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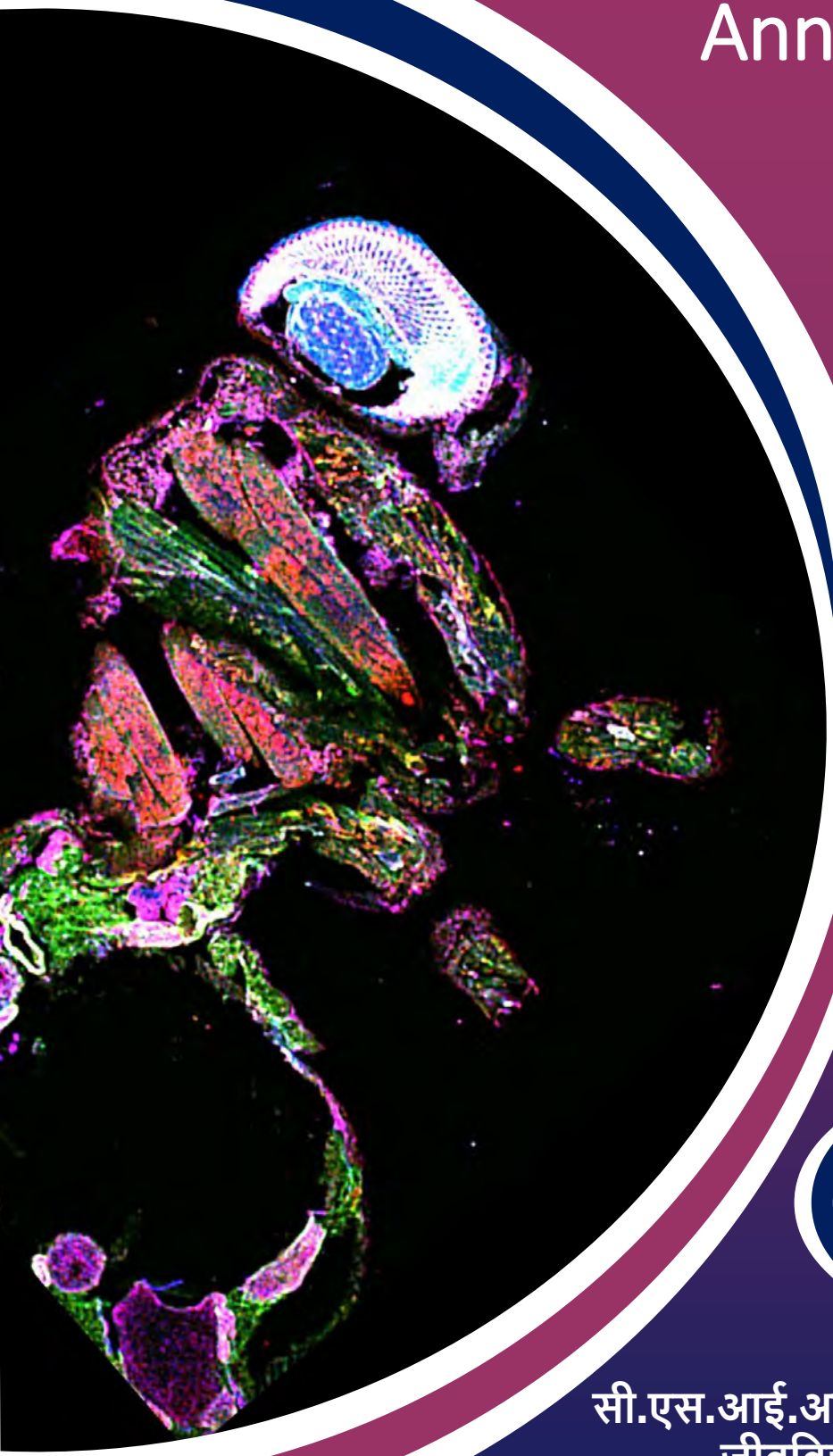
Annual Report
2023-24



सीएसआईआर
CSIR
भारत का नवाचार इंजन
The Innovation Engine of India

सीएसआईआर-आईआईसीबी
CSIR-IICB

सी.एस.आई.आर.-भारतीय रासायनिक जीवविज्ञान संस्थान, कोलकाता

CSIR-Indian Institute of Chemical Biology, Kolkata

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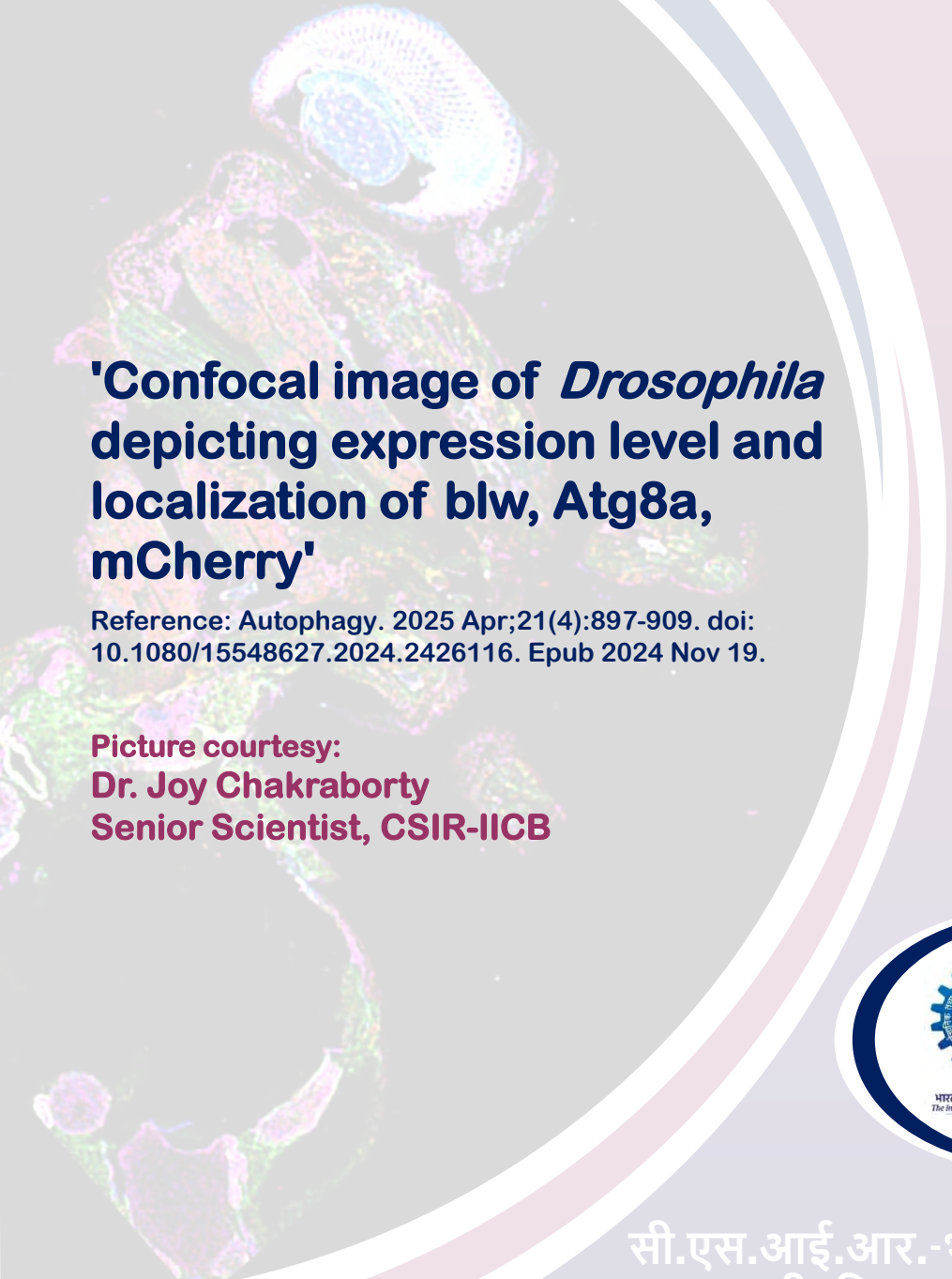
Annual Report
2023-24



'Confocal image of *Drosophila* depicting expression level and localization of blw, Atg8a, mCherry'

Reference: Autophagy. 2025 Apr;21(4):897-909. doi: 10.1080/15548627.2024.2426116. Epub 2024 Nov 19.

