh, M. K. (2015) Blood brain barrier: a challenge for effectual therapy of brain tumors. <i>Biomed Res Int</i> 2015 , 320941	0.633
199.	Bharitkar, Y.P, Hazra, A., Shah, S., Saha, S., Matoori, A.K., and Mondal, N.B. (2015) New flavonoid glycosides and other chemical constituents from <i>Clerodendrum phlomidis</i> leaves: isolation and characterisation. <i>Nat Prod Res</i> 29 ,1850-1856	0
200.	Mondal, A.(2015) Sonication Assisted Three Phase Partitioning for the Extraction of Palmitic Acid and Elaidic Acid from <i>Cassia sophera</i> Linn. <i>Sep Sci Technol</i> 50 , 1999-2003	0
201.	Pal, U., Pramanik, S.K., Bhattacharya, B., and Banerji, B. (2015). Binding interaction of a novel fluorophore with serum albumins: steady state fluorescence perturbation and molecular modeling analysis., <i>Springerplus</i> 4 , 548	0
202.	Banerji, B., and Pramanik, S. K. (2015) Binding studies of creatinine and urea on iron-nanoparticle. <i>Springerplus</i> 4 , 708	0
203.	Mandal, C., Schwartz-Albiez, R., and Vlasak, R. (2015) Functions and Biosynthesis of O-Acetylated Sialic Acids. <i>Top Curr Chem</i> 366 , 1-30	0

694.51/197
= 3.52

Doctorates From CSIR-IICB

Sl. No.	Recipient's Name	Title of the Thesis	University	Date of Award	Supervisor's Name	Division
1.	Manidip Shasmal	Investigation on ribosome structure and dynamics: Mycobacterium ribosome in focus.	Calcutta	16.10.2015	Dr. Jayati Sengupta	Structural Biology & Bioinformatics
2.	Sandip Mukherjee	Biophysical Characterization of Antimony Sensitive and Antimony Resistant Clinical Leishmani Donovanii Isolates and Interaction with Novel Antileishmanial Drug.	Calcutta	13.10.2015	Dr. Syamal Roy	Infectious Disease & Immunology
3.	Tapashi Mandal	Novel crosstalks in Stat3 regulation involving crucial signaling pathways: Implications in oncogenesis.	Calcutta	11.06.2015	Dr. Mrinal K Ghosh	Cancer Biology & Inflammatory Disorder
4.	Ranjib Banerjee	Studies on synchronization and enhancement in coupled oscillators.	Jadavpur	2015	Dr. Syamal Dana	Instrumentation
5.	Abhishek Nandy	Anticancer Role of Some of the Gold N-Heterocyclic Carbene Compounds.	Calcutta	01.02.2016	Dr. Krishna Das Saha	Department of Biotechnology
6.	Amrita Das	Protective Efficacy of Leishmanial Cysteine Proteases as Potent Vaccine Candidates against Experimental Visceral Leishmaniasis.	Calcutta	December, 2015	Dr. Nahid Ali	Infectious Disease & Immunology
7.	Anirban Chatterjee	Protein kinase CK2 evokes premature degradation of PML in cancer: implicative study of some crucial pro-oncogenic signaling dynamics.	Calcutta	28.11.2014	Dr. Mrinal K Ghosh	Cancer Biology & Inflammatory Disorder
8.	Aptarshi Roy	Glycobiological and immunological approach to understand the host pathogen interaction in Indian Visceral Leishmaniasis.	Calcutta	01.02.2016	Dr. Chitra Mandal	Cancer Biology & Inflammatory Disorder
9.	Arup Kumar Bag	Proteomic and Glycomic approaches in understanding of Disease Biology.	Calcutta	07.01.2016	Dr. Chitra Mandal	Cancer Biology & Inflammatory Disorder
10.	Ashok Behera	Synthesis of New Somatostatin Receptor Binding Radio-labelled peptides: Physico-chemical and Biological Evaluation and Scintigraphic Studies.	Jadavpur	27.06.2014	Dr. Mridula Misra, (CSIR-IICB), Dr. Sankha Chattopadhyay (VECC-BRIT), & Dr. Amalesh Samanta (Jadavpur University.)	Infectious Disease & Immunology Division
11.	Atul Katarkar	Signalin pathways and gene-gene network interaction in the pathogenesis of Oral submucous fibrosis: a precancerous condition.	Jadavpur	16.02. 2016	Dr. Keya Chaudhuri	Molecular genetics



Sl. No.	Recipient's Name	Title of the Thesis	University	Date of Award	Supervisor's Name	Division
12.	Bimolendu Das	Development of elegant methodologies for the synthesis of heterocycles and other compounds of biological interests.	Jadavpur	August, 2014	Dr. Chinmay Chowdhury	Organic & Medicinal Chemistry
13.	Biswajit Chakraborty	Synthesis of various analogues based on Andrographolide and Betulinic acid and evaluation of their anti-cancer potential	Jadavpur	30.11.2015	Dr. Chinmay Chowdhury	Organic & Medicinal Chemistry
14.	Bornita Das	Amelioration of arsenic toxicity by garlic and its major bioactive components.	Jadavpur	October, 2015	Dr. Keya Chaudhuri	Molecular genetics
15.	Chandrima Jash	Biophysical studies on the interaction of isoquinoline alkaloids with lysozyme.	Jadavpur	24.12.2015	Dr. G. Suresh Kumar	Organic & Medicinal Chemistry
16.	Chiranjit Acharya	Synthetic studies on chiral and achiral organic compounds using metal and biocatalysts.	Jadavpur	05.08.2015	Dr. P. Jaisankar	Organic & Medicinal Chemistry
17.	Chittaranjan Hens	Multiple attractor dynamics in coupled oscillators.	Jadavpur	2015	Dr. Syamal Dana	Instrumentation
18.	Debashree Chatterjee	Delineation of innate immune response of Vibrio cholerae and its outer membrane vesicles in an epithelial cell-dendritic cell co-culture model.	Jadavpur	May 2015	Dr. Keya Chaudhuri	Molecular genetics
19.	Debasmita Dutta	Evaluation of Molecular Mechanism Towards Apoptotic and Autophagic Effects of Betulinic acid Analogue and its Nanocapsulated Delivery.	Jadavpur	24.02.2016	Dr. Padma Das & Dr. Krishna Das Saha	Cancer Biology & Inflammatory Disorder
20.	Debdut Naskar	Role of Wnt5a-Fz5 Signaling in Innate Immunity.	Calcutta	Jan, 2015	Dr. Malini Sen	Cancer Biology & Inflammatory Disorder
21.	Deepak Kumar	Role of apoptosis, autophagy and mitochondrial dysfunction in anti leukemic activities of andrographolide and indole derivatives.	Jadavpur	25.08.2015	Dr. Padma Das & Dr. P. Jaisankar	Cancer Biology & Inflammatory Disorder
22.	Dipak Kumar Nayak	Potential of the [99mTc(CO) ₃ (H ₂ O) ₃] Moiety for the Labeling of Biomolecules for Infection Diagnosis.	Jadavpur	01.09. 2015	Dr. Mita Chatterjee Debnath	Infectious Diseases & Immunology Division