Picture courtesy:
Dr. Joy Chakraborty
Senior Scientist, CSIR-IICB

सी.एस.आई.आर.-भारतीय रासायनिक जीवविज्ञान संस्थान, कोलकाता
CSIR-Indian Institute of Chemical Biology, Kolkata

वार्षिक प्रतिवेदन

Annual Report

2023-24

सी.एस.आई.आर.-भारतीय रासायनिक जीवविज्ञान संस्थान

4, राजा एस. सी. मल्लिक रोड, यादवपुर, कोलकाता - 700032, भारत

CSIR-Indian Institute of Chemical Biology

4, Raja S. C. Mullick Road, Jadavpur, Kolkata - 700032, India

About CSIR-IICB

CSIR-Indian Institute of Chemical Biology stands as a premier biomedical research institute under the auspices of CSIR, leading cutting-edge research and development in understanding both infectious and non-infectious diseases biology. Our relentless efforts are directed towards the development of drug candidates, diagnostic tools, and therapeutic agents to address these challenges. CSIR-IICB's unique position, amalgamating medicinal chemistry and biology groups, empowers us to achieve ambitious targets in our quest for scientific excellence.

Vision

CSIR-Indian Institute of Chemical Biology stands at the forefront of biomedical sciences, uniquely integrating basic biological research with synthetic chemistry, phytochemistry, biophysical, and structural biology techniques. Presently, our innovative approach extends to the realms of Artificial Intelligence and Machine Learning. This multidisciplinary approach propels our mission to develop cutting-edge technologies and advance drug development, dedicated to addressing critical human diseases of national significance. Aligned with the CSIR's vision in healthcare research, IICB is committed to pioneering transformative solutions at the intersection of various scientific disciplines.

Mission

CSIR-IICB is dedicated to pioneering advancements in 5 key thematic areas:

- Innovative approaches in healthcare for communicable and non-communicable diseases
- Host-pathogen interactions in microbial colonization, infection, and disease
- Cell-based therapies, biological therapeutics (Biologics) for the management of autoimmune disorders (SLE, RA), Idiopathic Pulmonary Fibrosis, Solid Tumors (Breast, Ovarian, Pancreatic), and AML.
- Development of therapeutic agents and diagnostic probes from both synthetic and natural sources.
- Developing synthetic process technology for healthcare, pharmaceuticals & agrochemicals.

Our mission is to strategically expand and evolve in these thematic areas, charting a transformative course toward our Vision for 2030. Through a well-defined roadmap comprising short-term, mid-term, and long-term goals, we aim to propel our scientific pursuits. In the short term, we focus on ongoing projects, delineating achievable objectives over the next 2-3 years. Transitioning into the mid-term (till 2030), we harness insights from current initiatives to elevate our technologies for broader clinical and industrial impact. The long-term goals extend beyond 2030, propelling us into the next frontier of scientific and technological exploration in the healthcare sector.

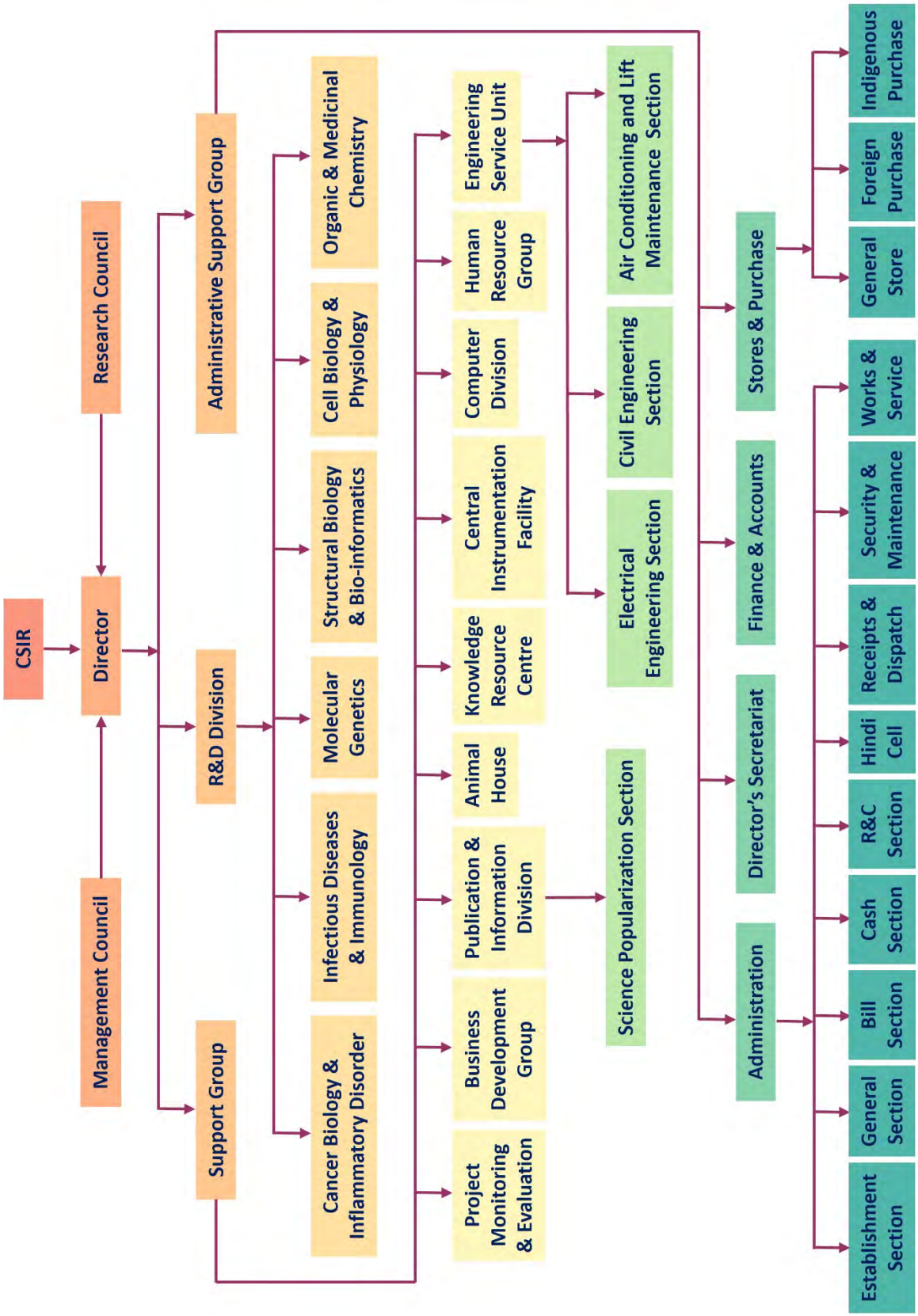
Mandate

In the coming year, CSIR-IICB is committed to a multifaceted mandate encompassing various strategic initiatives:

- Research Themes and Technology: Aligning our project proposals with CSIR Mission Mode Projects and external funding organizations, focusing on short-term and mid-term research goals within the specified thematic areas.
- Interdisciplinary Approach: Emphasizing our commitment to interdisciplinary research, evident in our short-, mid-, and long-term goals, fostering innovation and holistic scientific exploration.
- Facilities and Pilot Plants Establishment: Proposing the creation of a national drug screening facility, a pioneering initiative at CSIR, and a pilot plant for reactors to scale up in-house drug production. This contributes to sustainability, supports local industries, and generates revenue, fostering start-ups in the eastern region.
- Training and Mentorship Programs: Offering Ph.D. programs, training undergraduates, and participating in CSIR's Skill Development mission to provide short-term training, empowering individuals with biomedical and chemical research expertise.
- Research Collaboration: Strengthening collaborations with national and international universities, research institutes, hospitals, and industries to enhance project outcomes through shared expertise.
- Policy Contributions: Engaging in national policy and mission development related to biomedical research, sharing research findings, and contributing expertise to shape policies addressing public health challenges.
- Regular Assessment and Adaptation: Continuously evaluating ongoing projects, reassessing research priorities, and adapting strategies to align with emerging trends and advancements in the field.
- Translation of Research: Ensuring the translation of newly developed chemical resources and knowledge into practical solutions for specific diseases, exploring partnerships with industry and healthcare sectors to facilitate the application of research outcomes.
- Communication and Outreach: Conduct regular assessments of project progress, reassessing research priorities, and adapting strategies based on emerging trends and advancements.

Contents

CSIR-IICB Organisation Chart



Director's Message

It gives me great pleasure to present the CSIR-IICB Annual Report for the year 2023-24, reflecting on our achievements and activities as an institution.

This report is an overview of the research activities and achievements of the scientists of CSIR-IICB has been described under six divisions namely Cancer Biology & Inflammatory Disorder, Cell Biology & Physiology, Infectious Diseases and Immunology, Molecular Genetics, Organic & Medicinal Chemistry and Structural Biology & Bioinformatics. Our research covers all areas of Chemical Biology, in alignment with the mandate of CSIR-IICB. We have made significant contributions to a number of cutting-edge research projects and have initiated several new projects. As in previous years, this year also we have bagged a huge number of high-quality research papers published in reputable international journals. A good number of patents has been filed and granted in the India and abroad and several MoUs was signed. Our success is measured by the tangible results that are reflected in our Key Performance Indicators. Over the past year, our KPIs have provided invaluable insights into our research output.

Our commitment to society is demonstrated through our different outreach programmes. We conducted Skill Development programme to enhance both technical and soft skills of students and prepared them for their future endeavor. We arrange laboratory visits for college students to encourage their aspiration towards research. We have CSIR Jigyasa Programmes to foster young minds toward science. We also have a strong presence in social media to reach all segments of society.

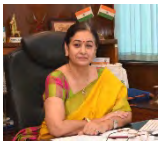
The efficient and smooth flow of our research is a result of our strong administrative and technical support divisions and facilities at CSIR-IICB. Our success is largely based on their behind-the-scenes contributions, providing essential services.

I would like to appreciate the efforts of our Scientists, researchers, staff, partners, and stakeholders who have contributed to our success. Their unwavering dedication are the driving forces behind our progress. I take this opportunity to extend my sincere thanks to DG, CSIR and our Mentor for their guidance. I express my sincere gratitude to our Research Council members and Management council members for their constant support. Together, we will continue to build a brighter future for the society.

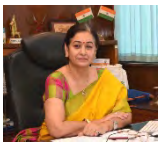
In the coming days, we will remain committed to our vision, mission and mandates and continue to contribute to the advancement of knowledge and make a meaningful impact on society.

Prof. Vibha Tandon
Director, CSIR-IICB

सीएसआईआर-आईआईसीबी अनुसंधान परिषद /
CSIR-IICB Research Council

	Dr. Tapas Kundu / **डॉ. तापस कुंडू** Former Director, CSIR-CDRI; Professor, JNCASR, Jakkur, Bengaluru / पूर्व निदेशक, सीएसआईआर-सीडीआरआई; प्रोफेसर, जेएनसीएएसआर, जक्कुर, बेंगलुरु	Chairman / अध्यक्ष
	Dr. T. Rajamannar / **डॉ. टी. राजमन्नार** Excecutive Vice President & Advisor to MD, Head, High Impact Innovations – Sustainable Health solution, Sun Pharmaceutical Industries Ltd. / कार्यकारी उपाध्यक्ष और एमडी के सलाहकार, प्रमुख, उच्च प्रभाव नवाचार - सतत स्वास्थ्य समाधान, सन फार्मास्युटिकल इंडस्ट्रीज लिमिटेड	External Member / बाहरी सदस्य
	Dr. V. Ravichandiran / **डॉ. वी. रविचंदीरन** Director, NIPER, Kolkata / निदेशक, एनआईपीईआर, कोलकाता	External Member / बाहरी सदस्य
	Dr. Arnab Mukhupadhyay / **डॉ. अर्नब मुखोपाध्याय** National Institute of Immunology, JNU, New Delhi / राष्ट्रीय प्रतिरक्षा विज्ञान संस्थान, जेएनयू, नई दिल्ली	External Member / बाहरी सदस्य
	Dr. Mukul Jain / **डॉ. मुकुल जैन** Senior Vice President, Zydus Research Center, Zydus Lifesciences Ltd. Ahmedabad / वरिष्ठ उपाध्यक्ष, ज़ाइडस रिसर्च सेंटर, ज़ाइडस लाइफसाइंसेज लिमिटेड, अहमदाबाद	External Member / बाहरी सदस्य
	Dr. Meenakshi Sharma / **डॉ. मीनाक्षी शर्मा** Division of Non-Communicable Diseases, Indian Council of Medical Research, New Delhi / गैर-संचारी रोगों का प्रभाग, भारतीय चिकित्सा अनुसंधान परिषद, नई दिल्ली	Agency Representative / एजेंसी प्रतिनिधि
	Dr. Sanjeev Khosla / **डॉ. संजीव खोसला** Director, CSIR-IMTech / निदेशक, सीएसआईआर-इमटैक	Sister Laboratory / सहयोगी प्रयोगशाला के निदेशक
	Prof. Vibha Tandon / **प्रो. विभा टंडन** Director, CSIR- IICB / निदेशक, सीएसआईआर- आईआईसीबी	Laboratory Director / प्रयोगशाला निदेशक
	Dr. Geetha Vani Rayasam / **डॉ. गीता वाणी रायसम** Council of Scientific & Industrial Research, New Delhi / वैज्ञानिक एवं औद्योगिक अनुसंधान परिषद, नई दिल्ली	DG's representative / महानिदेशक के प्रतिनिधि