Sl. No.	Recipient's Name	Title of the Thesis	University	Date of Award	Supervisor's Name	Division
23.	Goutam Kulsi	Design and Synthesis of Triazole based Peptidomimetic Macrocycles and other Heterocycles: Studies on the Self-Assembly and Anion Binding Property of the Macrocycles.	Jadavpur	2015	Dr. Partha Chattopadhyay & Dr. Krishnannanda Chattopadhyay	Organic & Medicinal Chemistry
24.	Indranil Paul	Role and Regulation of the E3 Ubiquitin Ligase CHIP in Glioma.	Jadavpur	09.12.2013	Dr. Mrinal K Ghosh	Cancer Biology & Inflammatory Disorder
25.	Joydeep Paul	TLR and immune response: Role of B-(1-4)-Galactose terminal Glycans in enhancements of immune response and protection against experimental Visceral Leishmaniasis.	Calcutta	08.10.2015	Dr. Krishna Das Saha & Late Dr. Tripti De	Cancer Biology & Inflammatory Disorder
26.	Kiran Kr. Naidu Guturi	Understanding the Molecular Mechanisms of Wnt/ β -Catenin Signalling in Cancer.	Jadavpur	27.08.2013	Dr. Mrinal K Ghosh	Cancer Biology & Inflammatory Disorder
27.	Manoj Kumar Singh	Antileishmanial Activity of Metal Compounds and Natural Extracts of Commonly Occurring Plants.	Calcutta	2014	Late Dr. Tripti De	Infectious Disease & Immunology Division
28.	Atanu Biswas	Biomolecular Assembly In Surface And Solution.	Jadavpur	17.09. 2015.	Dr. Surajit Ghosh	Organic & Medicinal Chemistry
29.	Pallashri Saha	Role of bioactive components of ginger and garlic in the reduction of Vibrio cholerae induced infection in model systems.	Calcutta Calcutta	March 02, 2016	Dr. Keya Chaudhuri	Molecular genetics
30.	Rajib Majumder	Regulatory Studies of Proteases from Filamentous Fungus Termitomyces clypeatus.	Calcutta	02.04. 2015.	Dr. Suman Khowala	Drug Development Diagnostics & Biotechnology
31.	Ranjita Das	Synergistic enhancement of Cytotoxicity of known chemo - therapeutic agents by mahanine in colon and cervical carcinoma.	Calcutta	Nov 2015	Dr. Chitra Mandal	Cancer Biology & Inflammatory Disorder
32.	Rumana Akhter	Studies on Death Associated Molecules in Alzheimer's Disease.	Calcutta	21.07. 2015	Dr. Subhas Chandra Biswas	Cell Biology & Physiology
33.	Sanchari Pradhan	Design, Development and Analysis of two Databases: IGDD and ProHspDb.	Calcutta	2015	Dr. Chitra Dutta & Dr. Kunal Ray	Molecular & Human Genetics
34.	Satyabrata Bag	Molecular characterizations of rel and rel-like genes of Mycobacterium tuberculosis	Calcutta	16 .19.2015	Dr. Rupak K. Bhadra	Infectious Diseases & Immunology Division



Sl. No.	Recipient's Name	Title of the Thesis	University	Date of Award	Supervisor's Name	Division
35.	Sayani Banerjee sayaniban@gmail.com	The role of intra-ovarian factors in the regulation of follicular death and survival, and management of ovarian lifespan.		03.04.2014	Dr. Syed. N Kabir	Cell Biology & Physiology Division
36.	Seemana Bhattacharya	Role and regulation of HAUSP in cancer.	Calcutta	20.02.2015	Dr. Mrinal K Ghosh	Cancer Biology & Inflammatory Disorder
37.	Soumendra Nath Das	Synthetic studies on novel chiral heterocycles and nucleosides from carbohydrate derivatives.	Jadavpur	18.02.2015	Dr. Sukhendu Bikas Mandal	Chemistry
38.	Souvik Ghosh	The effects of cellular context on miRNA activity in mammalian cells.	Calcutta	30.03.2015	Dr. Suvendra Nath Bhattacharyya	Molecular Genetics
39.	Subir Karmakar	Protective efficacy of Leishmanial Glycolipids in experimental model of Visceral Leishmaniasis	Jadavpur	08.07.2015	Dr. Syamal Roy Late Dr. Tripti De	Infectious Disease & Immunology Division
40.	Sukanta Jash sukantajash.iicb@gmail.com	Carrier assisted targeting of large functional RNA into mitochondria and its effect on cellular, molecular and physiological function.		29.10.2013	Dr. Samit Adhay	Genetic Engineering Laboratory, Molecular & Human Genetics Division
41.	Sumit Kumar Dey	Study of anticancer role of a few andrographolide derivatives and of a nano encapsulated form of andrographolide.	Calcutta	08.04.2015	Dr. Krishna Das Saha	Department of Biotechnology
42.	Trina Dutta	Deamidation and Protein Repair Studies of Bio-catalysts from Different Organisms.	Calcutta	09.12.2015	Dr. Anil K. Ghosh	Drug Development Diagnostics & Biotechnology
43.	Tuhin Suvro Banerjee	Alcohol Addiction: Molecular Basis and Therapy.	Calcutta	September 2015	Dr. Sumantra Das	Cell Biology & Physiology
44.	Abhishek Basu		Calcutta	26 June, 2015	Dr. Saumen Dutta	
45.	Somnath Paul	Evaluation of the Health Effects, Genetic Damage and DNA Methylation Induced by Arsenic Through Drinking Water.	Jadavpur	November 18, 2015	Dr. Ashok K. Giri & Dr. Arun Bandyopadhyay	Molecular Genetics Division, IICB
46.	Sumit Sen Santara	Biochemical Characterization of a Novel Heme-based Adenylate Cyclase from Leishmania major.	Jadavpur	31.12.2014	Dr. Subrata Adak	Structural Biology & Bioinformatics

Staff List of IICB as on March 31, 2016

STAFF STRENGTH AT A GLANCE

Director	1
Scientist – Gr. IV	52
Technical – Gr. III	44
Technician – Gr. II	34
Helper – Gr. I	15
Officers in Administration	11
Administrative Staff	43
Gr. C (Non-Technical)	8
Canteen Staff	8
Total	221

DETAILED STAFF LIST

	Sl. No.	EMP. ID	EMPLOYEE'S NAME	DEISGNATION	Revised Pay Band	Grade Pay
1	1	592	Samit Chattopadhyay Dr.	Director	HAG 67000-79000/-	
2	2	87	Sumantra Das Dr.	Chief Scientist	PB-4 37400-67000/-	10,000/-
3	3	95	Chitra Dutta Dr. (Mrs.)	Chief Scientist	PB-4 37400-67000/-	10,000/-
4	4	103	Nahid Ali Dr. (Mrs.)	Chief Scientist	PB-4 37400-67000/-	10,000/-
5	5	90	S. N. Kabir Dr.	Chief Scientist	PB-4 37400-67000/-	10,000/-
6	6	96	Debashish Bhattacharya Dr.	Chief Scientist	PB-4 37400-67000/-	10,000/-
7	1	105	G. Suresh Kumar Dr.	Senior Principal Scientist	PB-4 37400-67000/-	8900/-
8	2	115	R. Chowdhury Dr. (Mrs.)	Senior Principal Scientist	PB-4 37400-67000/-	8900/-
9	3	445	Arun Bandyopadhyay Dr.	Senior Principal Scientist	PB-4 37400-67000/-	8900/-
10	4	112	P. Jaisankar Dr.	Senior Principal Scientist	PB-4 37400-67000/-	8900/-
11	5	124	Rupak Kr. Bhadra Dr.	Senior Principal Scientist	PB-4 37400-67000/-	8900/-
12	6	120	S. R. Dungdung Dr. (Mrs.)	Senior Principal Scientist	PB-4 37400-67000/-	8900/-
13	7	521	Uday Bandopadhyay Dr.	Senior Principal Scientist	PB-4 37400-67000/-	8900/-