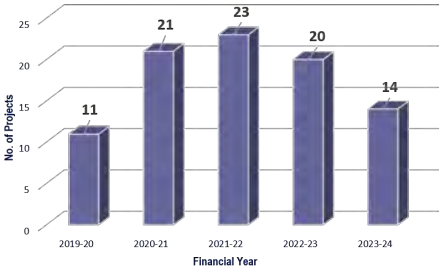
सीएसआईआर-आईआईसीबी प्रबंधन परिषद / CSIR-IICB Management Council

	Prof. Vibha Tandon / **प्रो. विभा टंडन** Director, CSIR- IICB / निदेशक, सीएसआईआर-आईआईसीबी	Chairman / अध्यक्ष
	Dr. Souvik Maity / **डॉ. शौविक मैती** Director, CSIR-IGIB, Kolkata / निदेशक, सीएसआईआर-सीजीसीआरआई, कोलकाता	Director of sister laboratory / सहयोगी प्रयोगशाला के निदेशक
	Dr. P. Jaisankar / **डॉ. पी. जयशंकर** Chief Scientist / मुख्य वैज्ञानिक	Scientist of the laboratory representing the staff of various age groups / विभिन्न आयु समूहों के कर्मचारियों का प्रतिनिधित्व करने वाले प्रयोगशाला के वैज्ञानिक
	Dr. Sarita Ghosh / **डॉ. सरिता घोष** Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक	
	Dr. Upasana Roy / **डॉ. उपासना रॉय** Principal Scientist / प्रधान वैज्ञानिक	
	Dr. Sourish Ghosh / **डॉ. सौरीश घोष** Senior Scientist / वरिष्ठ वैज्ञानिक	
	Dr. S.C. Biswas / **डॉ. एस.सी. बिस्वास** Chief Scientist / वरिष्ठ प्रधान वैज्ञानिक	Head, RPBD/PME of the Laboratory / प्रयोगशाला के प्रमुख, आरपीबीडी/पीएमई
	Dr. E. Padmanabam / **डॉ. ई. पद्मनाभम** Principal Technical officer / प्रधान तकनीकी अधिकारी	Representative of the technical personnel / तकनीकी कार्मिकों के प्रतिनिधि
	Finance & Accounts Officer, CSIR-IICB / वित्त एवं लेखा अधिकारी, सीएसआईआर-आईआईसीबी	CoFA/FAO of the laboratory / प्रयोगशाला के सीओएफए/एफएओ
	Sr. Controller of Administration / Administrative Officer, CSIR-IICB / सीनियर प्रशासन नियंत्रक/प्रशासनिक अधिकारी, सीएसआईआर-आईआईसीबी	Member Secretary / सदस्य सचिव

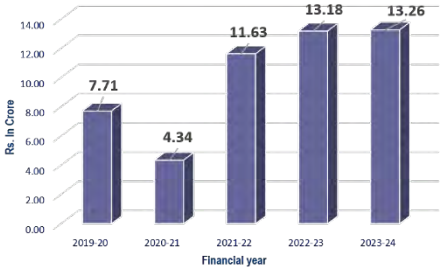
सीएसआईआर-आईआईसीबी पर एक नजर /
CSIR-IICB at a Glance

CSIR Funded Projects at CSIR-IICB

No. of CSIR projects

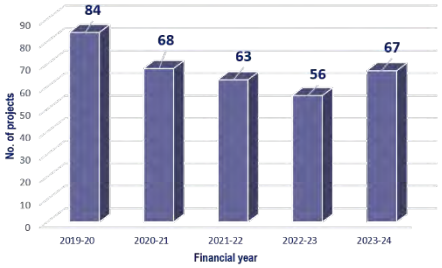


Funds received (In Crore)

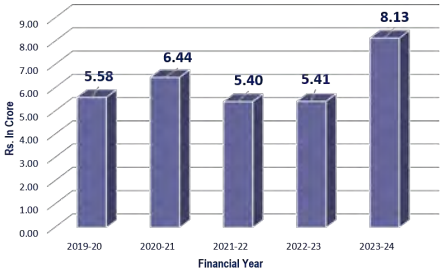


Externally Funded Projects at CSIR-IICB

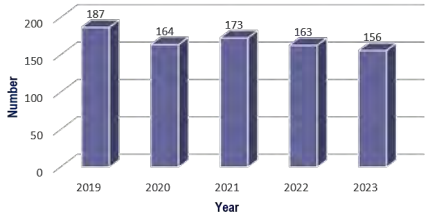
No. of Externally Funded Projects



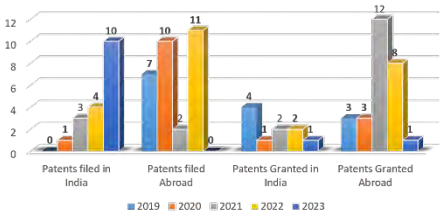
Funds Received (In Crore)



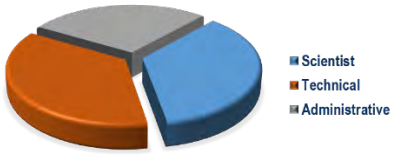
Publications in Last five years



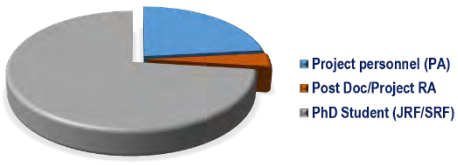
Patents Filed and Granted, Indian and Foreign



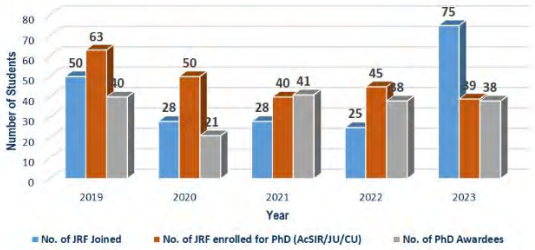
Permanent Staff



Research Personnel



CSIR-IICB: Student data



Research & Development @ CSIR-IICB

Cancer Biology & Inflammatory Disorder

In order for a normal cell to undergo functional deviation and proliferate at the expense of life, it must have a diverse array of aberrations. If viewed at the molecular level, the crucial signalling pathways are found to be extensively rewired. The long-term goals of this division are to focus on the comprehensive understanding of cancer at different levels ranging from the investigation of molecular and genetic basis of cancer, the elucidation of altered cellular processes during oncogenesis, immune response and inflammation associated with tumour development. The faculties of the division are engaged in investigating both basic and translational aspects of different cancer types, including lung, brain, oral, breast, pancreatic, colorectal, prostrate, cervical, ovarian cancer and leukemia.