14	8	473	S. Swarnakar Dr.(Miss)	Senior Principal Scientist	PB-4 37400-67000/-	8900/-
15	9	443	Sibsankar Ray Dr.	Senior Principal Scientist	PB-4 37400-67000/-	8900/-
16	1	110	M. Bhowmik Dr. (Miss)	Principal Scientist	PB-4 37400-67000/-	8700/-
17	2	99	Tushar K. Chakraborty Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
18	3	441	Aditya Konar Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
19	4	520	Chinmay Chowdhury Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
20	5	563	Rupasri Ain Dr. (Mrs.)	Principal Scientist	PB-4 37400-67000/-	8700/-
21	6	570	Sucheta Tripathi Dr. (Mrs.)	Principal Scientist	PB-4 37400-67000/-	8700/-
22	7	503	Soumen Datta Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
23	8	523	K.N. Chattopadhyay Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
24	9	524	Mrinal Kanti Ghosh Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
25	10	447	S. Chattopadhyay Dr.(Mrs)	Principal Scientist	PB-4 37400-67000/-	8700/-
26	11	472	Subrata Adak Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
27	12	530	S. N. Bhattacharya Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
28	13	122	N. V. M. Khalkho Dr. (Mrs.)	Principal Scientist	PB-4 37400-67000/-	8700/-
29	14	580	Saikat Chakrabarti Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
30	15	581	Surajit Ghosh Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
31	16	582	Debabrata Biswas Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
32	17	584	Umesh Prasad Singh Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
33	18	527	Malini Sen Dr. (Mrs.)	Principal Scientist	PB-4 37400-67000/-	8700/-
34	19	532	Jayati Sengupta Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
35	20	540	Biswadip Banerji Dr.	Principal Scientist	PB-4 37400-67000/-	8700/-
36	1	123	Debjani Mondal Dr. (Mrs.)	Senior Scientist	PB-3 15600-39100/-	7600/-
37	2	547	Subhas Ch. Biswas Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
38	3	551	Nakul Ch. Maiti Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
39	4	561	Partha Chakrabarti Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
40	5	566	Sanjoy Datta Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
41	6	568	Siddhartha Ray Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
42	7	571	Ranjan Jana Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
43	8	572	Arindam Talukdar Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-



44	9	574	Ramalingam Natarajan Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
45	10	575	Sujoy Mukherjee Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
46	11	576	Indu Bhusan Deb Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
47	12	577	Dipyaman Ganguly Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
48	13	578	Amitava Sengupta Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
49	14	583	Subhajit Biswas Dr.	Senior Scientist	PB-3 15600-39100/-	7600/-
50	1	528	Saraswati Garai Dr. (Miss)	Scientist	PB-3 15600-39100/-	6600/-
51	2	560	Indrajit Das Dr.	Scientist	PB-3 15600-39100/-	6600/-
52	3	601	Anil Kumar Mr.	Scientist	PB-3 15600-39100/-	6600/-
53	1	143	Krishna Das Saha Dr. (Mrs.)	Principal Technical Officer	PB-4 37400-67000/-	8700/-
54	2	145	S.E. Besra Dr. (Mrs.)	Principal Technical Officer	PB-4 37400-67000/-	8700/-
55	3	432	M Chatterjee Debnath Dr.	Principal Technical Officer	PB-4 37400-67000/-	8700/-
56	4	164	S. Majumdar Dr.	Principal Technical Officer	PB-4 37400-67000/-	8700/-
57	5	467	Shekhar Ghosh Sri	Principal Technical Officer	PB-4 37400-67000/-	8700/-
58	6	494	Sandip Saha Sri	Principal Technical Officer	PB-4 37400-67000/-	8700/-
59	1	535	Chirantan Debdas Sri Sr.	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
60	2	499	Narayan ch. Ghosh Dr.	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
61	3	448	Binayak Pal Sri	Sr. Technical Officer (3)	PB-3 15600-39100/-	600/-
62	4	449	Aparna Laskar Dr. (Mrs.)	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
63	5	174	Sankar Kumar Maitra Dr.	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
64	6	175	Ardhendu Kr. Mandal Dr.	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
65	7	177	Tapas Sarkar Dr.	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
66	8	179	Subhagata Ghosh Dr. (Miss)	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
67	9	180	Arupesh Majumder Sri	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
68	10	185	R.N.Mandi Sri	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
69	11	184	Ramdhan Majhi Dr.	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
70	12	187	Asish Mullick Sri	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
71	13	188	Dipika Roy Mrs.	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
72	14	173	Purnima Chatterjee Mrs.	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-
73	15	176	Banasri Das Mrs.	Sr. Technical Officer (3)	PB-3 15600-39100/-	7600/-



74	1	186	P. Gangopadhyay Sri	Sr. Technical Officer (2)	PB-3 15600-39100/-	6600/-
75	2	178	Diptendu Bhattacharya Sri	Sr. Technical Officer (2)	PB-3 15600-39100/-	6600/-
76	3	182	Pratap Ch. Kayal Sri	Sr. Technical Officer (2)	PB-3 15600-39100/-	6600/-
77	4	496	E. Padmanaban Sri	Sr. Technical Officer (2)	PB-3 15600-39100/-	6600/-
78	5	162	Kshudiram Naskar Sri	Sr. Technical Officer (2)	PB-3 15600-39100/-	6600/-
79	6	514	Susanta Ray Sri	Sr. Technical Officer (2)	PB-3 15600-39100/-	6600/-
80	1	411	Sandip Chowdhury Sri	Sr. Technical Officer (1)	PB-3 15600-39100/-	5400/-
81	1	463	Arti Khetrapaul Mrs.	Technical Officer	PB-2 9300-34800/-	4600/-
82	2	465	Swapan Kr. Mondal Sri	Technical Officer	PB-2 9300-34800/-	4600/-
83	3	495	Jishu Mandal Sri	Technical Officer	PB-2 9300-34800/-	4600/-
84	4	466	Nirali Bage Mrs.	Technical Officer	PB-2 9300-34800/-	4600/-
85	5	513	Debashis Banik Sri	Technical Officer	PB-2 9300-34800/-	4600/-
86	6	516	Sandip Chakraborty Sri	Technical Officer	PB-2 9300-34800/-	4600/-
87	1	539	Muruganandan T. Sri	Technical Assistant	PB-2 9300-34800/-	4200/-
88	2	550	Karri Suresh Kumar Sri	Technical Assistant	PB-2 9300-34800/-	4200/-
89	3	552	M. Vigneshwaran Sri	Technical Assistant	PB-2 9300-34800/-	4200/-
90	4	556	Santu Paul Sri	Technical Assistant	PB-2 9300-34800/-	4200/-
91	5	557	Sandip Kundu Sri	Technical Assistant	PB-2 9300-34800/-	4200/-
92	6	559	Debasree Das Ms	Technical Assistant	PB-2 9300-34800/-	4200/-
93	7	569	Pradeep Sypureddi	Technical Assistant	PB-2 9300-34800/-	4200/-
94	8	579	Soumik Laha Sri	Technical Assistant	PB-2 9300-34800/-	4200/-
95	9	589	Sourin Ghosh Sri	Technical Assistant	PB-2 9300-34800/-	4200/-
96	10	529	Ujjal Roy Sri	Technical Assistant	PB-2 9300-34800/-	4200/-
97	11	600	Shubhendu Ghosh Shri	Technical Assistant	PB-2 9300-34800/-	4200/-
98	1	236	P. K. Chanda Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
99	2	241	S. C. Das Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
100	3	251	S. R. Tudu Sri Sr.	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
101	4	244	Swapan Kumar Naskar Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
102	5	344	Ayub Shah Md.	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
103	6	242	Sheo Shankar Verma Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-



104	7	246	Tapas Chowdhury Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
105	8	383	Pradip Mondal Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
106	9	247	Tarak Prasad Nandi Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
107	10	248	Sutapa Ganguly Mrs.	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
108	11	249	Sanjib Biswas Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
109	12	250	R. P. Gorh Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
110	13	252	Nishikanta Naskar Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
111	14	253	Pallab Mukherjee Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
112	15	345	Ranjit Das Sri	Sr. Technician (2)	PB-2 9300-34800/-	4600/-
113	1	450	Abhijit Paul Sri	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
114	2	410	Anirban Manna Sri	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
115	3	426	Samir Majumder Sri	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
116	4	360	M. Ahmed Md.	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
117	5	409	Paresh Sarkar Sri	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
118	6	416	Sujit Kr. Majumdar Sri	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
119	7	419	Mahua Bhattacharjee Mrs.	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
120	8	418	Prabin Kr. Das Sri	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
121	9	460	Tapan Das Sri	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
122	10	417	Atanu Maitra Sri	Sr. Technician (1)	PB-2 9300-34800/-	4200/-
123	1	534	Anup Karmakar Sri	Technician (1)	PB-1 5200-20200/-	1900/-
124	2	546	Soumalya Sinha Sri	Technician (1)	PB-1 5200-20200/-	1900/-
125	3	553	Nita Chakraborty Ms	Technician (1)	PB-1 5200-20200/-	1900/-
126	4	554	Akash Gupta Sri	Technician (1)	PB-1 5200-20200/-	1900/-
127	5	555	Samir Thami Sri	Technician (1)	PB-1 5200-20200/-	1900/-
128	6	585	Avijit Paul Sri	Technician (1)	PB-1 5200-20200/-	1900/-
129	7	586	Tanmoy Biswas Sri	Technician (1)	PB-1 5200-20200/-	1900/-
130	8	590	Shiv Kumar Gupta Sri	Technician (1)	PB-1 5200-20200/-	1900/-
131	9	591	Hari Sankar Beni Sri	Technician (1)	PB-1 5200-20200/-	1900/-
132	1	272	Sunil Nath Sri	Lab. Assistant	PB-1 5200-20200/-	2800/-
133	2	274	R. N. Jana Sri	Lab. Assistant	PB-1 5200-20200/-	2800/-