Dr. Amit Kumar Srivastava and his group members

Understanding and targeting DNA polymerase eta-mediated translesion DNA synthesis in cancer

Research Activities

Targeting DNA polymerase eta-mediated mutagenic translesion DNA synthesis by small molecules

Development of chemoresistance and tumor relapse is the major challenges associated with successful chemotherapy. Accumulated pieces of evidence including data from our laboratory suggest that targeting Pol η mediated-mutagenic translesion synthesis (TLS) is a potential strategy for improving chemotherapy. Therefore, targeting Pol η with small-molecule inhibitors is a promising strategy for combating chemoresistance in certain types of cancer. However, the identification of small molecules which specifically target Pol η -mediated TLS with high *in vivo* efficacy has been challenging. Using *in silico* screening approach, we have identified a small-molecule inhibitor, chrysin that can bind with Pol η more efficiently out of active 230 compounds screened (Saha et al., 2020). A few of the reported interacting residues (Arg 93, Arg 111) are the ones that impart stability to the palm domain of Pol η. We have also performed molecular dynamics studies of this small molecule-target complex. Further, we demonstrated that chrysin treatment sensitizes the ovarian cancer stem-like cells to cisplatin treatment via inhibiting η-mediated TLS. Remarkably, chrysin treatment inhibits Pol η expression and enhances the cisplatin-induced cell death in ovarian CSLCs both *in vitro* and *in vivo*. Pre-treatment with chrysin attenuates cisplatin-induced hematological toxicity and suppresses tumor growth in ovarian cancer human xenografts. These results establish chrysin as a novel class of TLS inhibitors and highlight its potential as a chemotherapy adjuvant for overcoming chemoresistance and improving treatment outcomes in ovarian cancer (Figure 1).

Deciphering the role of miRNAs in ovarian cancer progression and chemoresistance

Cancer stem cells (CSCs) are considered to play a central role in the process of tumor initiation, progression, invasion, metastasis and therapy resistance. MicroRNAs (miRNAs) have important roles in regulating CSC properties like self-renewal, differentiation and stemness, and are considered to be potential pharmacological targets. Altered expressions of various miRNAs have been reported in ovarian cancer cells. However, only few miRNAs have been reported to link with stemness, chemoresistance and progression of ovarian cancer. Tumor suppressive role of miR-379-5p have been

reported in various malignancies such as breast, gastric, non-small cell lung carcinoma and hepatocellular carcinoma. However, we still lack evidence for the inhibitory function of miR-379-5p in ovarian cancer metastasis and chemoresistance. Herein, we showed that miR-379-5p is downregulated in several OC cell populations in both cell lines and primary patient tumors. Furthermore, miR-379-5p overexpression effectively inhibits CSLCs and counters cisplatin-induced expansion of CSCs. Mechanistic investigations identify Rad18, a DNA repair protein involved in translesion DNA synthesis (TLS), as direct target of miR-379-5p. Moreover, a negative correlation between miR-379-5p and Rad18 expression is observed in ovarian CSLCs isolated from OC patients. The downregulation of Rad18 inhibits stem-like phenotypes and enhances sensitivity of ovarian CSLCs to cisplatin treatment. miR-379-5p mediated inhibition of RAD18 prevents the repair synthesis in CSCs causing DNA damage accumulation. The xenograft study reveals an enhanced DNA damage in presence of miR-379-5p which consequently prevents tumor proliferation in athymic nude mice. Notably, miR-379-5p targeting of RAD18 prevents monoubiquitination of PCNA resulting in reduced DNA Polymerase η (a TLS polymerase that helps to bypass DNA lesions) recruitment to lesion sites. In the absence of Pol η the persisting DNA lesions cause activation of cell cycle arrest and apoptosis pathway in CSLCs. Therefore, our findings unveil a novel mechanism in which miR-379-5p overexpression curtails CSLCs by modulating Rad18/Pol η axis.

Future Research Plans

In next few years, the major focus of our lab would be unravelling the mechanisms lead to development of acquired drug resistance in ovarian cancer. Our long-term goal is to develop small molecules/small molecule-anti-cancer drug conjugate for targeting molecular signalling pathways leading to chemoresistance.

Extramural / CSIR Funding

1. Understanding the role of translesion DNA synthesis in chemoresistance of lung adenocarcinoma (GAP-435), ICMR, New Delhi, 2021-2024, 41 lakhs, 2020-4993/SCR/ADHOC-BMS.
2. Evaluation of anti-cancerous potential: in silico phrenological analysis and molecular mechanism of in ovarian cancer μTumor spheroids, and in in vivo models (GAP-438), CCRAS, Ministry of Ayush, 2023-25, 44.64 lakhs, 1306/2022-23.
3. DBT-Ramalingaswami Fellowship, DBT, New Delhi, Govt. of India, 2018-2023, 32.5 lakhs, BT/HRD/35/02/2006.
4. Anticancer potential and molecular mechanism of Rasa sindhoor on Ovarian Cancer Cells (GAP-455), CCRAS, Ministry of Ayush, 2023-2025, 40.64 lakhs, 761/2022-23.
5. Evaluation of cytotoxicity, pharmacokinetics, anti-cancer activity, detailed molecular mechanisms of Bhallatakadi Modka in in vitro and in vivo tumor xenograft models, CCRAS, Ministry of Ayush, 2021-2023, 23.91 lakhs, 480/2021-22.
6. Utilizing the Principles of Coordination Chemistry to Develop Combination Prodrugs and Nanotherapeutics with a Synthetic Lethality-Like Concept (GAP-462), SERB Govt. of India, 2023-2025, 8.37 lakhs, CRG/2022/005874.
7. Chemopreventive effects of opuntia elatior fruits against chemotherapy-induced toxicity in ovarian cancer pre-clinical models'(GAP-478), CCRAS, Ministry of Ayush, 2024-2026, 37.65 lakhs, 1280/2023-24.
8. Development of Genetically Engineered “off the Shelf” Inducible CAR-T Cells for the Cancer Therapeutics (GAP-448), DBT, New Delhi, Govt. of India, 2022-2025, 53.97 lakhs, BT/PR40619/MED/30/2294/2020.

Publications

1. Chatterjee, B., Sarkar, M., Bose, S., Alam, M. T., Chaudhary, A, A., Dixit, A. K., Tripathi, P. P., Srivastava, A. K. (2023) MicroRNAs: Key modulators of inflammation-associated diseases. *Seminars in Cell & Developmental Biology.* 154, 364-373.
2. Prasad, S., Saha, P., Chatterjee, B., Chaudhary, A.A., Lall, R., Srivastava A. K. (2023) Complexity of tmor microenvironment: Therapeutic role of curcumin and its metabolites. *Nutrition and Cancer.* 75, 1-13.
3. Mandal, T., Shukla, D., Pattanayak, S., Barman, R., Ashraf, R., Dixit, A.K., Kumar, S., Kumar, D., Srivastava, A. K. (2024) Ellagic acid induces DNA damage and apoptosis in cancer stem-like cells and overcomes cisplatin resistance. *ACS Omega* (In press).
4. Shukla, D., Mandal, T., Srivastava, A. K. (2024) Neil1 deficiency facilitates chemoresistance through upregulation of RAD18 expression in

ovarian cancer stem cells. *Biochem Biophys Res Commun*. 18, 712-713.

5. Roy, S., Das, A., Bairagi, A., Das, D., Jha, A., Srivastava, A.K., Chatterjee N. (2024) Mitochondria act as a key regulatory factor in cancer progression: Current concepts on mutations, mitochondrial dynamics, and therapeutic approach. *Reviews in Mutation Research* (In press).

Patents

A recombinant construct for screening drugs against SARS-COV-2 spike protein. 04.05.2023, PCT/IN2022/050949, Co-inventor.

Conferences Attended

National seminar on "Trends in Biomedical Research: Advances and Challenges" from 29th January to 30th January, 2024 organized by CCRAS-CARI, Kolkata.

Dr. Amit Kumar Srivastava, Senior Scientist

Group Members: Ananya Ganguly, Project-SRF; Devendra Shukla, CSIR-SRF; Tanima Mandal, CSIR-SRF; Bilash Chatterjee, UGC-SRF; Subhankar Bose, CSIR-SRF; Debanjan Ghosh, Project-JRF; Sangita Mishra, Project-JRF

Collaborators: Prof. Ramesh Ganju, PhD, Department of Pathology, The Ohio State University, Columbus, USA; Prof. Qi-En Wang, PhD, Department of Radiology, The Ohio State University, Columbus, USA

Dr. Amitava Sengupta and his group members

Epigenetic regulation of acute myeloid leukemia hematopoiesis

Research Activities

Physiological aging is associated with the onset of chronic and lifestyle diseases including cancer. Hematopoietic aging is characterized by clonal expansion of myeloid-biased hematopoietic stem cells/ progenitors and by increased risk of development of myeloid leukemia. Although the majority of patients with acute myeloid leukemia (AML) initially respond to chemotherapy, many of them subsequently relapse, and the mechanistic basis for AML persistence following chemotherapy remains poorly understood. We are trying to test the hypothesis that epigenetic dysregulation within hematopoietic compartment is involved in hematopoietic aging and causes AML pathogenesis. We are particularly interested at understanding the cell-autonomous and non-cell-autonomous molecular determinants that regulate HSC self-renewal, differentiation and interaction with hematopoietic microenvironment or niche. Our overarching aim is identification of altered and unique epigenetic fingerprints in human myeloid leukemia, and characterization of epigenetic vulnerabilities in AML.

AML is a heterogeneous, aggressive malignancy with dismal prognosis and with limited availability of targeted therapies. Epigenetic deregulation contributes to AML pathogenesis. KDM6 proteins are histone-3-lysine-27-demethylases that play context-dependent roles in AML. Recently we have identified that KDM6-demethylase function critically regulates DNA-damage-repair-(DDR) gene expression in AML. Mechanistically, KDM6 expression is regulated by genotoxic stress, with deficiency of KDM6A-(UTX) and KDM6B-(JMJD3) impairing DDR transcriptional activation and compromising repair potential. Acquired KDM6A loss-of-function mutations are implicated in chemoresistance, although a significant percentage of relapsed-AML has upregulated KDM6A. Olaparib treatment reduced engraftment of KDM6A-mutant-AML-patient-derived xenografts, highlighting synthetic lethality using Poly-(ADP-ribose)-polymerase-(PARP)-inhibition.

Crucially, a higher KDM6A expression is correlated

with venetoclax tolerance. Loss of KDM6A increased mitochondrial activity, BCL2 expression, and sensitized AML cells to venetoclax. Additionally, BCL2A1 associates with venetoclax resistance, and KDM6A loss was accompanied with a downregulated BCL2A1. Corroborating these results, dual targeting of PARP and BCL2 was superior to PARP or BCL2 inhibitor monotherapy in inducing AML apoptosis, and primary AML cells carrying KDM6A-domain mutations were even more sensitive to the combination. Together, our study illustrates a mechanistic rationale in support of a novel combination therapy for AML based on subtype-heterogeneity, and establishes KDM6A as a molecular regulator for determining therapeutic efficacy. Unlike solid tumors, hematologic malignancies do not frequently harbor BRCA1/2 mutations. PARP inhibition as a therapeutic strategy in blood disorders, therefore, did not receive the same importance. However, underlying epigenetic plasticity and leveraging transcriptional dependencies across molecular subtypes of leukemia has invigorated PARP inhibition-guided synthetic lethality in hematologic malignancies (Figure 1).

Future Research Plans

We aim to examine 1) epigenetic mechanisms of AML pathogenesis, 2) interrogate evolution of AML immune microenvironment heterogeneity and inflammatory signaling, and 3) characterize immunomodulatory therapy.

Extramural / CSIR Funding

Harnessing epigenetic dependencies for immunomodulation in acute myeloid leukemia, Institutional Research Project Grant, Lady Tata Memorial Trust, March 2024-March 2027, 100 lakhs, GAP-480.

Publlications

1. Boila, L. D., Sengupta, A. Unifying targeted therapy for leukemia in the era of PARP inhibition. (2023). *Exp Hematol.* 124, 1-14.
2. Boila, L. D., Ghosh, S., Bandyopadhyay, S. K., Sengupta, A. (2023). KDM6 demethylases integrate DNA repair gene regulation and loss of KDM6A sensitizes human acute myeloid leukemia to PARP and BCL2 inhibition. *Leukemia* 37, 751-764.
3. Bandyopadhyay, S. K., Bose, A., Chattopadhyay, A., Ghosh, S., Bhowmik, S., Samanta, S. K., Bhattacharyya, M., Sengupta, A. Histone lysine demethylase modulate anti-tumor immune response in AML (2023). *Blood* 142, 2753. (Abstract for 65th American Society of Hematology Annual Meeting, CA, USA).

Invited Lectures

Epigenetic insights for acute myeloid leukemia targeted therapy. ACTREC, Navi Mumbai. 42nd Annual Conference of Indian Association for Cancer Research, 12-16 January 2023.

Conferences Attended

42nd Annual Conference of Indian Association for Cancer Research, ACTREC, Navi Mumbai. 12-16 January 2023.

Awards

S Ramachandran National Bioscience Award for Career Development, DBT, CGO Complex, Lodhi Road, New Delhi, 2023

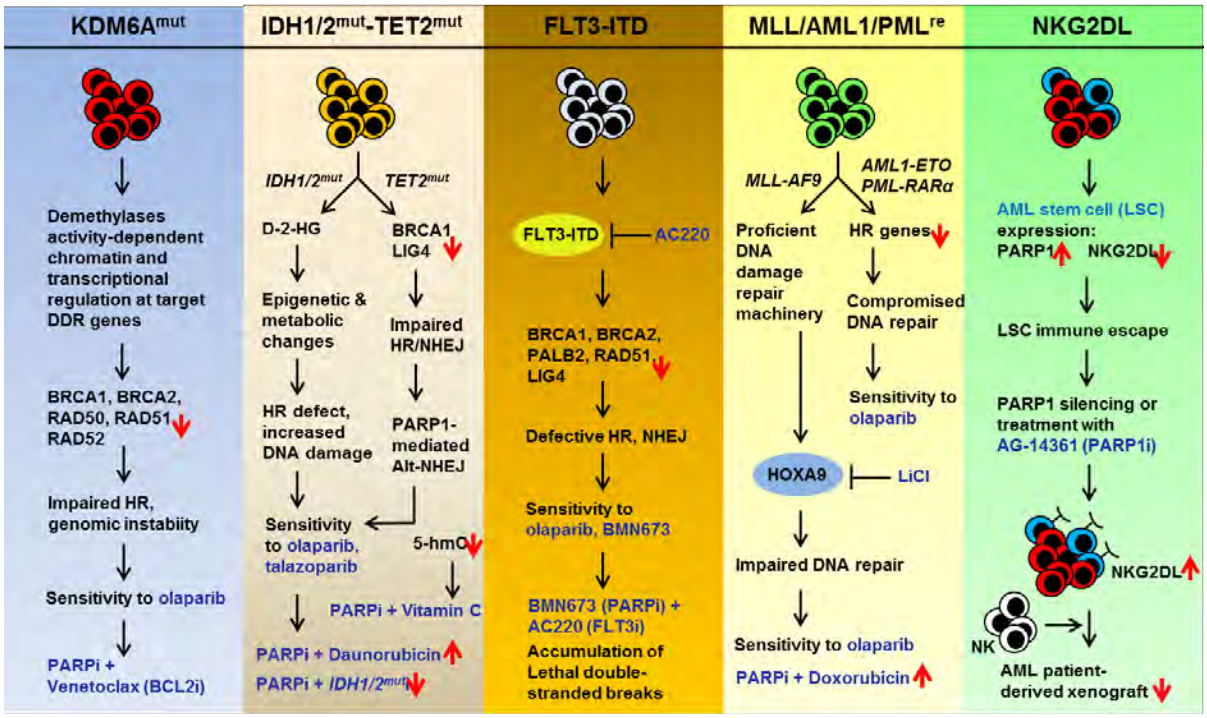


Figure 1: AML cells with varying moleculars ubtypes are sensitive to PARP inhibition.