134	3	275	Prahlad Das Sri	Lab. Assistant	PB-1 5200-20200/-	2800/-
135	4	440	Bhaskar Basu Sri	Lab. Assistant	PB-1 5200-20200/-	2800/-
136	5	279	Shyamal Das Sri	Lab. Assistant	PB-1 5200-20200/-	2800/-
137	6	479	Madan Halder Sri	Lab. Assistant	PB-1 5200-20200/-	2800/-
138	7	280	Amerika Das Sri	Lab. Assistant	PB-1 5200-20200/-	2800/-
139	8	282	Nimai Charan Prodhan Sri	Lab. Assistant	PB-1 5200-20200/-	2800/-
140	1	351	Sambhu Raul Sri	Lab. Attendant (2)	PB-1 5200-20200/-	1900/-
141	2	353	Suresh Balmiki Sri	Lab. Attendant (2)	PB-1 5200-20200/-	1900/-
142	3	352	Nanda Lal Routh Sri	Lab. Attendant (2)	PB-1 5200-20200/-	1900/-
143	4	361	S. K. Banik Sri	Lab. Attendant (2)	PB-1 5200-20200/-	1900/-
144	5	501	Ashoke Sardar Sri	Lab. Attendant (2)	PB-1 5200-20200/-	1900/-
145	6	502	Ram Kumar Sarkar Sri	Lab. Attendant (2)	PB-1 5200-20200/-	1900/-
146	7	519	Shyamal Nath Sri	Lab. Attendant (2)	PB-1 5200-20200/-	1900/-
				Lab. Attendant (1)	PB-1 5200-20200/-	1800/-
				ADMINISTRATION		
147	1	603	B.C. Sahoo Sri	Administrative Officer	PB-3 15600-39100/-	6600/-
148	2	573	Sudipto Chatterjee Sri	Finance & Accounts Officer	PB-3 15600-39100/-	6600/-
149	3	602	A.K. Pandey Sri	Stores & Purchase Officer	PB-3 15600-39100/-	6600/-
150	4	518	Asim Kr. Jha Sri	Finance & Accounts Officer	PB-3 15600-39100/-	6600/-
151	5	485	Siddhartha Dey Sri	Section Officer (G)	PB-3 15600-39100/-	5400/-
152	6	587	V.K. Gond Shri	Section Officer (G)	PB-3 15600-39100/-	5400/-
153	7	525	Shampoo Sengupta Mrs.	Section Officer (G)	PB-3 15600-39100/-	5400/-
154	8	308	Anjana Mandi Mrs.	Section Officer (G)	PB-2 9300-34800/-	4800/-
155	9	392	Kanu Mondal Sri.	Section Officer (G)	PB-2 9300-34800/-	4800/-
156	10	588	Monoj Kumar Sri	SO(F&A)	PB-3 15600-39100/-	5400/-
157	11	397	Ratan Bage Sri	SO(SP)	PB-3 15600-39100/-	5400/-
158	1	427	Sanhita Ganguly Mrs.	ASSTT. (GEN.) GR.I(MACP)	PB-2 9300-34800/-	4800/-
159	2	428	M. Bhattacharya Mrs.	ASSTT. (GEN.) GR.I(MACP)	PB-2 9300-34800/-	4800/-
160	3	334	R.N. Hansda Sri	ASSTT. (GEN.) GR.I(MACP)	PB-2 9300-34800/-	4800/-
161	4	335	Prem Singh Sri	ASSTT. (GEN.) GR.I(MACP)	PB-2 9300-34800/-	4800/-



162	5	340	D. K. Kisku Sri	ASSTT. (GEN.) GR.I	PB-2 9300-34800/-	4600/-
163	6	396	Alok Ray Sri	ASSTT. (GEN.) GR.I	PB-2 9300-34800/-	4600/-
164	7	510	Jayanta Pal Sri	ASSTT. (GEN.) GR.I	PB-2 9300-34800/-	4600/-
165	8	511	Saugata Das Sri	ASSTT. (GEN.) GR.I	PB-2 9300-34800/-	4600/-
166	1	508	Tarun Kr. Sinha Roy Sri	ASSTT. (G) GR.II	PB-1 5200-20200/-	2400/-
167	2	507	Raju Pal Sri	ASSTT. (G) GR.II	PB-1 5200-20200/-	2400/-
168	3	509	Ranjit Debnath Sri	ASSTT. (G) GR.II	PB-1 5200-20200/-	2400/-
169	4	512	Sukhendu Biswas Sri	ASSTT. (G) GR.II	PB-1 5200-20200/-	2400/-
170	5	565	Anirudha Das Sri	ASSTT. (G) GR.II	PB-1 5200-20200/-	2400/-
171	1	593	Tanumoy Sen Shri	ASSTT. (G)GR.III	PB-1 5200-20200/-	1900/-
172	2	594	Raju Kumar Shri	ASSTT. (G)GR.III	PB-1 5200-20200/-	1900/-
173	3	595	Debtanu Pal Shri	ASSTT. (G)GR.III	PB-1 5200-20200/-	1900/-
174	4	596	Sumit Kumar Singh Shri	ASSTT. (G)GR.III	PB-1 5200-20200/-	1900/-
175	5	597	Ram Kanai Mondal Shri	ASSTT. (G)GR.III	PB-1 5200-20200/-	1900/-
176	1	327	A. K. Chanda Sri	ASSTT. (F&A.) GR.I (MACP)	PB-2 9300-34800/-	4800/-
177	2	476	Banani Dutta Mrs.	ASSTT. (F&A.) GR.I (MACP)	PB-2 9300-34800/-	4800/-
178	3	343	Sanjoy Mukhopadhyay Sri	ASSTT. (F&A.) GR.I (MACP)	PB-2 9300-34800/-	4800/-
179	4	336	Asit Kr. Roy Sri	Asstt.(F&A),Gr.I	PB-2 9300-34800/-	4600/-
180	1	338	M. K. Dutta Sri	ASSTT. (F & A) GR.II(MACP)	PB-1 5200-20200/-	2800/-
181	2	506	Vishal Agarwal Sri	ASSTT. (F & A) GR.II	PB-1 5200-20200/-	2400/-
182	1	598	Chaitali Sarkar Miss	ASSTT. (F & A) GR.III	PB-1 5200-20200/-	1900/-
183	1	328	A. B. S. Roy Sri	ASSISTANT (SP) GR.I	PB-2 9300-34800/-	4800/-
184	2	536	Rajib Ray Sri	ASSISTANT (SP) GR.I	PB-2 9300-34800/-	4600/-
185	3	342	Bisweswar Das Sri	ASSISTANT (SP) GR.I	PB-2 9300-34800/-	4600/-
186	4	363	Bula Pal Mrs.	ASSISTANT (SP) GR.I	B-2 9300-34800/-	4600/-
187	1	505	Pradipta Sarkar Sri	ASSISTANT (SP) GR.II	PB-1 5200-20200/-	2400/-
188	2	504	Arnab Sen Sri	ASSISTANT (SP) GR.II	PB-1 5200-20200/-	2400/-
189	1	599	Shyama Chanran Bose Sri	ASSISTANT (SP) GR.III	PB-1 5200-20200/-	1900/-
190	1	318	Dipak Kr. Guin Sri	SR. STENO (ACP & MACP)	PB-2 9300-34800/-	5400/-
191	2	323	Asim Roy Sri	SR. STENO (ACP & MACP)	PB-2 9300-34800/-	5400/-