Dr. Amitava Sengupta, Senior Principal Scientist
Group Members: Subham K. Bandyopadhyay, DBT-SRF; Subhadeep Ghosh, CSIR-SRF; Satyaki Bhowmik, CSIR-JRF; Anwesha Bose, CSIR-JRF
Collaborators: Dr. Maitreyee Bhattacharyya, Institute of Hematology & Transfusion Medicine, Medical College & Hospital, Kolkata; Dr. Arnab Chattopadhyay, IHTM, Medical College & Hospital, Kolkata; Dr. Sambit K. Samanta, IHTM, Medical College & Hospital, Kolkata; Dr. Prakas K. Mandal, NRS Medical College & Hospital, Kolkata; Dr. Debasis Banerjee, Ramakrishna Mission Seva Pratisthan, Kolkata; Dr. Arindam Maitra, National Institute of Biomedical Genomics, Kalyani

Dr. Debasis Nayak and his group members

Exploring the metabolic vulnerabilities of pancreatic and colorectal cancer cells for targeted therapeutic development

Research Activities

The solid tumor microenvironment (TME) is a nutrient-poor environment wherein the cancer cells strive for their survival and expansion. Moreover, the cancer cells undergoing epithelial-mesenchymal transition (EMT), surviving in the circulation or migrating to a secondary organ site experience various stresses such as hypoxia, nutrient stress, oxidative stress and nitrosative stress. Under such stressed conditions, cancer cells rewire many metabolic pathways and regulate numerous proteins to adapt to the changing environment and fulfill their nutritional requirements. One important class of proteins, which alter during such metabolic adaptations in cancer cells are the solute carriers (SLCs). SLCs are membrane transport proteins, expression of which occurs mainly on the cell membrane and on the membranes of cell organelles such as mitochondria and lysosomes. There are about more than 450 individual SLC proteins grouped into 65 sub-families; together they constitute a superfamily, which is the second largest family of membrane proteins after the G protein-coupled receptors family. SLCs are involved in the transport of various nutrients such as carbohydrates, amino acids and ions across the membrane for performing various cellular activities and thus, they are regarded as metabolic gatekeepers of cells. They are also involved in removal of waste materials from the cells, thus help in maintaining cellular homeostasis. Proliferating cancer cells exploit various SLCs to fulfill their increased nutritional requirements, and hence, aberrant expression of different SLCs are observed at various stages of cancer progression. Therefore, SLCs are crucial drug targets to interfere with the metabolic supply of cancer cells for inhibiting tumor growth and metastasis.

Currently my research group is focusing on studying the biology, mechanism and therapeutic targeting of some crucial SLCs in pancreatic and colorectal cancer. We have the following research questions:

1: How SLC22A15 is involved in pancreatic and colorectal cancer progression and whether we can target it to achieve therapeutic benefits?

SLC22A15 (Solute carrier family 22, member 15) is recently reported for its tumor promoting role in pancreatic, colorectal and hepatocellular carcinoma. Analysis of the previously performed RNA-sequencing results of SLC22A15-overexpressing clones demonstrate that SLC22A15 upregulates genes related to cancer stemness such as ROR1, ROR1-AS1 and ALDH1A1 in pancreatic cancer. Furthermore, The Cancer Genome Atlas (TCGA) and GEPIA database search for SLC22A15 expression suggests that this gene is highly expressed in pancreatic and colorectal cancers and its high expression is positively correlated with poor overall patient survival. In addition, SLC22A15 triggers genes and signaling pathways that lead to fatty acid metabolism and lipogenesis in cancer. Therefore, keeping these observations in mind, we are now investigating whether SLC22A15 promotes stemness in pancreatic and colorectal cancers and what is its mechanism of action. This will lead to exploration of pathways/nodes and open avenues for identifying small molecule modulators of SLC22A15 or its downstream targets for pharmacological intervention. Illustrated in Figure 1A.

2: How SLC28A3 (a nucleoside analog drug transporter) gets downregulated in advanced pancreatic cancers and whether we can restore its expression to get improved treatment outcomes?

SLC28A3 (Solute carrier family 28, member 3), also called concentrative nucleoside transporter 3 (CNT3) is a membrane transporter protein mainly involved in sodium-dependent transport of endogenous nucleosides and nucleoside analog anticancer and antiviral drugs (e.g. gemcitabine, azacitide, ribavirin) into the cells [4]. Immunohistochemistry (IHC) analysis of this protein in pancreatic cancer patient tissues demonstrated that expression of CNT3 is downregulated in undifferentiated tumors compared to differentiated tumor tissues and adjacent normal tissues. TNMplot database search also revealed that SLC28A3 expression is remarkably downregulated in metastatic pancreatic cancer tissues compared to primary tumor and normal tissues. Moreover, a study by Zheng et al. demonstrated that CNT3 expression was augmented in tissues of genetically engineered mouse models of pancreatic cancer knockout for transcription factors SNAIL1 and TWIST1 (genes promoting epithelial-mesenchymal transition (EMT)) [5]. We are currently investigating (i) how CNT3 is lost in pancreatic cancer, (ii) whether CNT3 expression influences EMT and its mechanism of action and (iii) whether restoration of CNT3 can increase nucleoside analog drug uptake and better therapeutic efficacy in pancreatic cancer. Illustrated in Figure 1B.

Future Research Plans

- How mitochondrial SLCs play roles during nutrient-deprivation in pancreatic cancer cells?
- How fatty acid metabolism and lipogenesis influence drug transporters and drug efficacy in colorectal cancer?
- How gut microbiome impacts pancreatic cancer progression and chemoresistance?

Publications

Persaud, A. K., Bernier, M. C., Massey, M. A., Agrawal, S., Kaur, T., Nayak, D., Govindarajan, R. (2023). Increased renal elimination of endogenous and synthetic pyrimidine nucleosides in concentrative nucleoside transporter 1 deficient mice. *Nature Comm*, 14, 3175.

Book Chapters

Nayak, D., Weadick, B., Govindarajan, R. (2023). Combination of Tissue Microarray Profiling and Multiplexed IHC Approaches to Investigate Transport Mechanism of Nucleoside Analog Drug Resistance. In Cancer Systems and Integrative Biology: *Methods in Molecular Biology Book Series*, 95-121. New York, NY: Springer US.