192	3	324	Pratima Banerjee Mrs.	SR. STENOGRAPHER(MACP)	PB-2 9300-34800/-	4800/-
193	4	325	Shankar Bhakta Sri	SR. STENOGRAPHER(MACP)	PB-2 9300-34800/-	4800/-
194	5	393	Rabindranath Das Sri	SR. STENOGRAPHER(MACP)	PB-2 9300-34800/-	4800/-
195	6	405	Saibal Giri Sri	SR. STENOGRAPHER(MACP)	PB-2 9300-34800/-	4800/-
196	7	490	Sankar Santra	SR. STENOGRAPHER	PB-2 9300-34800/-	4600/-
197	8	453	Gautam Saha Sri	SR. STENOGRAPHER	PB-2 9300-34800/-	4600/-
198	9	491	Moumita Majumdar Mrs.	SR. STENOGRAPHER	PB-2 9300-34800/-	4600/-
				ISOLATED POST		
199	1	321	Ambalika Nag Mrs.	Hindi officer	PB-2 9300-34800/-	5400/-
200	2	567	Sabyasachi Karmokar Sri	Security Officer	PB-2 9300-34800/-	4600/-
201	1	348	Ashok Ram Sri	GR-C (NT) (ACP & MACP)	PB-1 5200-20200/-	2400/-
202	2	365	Kailash Ch. Nayak Sri	GR-C (NT) (MACP)	PB-1 5200-20200/-	2000/-
203	3	364	Gita Ghosh Mrs.	GR-C (NT) (MACP)	PB-1 5200-20200/-	1900/-
204	4	401	Soma Devi Sharma Mrs	GR-C (NT) (MACP)	PB-1 5200-20200/-	1900/-
205	5	412	Gopal Ch. Mandal Sri	GR-C (NT)	PB-1 5200-20200/-	1900/-
206	6	413	Asit Mitra Sri	GR-C (NT)	PB-1 5200-20200/-	1900/-
207	7	431	Janmanjoy Midya Sri	GR-C (NT)	PB-1 5200-20200/-	1900/-
208	8	430	Pasupati Midya Sri	GR-C (NT)	PB-1 5200-20200/-	1900/-
209	9	423	Shyamal Kr. Ghosal Sri	GR-C (NT)	PB-1 5200-20200/-	1900/-
210	10	414	P. C. Dehury Sri	GR-C (NT)	PB-1 5200-20200/-	1900/-
211	11	425	Manoranjan Adhikary Sri	GR-C (NT)	PB-1 5200-20200/-	1900/-
212	12	424	Tapan Sarkar Sri	GR-C (NT)	PB-1 5200-20200/-	1900/-
213	13	451	Dinesh Mahali Sri	GR-C (NT)	PB-1 5200-20200/-	1900/-
214	1	369	Amal Dutta Sri	CLERK (MACP)	PB-2 9300-34800/-	4600/-
215	2	373	Sudhangshu Halder Sri	TEA MAKER(MACP)	PB-1 5200-20200/-	2400/-
216	3	372	Bimal Das Sri	BEARER(MACP)	PB-1 5200-20200/-	2400/-
217	4	371	Ashok Sadhukhan Sri	BEARER(MACP)	PB-1 5200-20200/-	2400/-
218	5	370	Badal Halder Sri	BEARER(MACP)	PB-1 5200-20200/-	2400/-
219	6	374	Jagabandhu Biswas Sri	WASH BOY(MACP)	PB-1 5200-20200/-	2400/-
220	7	375	Nirapada Halder Sri	SWEEPER	PB-1 5200-20200/-	2000/-
221	8	376	Mantu Das Sri	SWEEPER	PB-1 5200-20200/-	2000/-



LIST OF EMERITUS SCIENTISTS AND OTHER PRESTIGIOUS FELLOWSHIP AWARDEES

Sl. No.	Name of the Emeritus Scientist	Designation	I.D. Number	Date of Joining	Tenure Upto
1	Dr. Siba Brata Mukhopadhyay	Emeritus Scientist	5051	04-01-2011	31/03/2016
2	Dr. Anil K. Ghosh	Emeritus Scientist	5032	01-02-2012	31/07/2016
3	Dr. Nirmalendu Das	Emeritus Scientist	5052	01-02-2012	31/01/2016
4	Professor Samaresh Mitra	Senior Scientist, INSA	5053	01-01-2011	31/12/2015
5	Dr. Alok Kr. Datta	Senior Scientist, INSA	5054	02-05-2012	30/04/2017
6	Dr. A.K. Giri	Emeritus Scientist	5021	07-02-2012	31/07/2017
7	Dr. H.K. Majumder Raja Ramanna	Fellow (DAE)	5024	11-01-2012	31/10/2015
8	Dr. N.B. Mondal	Emeritus Scientist	5028	01-05-2013	30/04/2017
9	Dr. Syamal Kr. Dana	Emeritus Scientist	5029	13-05-2013	31/05/2016
10	Dr. Nanda Ghoshal	Emeritus Scientist	5031	08-01-2013	30/04/2017
11	Dr. Keya Chaudhuri	Emeritus Scientist	5036	02-03-2014	31/01/2017
12	Dr. A.K. Sen	Emeritus Scientist	5038	01-05-2014	30-04-2017
13	Dr. Pijush K Das	Senior Scientist, NASI	5056	01-01-2015	31-12-2015
14	Professor P.K. Sarkar	Honorary Scientist, INSA			February'2015
15	Prof. Chitra Mandal	Distinguished Biotechnology Research Professor	5068	01.04.2016	31.03.2019
16	Dr. Samit Adhya	Emeritus Scientist	5067	01.04.2016	31.03.2019
17	Dr. Md. Wasim Khan	Inspire Faculty	5018	09-09-2012	08-09-2017
18	Dr. Smrutisanjita Behera	Inspire Faculty	5069	28.03.2016	27.03.2021



RETIREES



Dr. Susanta Roychowdhury
Chief Scientist
30.04.2015



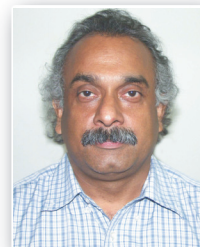
Dr. Suman Khowala
Principal Scientist
30.04.2015



Dr. Prasanta Chakraborty
Sr. TO (3)
01.05.2015(VR)



Dr. Santu Bandopadhyay
Chief Scientist
31.08.2015 (Extn)



Dr. K.P. Mohanakumar
Chief Scientist
30.09.2015



Dr. Padma Das
Principal Scientist
30.09.2015



Sri Balaram Panda
Halwai-Cum-Cook
30.09.2015



Dr. Samit Adhya
Outstanding Scientist
30.09.2015 (Extn)



Dr. P. Chattopadhyay
Chief Scientist
30.09.2015 (Extn)



Dr. Chitra Mandal
Outstanding Scientist
30.09.2015 (Extn)



Sri Debdas Guhathakurta
Private Secretary
30.11.2015



Mrs. Indira Kundu
Asstt. (G) Gr. I (MACP)
30.11.2015



Sri A.K. Sen
Sr. Technician (1)
31.12.2015



Dr. Syamal Roy
Chief Scientist
31.01.2016 (Extn)



Dr. S. N. Kabir
Chief Scientist
31.03.2016 (Extn)



NEW APPOINTMENTS



Shri Sourin Ghosh
Technical Assistant
08-04-2015



Shri Shiv Kumar Gupta
Technician (1)
23-06-2015



Shri Hari Sankar Beni
Technician (1)
02-07-2015



Shri Raju Kumar
Asst. (G) Gr. III
17-08-2015



Miss Chaitali Sarkar
Asst. (F&A) Gr. III
17-08-2015



Shri Debtanu Pal
Asst. (G) Gr. III
17-08-2015



Shri Sumit Kumar Singh
Asst. (G) Gr. III
17-08-2015



Shri Ram Kanai Mondal
Asst. (G) Gr. III
17-08-2015



Shri Tanumoy Sen
Asst. (G) Gr. III
17-08-2015



Shri Shyama Charan Bose
Assistant (S&P) Gr. III
19-08-2015



Dr. Samit Chattopadhyay
Director
25-08-2015



Shri Shubhendu Ghosh
Technical Assistant
19-10-2015



Shri Anil Kumar
Scientist
10-11-2015

APPOINTMENTS ON TRANSFER



Shri Monoj Kumar
Section Officer (F&A)
10-04-2015



Shri A.K. Pandey
SPO
19-08-2015



Shri B.C. Sahoo
Administrative Officer
02-12-2015



Shri Kanu Mondal
Section Officer (G)
22-02-2016



EVENTS

April 10, 2015	59TH IICB Foundation Day: Foundation Day Celebration of CSIR-IICB was held on Friday, April 10, 2015. Prof Siddharth Roy Director, Bose Institute Was Guest in chief. Dr. Prof. Peter Walden, Department of Dermatology, Charite', Humboldt University, Berlin, Germany was the Special Guest on the occasion. Prof. C. P. Thakur, Balaji Utthan Sansthan, Kala-azar Research Centre, Patna delivered the XXVIIth J.C. Ray Memorial Lecture. Prof. Subhash C. Basu, University of Notre Dame, USA delivered the 1st B.K. Bachhawat Memorial Lecture
April 13, 2015	Eighteen (18) post Graduate Students of M.Sc. Biotechnology along with one faculty of St. Anthony's college, Shillong, Meghalaya, visited CSIR-IICB for a one day scientific exposure tour
April 17, 2015	A one day National Seminar on "Recent Advances in Biotechnology" was jointly organized by CSIR-Indian Institute of Chemical Biology (CSIR-IICB) & Jadavpur University Kolkata Chapter of BRSI, The Biotech Research Society (India) on 17th April, 2015 at CSIR-IICB, Kolkata. The seminar was attended by about 262 delegates, invitees, faculties, researchers, students and volunteers from different parts of India and from colleges, universities and institutes in and around Kolkata
June 5, 2015	CSIR-IICB organized 3rd Annual Research Festival of its faculty scientists in a one day meet on 5th June 2015 at the Salt Lake Campus of this Institute. Eleven faculties presented their works in three different scientific sessions dedicated for "Structure, Function and Biology of Macromolecules", "Chemistry of Biomolecules" & "Biology of Diseases"
June 7, 2015	Half Day Symposium was organized by CSIR-IICB jointly with Bangiya Bijan Parishad to observe the World Environment Day on 7th June 2015 in the B. K. Bachawat Memorial Hall
September 15, 2015	Hindi Day was observed on 15th September, 2015 which was also the concluding day for a weeklong celebration for Hindi Week in the institute, when recitation and extempore competition in Hindi were held. Senior Prof of Hindi Calcutta University was the chief guest of the day. Sri. Satish Kumar Pandey Asst. Director of Central Translation Bureau was the special guest of the day. Dr. Chitra Mandal presided on the occasion and requested all the members of the Institute to work in Hindi
September 22, 2015	Foundation Day Quiz was organized at J.C. Ray Auditorium CSIR-IICB Jadavpur Campus
September 24, 2015	OPEN HOUSE was organized on Friday 24th September, 2015 at CSIR-IICB. One hundred and thirty three, Students from eight suburb schools of Kolkata participated in one day scientific exposure trip to various laboratories and other scientific facilities of the institute
September 26, 2015	CSIR-IICB, Kolkata, observed the 73rd Foundation Day of CSIR on Saturday, September 26, 2015 at Dr. J. C. Ray Memorial Auditorium of the institute. Dr. Samit Chattopadhyay, Director, CSIR-IICB presided over the function in which Prof. Samir Bhattacharya, Emeritus Professor, Centre for Advance Studies in Zoology, School of Life Sciences, Visva-Bharti, Santiniketan and former Director of CSIR-IICB was present as Guest-in chief. Dr. Amit Ghosh, Emeritus Scientist, National Institute of Cholera & Enteric Diseases, Kolkata and former Director of CSIR-IMTECH, Chandigarh delivered the Foundation Day invitation lecture
November 4, 2015	Sixteen (16) post Graduate Students of M.Sc. Environmental Science along with one faculty of University of Calcutta, visited CSIR-IICB for a one day scientific exposure tour
December 4, 2015	Twenty eight (28) Graduate Students of B.Sc. Environmental Biotechnology & Biochemistry along with two faculty, St. Anthony's college, Shillong, Meghalaya, visited CSIR-IICB for a one day scientific exposure tour
December 22-24, 2015	XVII All India Congress of Cytology and Genetics & International Symposium on "Exploring Genomes: The New Frontier" was Jointly Organized by CSIR-Indian Institute of Chemical Biology and Archana Sharma Foundation of Calcutta
December 29, 2015	Honorable Minister of State for Science & Technology, Y .S. Chowdary visited CSIR-IICB on 29th December, 2015 to discuss the issue related to re-structuring of Vision, Mission and Objectives of the institute for achieving mandate. Proper mapping of manpower and budget allocation
January 14, 2016	Fifteen (15) post Graduate Students of M.Sc. Biotechnology along with one faculty of Sambalpur University, visited CSIR-IICB for a one day scientific exposure tour
January 22, 2016	Lal Bahadur Shastri National Academy of Administrative (LBSNA), the pioneer training institute for civil servants has chosen CSIR-IICB, Kolkata for a Winter Study Visit organized for Officers Trainees 2015 batch. CSIR-IICB, Kolkata is a pioneer institute under the aegis of Ministry of Science & Technology, Government of India. The institute is engaged in research and development in the field of bio-medical research. CSIR-IICB is welcomed a batch of 18 IAS Officers Trainees on Friday, January 22, 2016 for Winter Study Tour.



January 26, 2016	67th Republic Day was observed with great show of strength
February 5, 2016	The week long symposium held in eight different research institutes in India was organized as part of a Government of India and the European Molecular Biology Organisation (EMBO) partnership to induct India as a member state of the EMBC and EMBO. CSIR-IICB was one of the venues of this programme. Half Day EMBO partnership symposium was organized at CSIR-IICB. Dr. Suvendra Bhattacharyya served as the convenor of this event in CSIR-IICB. Dr. Gerlind Wallon and Dr. Luis Valente had represented EMBO in this event. As part of the agreement, Indian scientists now will be able to participate in the same EMBO programmes as researchers from all other member states
February 8, 2016	The Kolkata-based CSIR-Indian Institute of Chemical Biology (IICB) recently entered into a Memorandum of Understanding (MoU) with the National Research Development Corporation (NRDC) to promote entrepreneurship. The MoU was signed in the presence of Dr. Harsh Vardhan, Minister of Science & Technology
February 8, 2016	Union Minister for Science & Technology & Earth Sciences Dr. Harsh Vardhan inaugurated a Translational Research Unit of Excellence (TRUE) at the Council of Scientific & Industrial Research - Indian Institute of Chemical Biology (CSIR-IICB) Kolkata on Monday (February 8, 2016) in the presence of the Minister-in-charge, Science Technology & Biotechnology, Govt. of West Bengal Dr. Rabiranjana Chattopadhyay. This 'TRUE' is conceived as a productive platform for successful industry-institute liaison for translating previously achieved and ongoing biomedical discoveries by IICB scientists into biomedical deliverables
February 25, 2016	Swatchhta Campaign, a Safai Aviyan was organized in the institute where all Scholars and staff members actively participated and took a special drive to clean the outside premises of the Institute
March 4, 2016	(4) Post Graduate Students of M.Sc. Zoology along with one faculty of Serampore College, Calcutta University, visited CSIR-IICB for a one day scientific exposure tour
March 22, 2016	Sixteen (16) Post Graduate Students of M.Sc. Zoology along with one faculty of Gauhati University, visited CSIR-IICB for a one day scientific exposure tour



CSIR-IICB Scientist represented CSIR at one of the world's largest Trade Fair and Exhibition of Technology held at Hannover Messe, Germany



CSIR-IICB scientist attending address by Honorable Minister of State for Science & Technology, Mr. Y. S. Chowdary



25th Annual General Meeting, 23.02.2016



Joining of Dr. Samit Chattopadhyay as a Director, CSIR-IICB on 25.08.2015



European Molecular Biology Organisation (EMBO) Partnership to Induct India as a Member State of the EMBC and EMBO. CSIR-IICB was one of the venues of this programme



CSIR-IICB Ward's Essay Competition during IICB Foundation Day on 22.9.15



World Environment Day, 07.06.2015



Hindi Drama on Hindi Day, 15.9.15



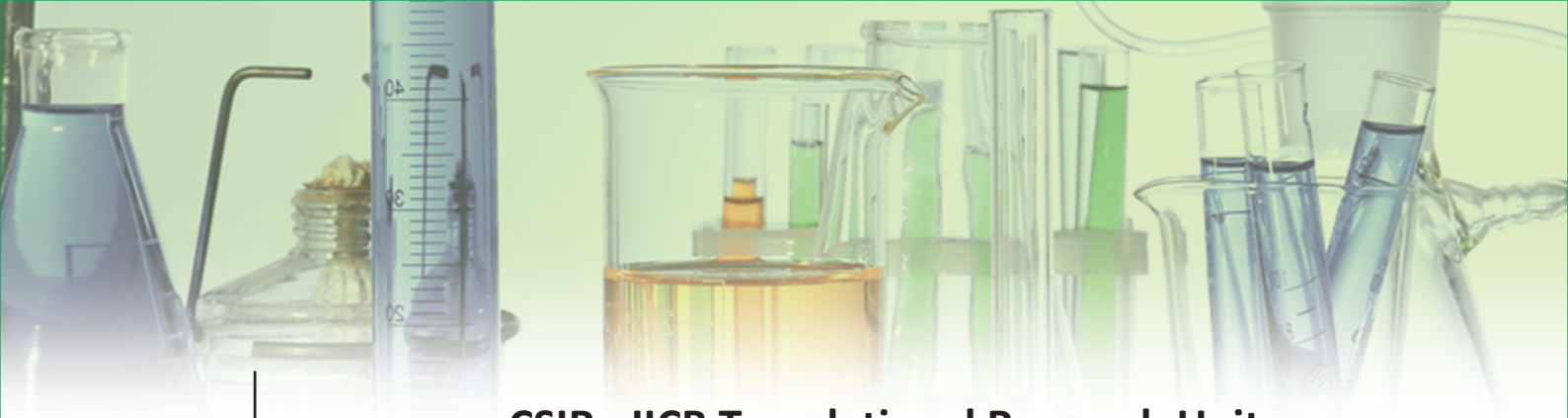
Republic Day, 2016



Inaugural Song by Research Scholars on the occasion of Republic Day, 2016



Blood Donation Camp by CSIR-IICB Club on 23.9.15



CSIR - IICB Translational Research Unit of Excellence (TRUE)

Salt Lake, Kolkata

CSIR-IICB, Jadavpur, Kolkata is engaged in R & D on diseases and certain biological problems of global interest. CSIR-IICB is one of the major institutes in India which initiated, right from its inception, multidisciplinary concerted efforts for conducting basic research on infectious diseases, specifically leishmaniasis and cholera, along with the development of technologies for the diagnosis, immunoprophylaxis and chemotherapy of the diseases. The institute is paying substantial attention in developing drugs from indigenous and natural resources like native Indian medicinal plants.



Inside a Lab in TRUE



TRUE – Front View



In order to strengthen the basic research and to attain translational objectives, a second campus with a four storey building was constructed at Salt Lake, Kolkata. The unit is named CSIR-IICB Translational Research Unit of Excellence (TRUE), the overall mandate of it being translation of the state-of-the-art fundamental and indigenous innovations to

affordable technology for societal benefits of the common man. At the nascent stage of the TRUE unit, it is planned to adopt a three way program - facilitation, incubation and translation, for meaningful transfer of research output into successful technology and subsequent contribution towards economic growth of the country.



Director sharing dais with the Ministers



Director presenting memento to Union Minister



On February 08, 2016 CSIR-IICB TRUE was inaugurated by, Dr. Harsh Vardhan, Hon'ble Union Minister for Science & Technology and Earth Sciences and Vice President of CSIR. Dr. Rabiranjan Chattopadhyay, Minister in-Charge for Science & Technology, Biotechnology, Govt. of West Bengal was present in the occasion

as a Distinguished Guest. This establishment is conceived as a productive platform for successful industry-institute cooperation for translating previously achieved and ongoing biomedical discoveries by CSIR-IICB scientists into biomedical deliverables with a view to contribute into country's start-up movement.



Honourable Minister lighting the lamp



Inauguration of the facilities



The major scope and the roadmap set for the new unit includes Research facilitation by establishing advanced technological platforms, establishing a Biomedical Incubation Center for MSMEs, start-up companies and translating discoveries made by CSIR-IICB scientists. Approximately 1000 sq. ft area in the TRUE building is planned to be allocated for the core facility centre. Around 10,000 sq. ft area (including the core facility) in the TRUE building is planned to be allocated for the incubation centre.

Dr. Harsh Vardhan appreciated the significant contribution of CSIR-IICB in areas of Cholera and Leishmaniasis. He was also happy to know that several herbal medicines have been developed and marketed by CSIR-IICB and many more are in the pipe-line to be marketed soon. The minister stressed the importance of units like the TRUE, a productive platform for successful industry-institute liaison for technology facilitation and transfer. "Be it scientists or institutes, today the most important factor is innovation coefficient and our government is keen on developing this coefficient. With the impetus by the start-up movement and centres like the TRUE, we are confident of turning lab researches into solutions for the common man," he said during his address.

Dr. Rabiranjana Chattopadhyay, expressed his appreciation for the creation of the unique Incubation Center for doing translational research with high end sophisticated equipments. He expressed the hope that the State Government and this newly created CSIR-IICB TRUE would work together for the benefit of the people.



Dr. Harsh Vardhan delivering his speech



Dr. Rabiranjana Chattopadhyay delivering his speech



Audience



The programme was followed by an Exhibition on Industry-Institute partnership where the products from CSIR-IICB were exhibited by Industries and the most promising technologies in pipeline were exhibited by the scientists of the institute.

The National Research Development Corporation (NRDC) entered into a Memorandum of Understand (MoU) with CSIR-IICB to promote entrepreneurship. Chairman and Managing Director, NRDC, Dr. H. Purushotham, Prof. Samit Chattopadhyay, Director, CSIR IICB and Dr. Suresh Kumar, Head, Business Development signed and exchanged the MoU in the presence of Dr. Harsh Vardhan and Dr. Rabiranjan Chattopadhyay. After signing MoU, Dr. Purushotham said that the partnership

between NRDC and CSIR-IICB will contribute to the “Start-up India” and “Make in India” Missions of Govt. of India by way of promoting Entrepreneurships, Incubation, IPRs and Technology Transfer.



MoU signed between CSIR-IICB and NRDC



Dr. Harsh Vardhan examining CSIR-IICB products exhibited



IICB RESEARCH COUNCIL MEMBERS 2013-2016

Prof. M. Vijayan

Chairman (August 2013-August 2015)

INSA Albert Einstein Professor

Molecular Biophysics Unit

Indian Institute of Science

Bengaluru - 560012

Dr. Kanury V.S. Rao

Chairman (September 2015 onwards)

Group Leader

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External expert

Director

National Brain Research Centre (NBRC)

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Dr. Mammen Chandy

External expert

Director

Tata Medical Center

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Dr. G.V.M. Sharma

External expert

Chief Scientist

CSIR-Indian Institute of Chemical Technology

Hyderabad - 500607

Prof. D. J. Chattopadhyay

External expert

Pro-Vice-Chancellor (Academic Affair)

Department of Biotechnology

B. C. Guha Centre for Biotechnology and Genetic Engineering

Calcutta University

35, Ballygunge Circular Road

Kolkata - 700 019

Prof. Rentala Madhubala

External expert

Director, AIRF

School of Life Sciences

Jawaharlal Nehru University

New Delhi - 110067

Dr. T.S. Balganes

CSIR Distinguished Scientist

CSIR Fourth Paradigm Institute

NAL Belur Campus, Bengaluru - 560037

Dr. Sukdeb Sinha

Representative of Scientific Department

Adviser

Department of Biotechnology

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New Delhi - 110 003

Dr. Balaram Ghosh

Scientist from Sister Laboratory

CSIR-Institute of Genomics and Integrative Biology

Mall Road, New Delhi - 110 007

Dr. Ch. Mohan Rao

DG Nominee

CSIR-Centre for Cellular and Molecular Biology

Hyderabad - 500007

Director

CSIR-Indian Institute of Chemical Biology

4 Raja S. C. Mullick Road

Kolkata - 700032

Dr. Sudeep Kumar

Permanent Invitee

Head

Planning & Performance Division (PPD)

Council of Scientific and Industrial Research

Anusandhan Bhawan, 2, Rafi Marg

New Delhi - 110001

Prof. Umesh Varshney

Special invitee

Dept of Microbiology & Cell Biology

Indian Institute of Science, Bengaluru - 560012

Prof. Amitabha Chattopadhyay

Special invitee

Outstanding Scientist

CSIR- Centre for Cellular & Cell Biology

Uppal Road, Hyderabad - 500007



MANAGEMENT COUNCIL

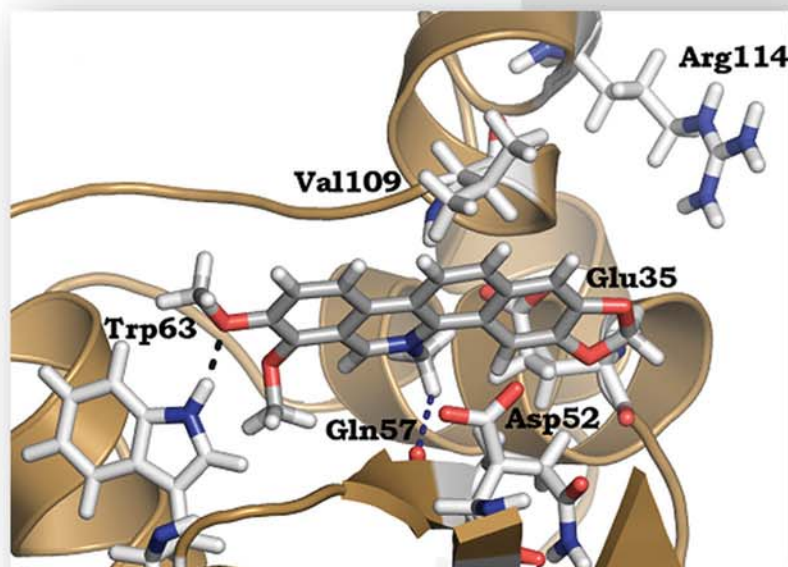
(For the period from 01.01.2014 to 31.12.2015)

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Dr. K. P. Mohanakumar, Chief Scientist, IICB	Member
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Dr. Indrajit Das, Scientist, IICB	Member
Dr. Mita Chatterjee Debnath, Principal Technical Officer, IICB	Member
Mr. Sudipto Chatterjee, F&Ac. Officer, IICB	Member
Mr. K. Bhattacharya, Administrative Officer, IICB	Member Secretary

MANAGEMENT COUNCIL

(For the period from 01.01.2016 to 31.12.2017)

Dr. Samit Chattopadhyay, Director	Chairman
Dr. Rajesh S. Gokhale, Director, CSIR-IGIB	Member
Dr. Ayyappanpillai Ajayaghosh, Director, CSIR-NIIST, Thiruvananthapuram	Member
Dr. G. Suresh Kumar, Sr. Principal Scientist & Head PME, IICB	Member
Dr. Arun Bandyopadhyay, Sr. Principal Scientist	Member
Dr. Sucheta Tripathy, Principal Scientist	Member
Dr. Subhajit Biswas, Senior Scientist	Member
Mr. Anil Kumar, Scientist	Member
Dr. Siddhartha Majumdar, Principal Technical Officer	Member
Mr. Sudipto Chatterjee, F&AO, IICB	Member
Dr. B. C. Sahoo, Administrative Officer, IICB	Member Secretary



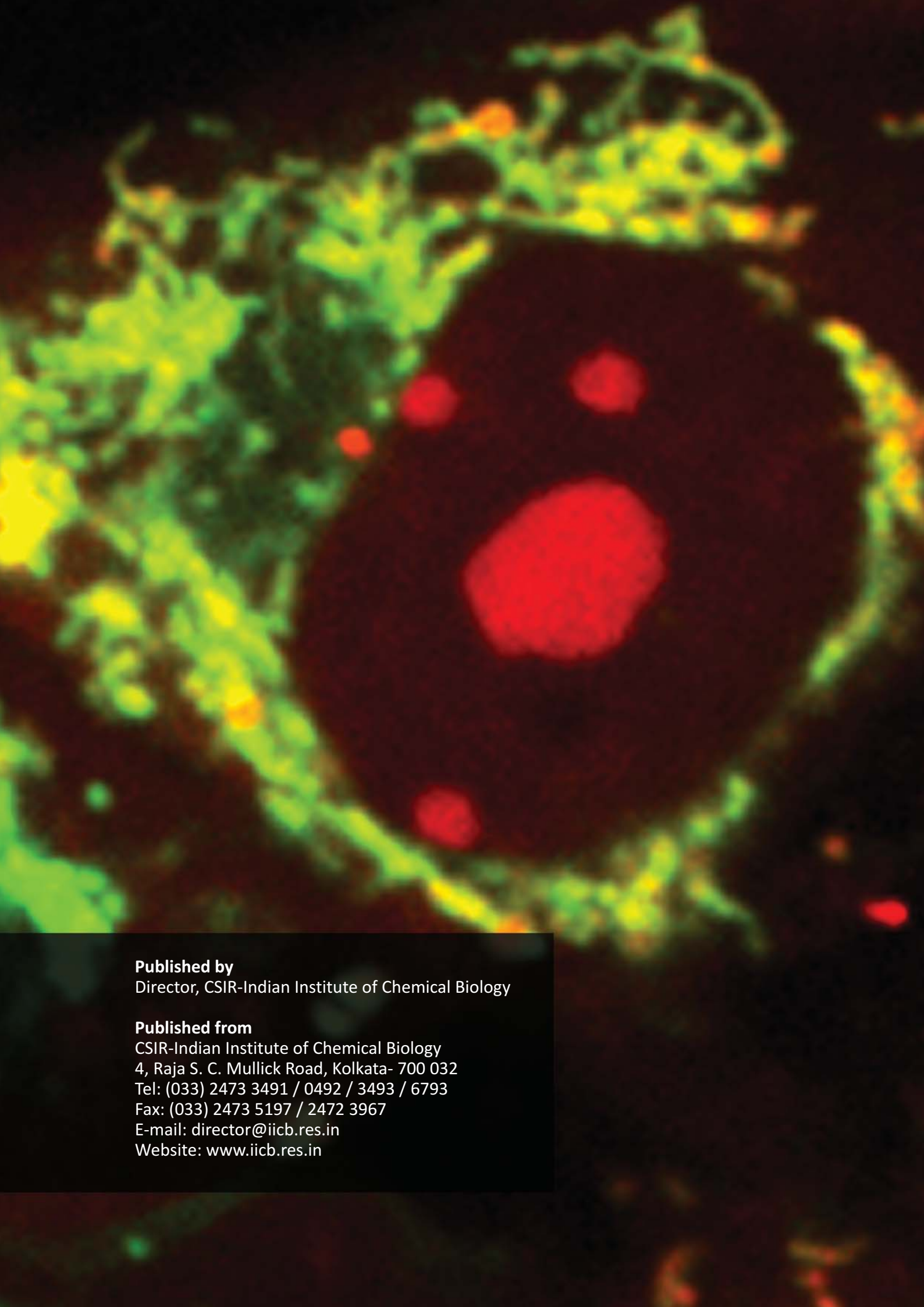
Crucial H-bond interactions (classical and non-classical) of iminium. Black and blue dotted line denote the classical and the non-classical H-bonds, respectively.

Courtesy: Dr. G. Suresh Kumar

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