Invited Lectures

1. Targeting solute carrier (SLC) transporters in cancer- A promising aspect towards therapeutic development, National Conference on Recent Advances in Cancer Research and Diagnostic Approaches, Department of Biochemistry, Prof. Dhanapalan College of Science and Management, Padur, Chennai 603103, October 06, 2023.
2. Understanding the role of solute carrier (SLC) transporters in pancreatic cancer- molecular mechanisms and therapeutic targeting, Annual Research Conclave, CSIR-Indian Institute of Chemical Biology, Kolkata, January 25, 2024.

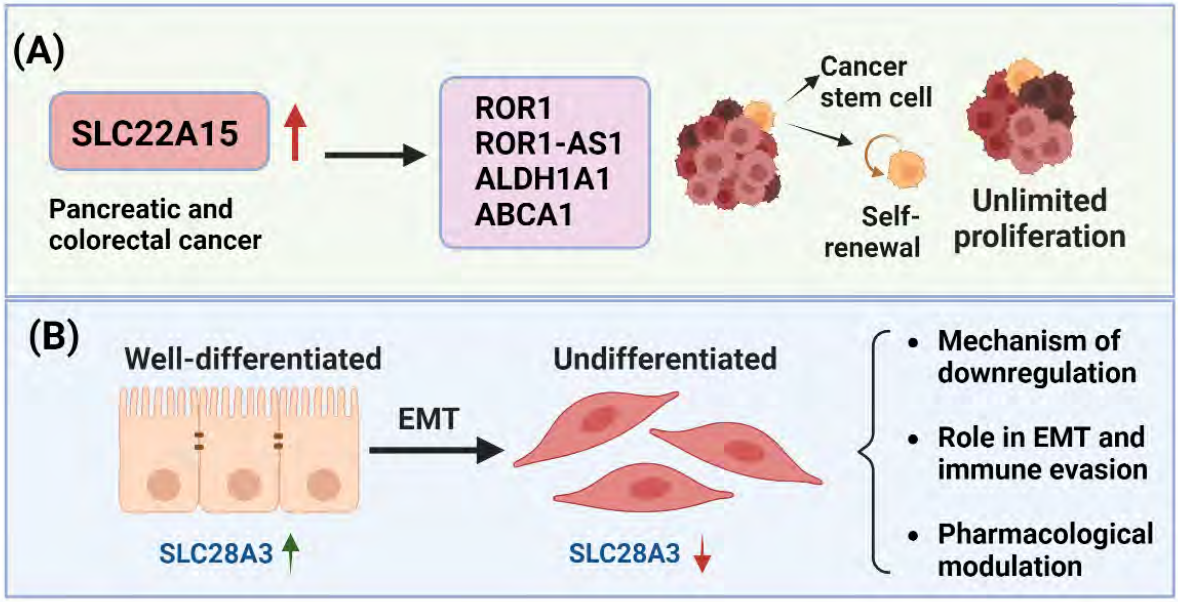
Conferences Attended

1. International Conference on Metabolic Diseases (ICMD) 2023, CSIR-Indian Institute of Chemical Biology, Kolkata, August 19, 2023.

2. 15th Annual Meeting of NEUROUPDATE 2023, Neuroupdate, CSIR-Indian Institute of Chemical Biology, Kolkata, November 25-26, 2023.
3. Chaired a Scientific Session of Society of Biological Chemists (I) (Kolkata Chapter), 6-8 April 2024, Shankarpur, West Bengal.

Member of Society

1. Indian Association of Cancer Research (IACR)
2. American Association of Pharmaceutical Scientists (AAPS)



Dr. Debasis Nayak, Scientist
Group Members: Ritwik Mandal, JRF; Tanaya Mondal, JRF; Bappaditya Mitra, JRF; Anup Hazra, JRF; Tania Karmakar, Research Intern; Anushree Biswas, Research Intern

Dr. Dipyaman Ganguly and his group members

Exploring plasmacytoid dendritic cell biology in the clinical contexts of autoreactive inflammation and role of Piezo1 mechanosensors in regulation of human immunocellular functions

Research Activities

Ours is a human cellular immunology and cell biology laboratory. Our research broadly concentrates on role of innate immune axis in diverse clinical contexts of autoreactive inflammation (*Diabetes, 2016; Trends Immunol, 2018; J Immunol, 2019; Front Immunol, 2019; Front Immunol, 2021; Obesity, 2023; J Immunol, 2024*). We are inspired by a holobiotic view of the immune system, wherein a multidimensional regulatory model is envisaged to influence systemic immune functions, which include genome, epigenome, microbiome and metabolome. Our laboratory is also interested in how mechanical cues can modulate immune functions in different immune cells, in terms of their migration, activation and other cell biological phenomena (*J Immunol, 2018; Crit Rev Immunol, 2020, eLife 2024, J Med Chem, 2024*).

We collaborate with medicinal chemists to develop small molecules that can target crucial innate immune events for potential therapeutic usage (*ChemMedChem, 2023; J Med Chem, 2022; J Med Chem, 2021; J Med Chem, 2020; Eur J Med Chem, 2020; J Med Chem, 2019; Eur J Med Chem, 2018; Eur J Med Chem; 2017*).

Our laboratory also led a randomized control trial on convalescent plasma therapy in severe COVID-19 along with immunopathogenic studies during the COVID-19 pandemic (*mBio, 2023; Gut Pathog, 2023; Nat Commun, 2022; JAMA Netw Open, 2022; J Infect Dis, 2021*).

Future Research Plans

Utilizing their experience of working with primary human pDCs and employing gene-targeting techniques we want to explore novel molecular regulators of human dendritic cell function. Major focus is on identifying regulators of, a) endosomal maturation, b) endosomal pH regulation and c) differential cytokine induction by dendritic cell subsets.

Based on preliminary studies done earlier, our laboratory is going to explore role of plasmacytoid

dendritic cells and type I IFNs in the clinical contexts of neuroinflammation.

Based on our work on the role of Piezo1 mechanosensors in human immune cells, our laboratory is exploring crucial immunocellular events for plausible influence of physical cue sensing by Piezo1.

We are also currently contributing in a phase II/III randomized control trial for an indigenously developed hepatitis-E vaccine in a multi-institutional collaborative project and a post-vaccination follow-up study for COVID-19.

Extramural / CSIR Funding

1. Indo-Italian Grant for Significant Research: Exploring the heterogeneity of systemic lupus patients based on autoantibodies distribution and multi-omics approaches compared in two ethnic cohorts (Principal Investigator, India; Other institutions: ISI, IPGMER). DST, India,1.38 Crores, 2021-23, INT/Italy/P-25/2022, GAP403.
2. Phase II/III clinical trial of an indigenously developed hepatitis-E vaccine (Co-investigator, PI: Prof. Rakesh Aggarwal, JIPMER; other institutions: JIMPER, SGPGI, SNU, Zydus). BIRAC, India, 33.8 lakhs, 2022-24, BT/NBM0371/NBM/09/20, GAP445.
3. Multicentric post-vaccination immune response against COVID-19 (Co-investigator, PI: Dr. Vivek Rao, CSIR-IGIB; Other institutions: IMTech, CDRI, CCMB), CSIR, India, 108 lakhs, 2021-23, MLP2105.
4. Indo-French Collaborative Research Project: Exploring the role of DNAse1L3 in obesity-associated metaflammation and type 2 diabetes (Principal Investigator, India), CEFIPRA, 60 lakhs, 2021-23, CEFIPRA-6203-1, GAP433.
5. Niche Creating Project: Deriving a pan-omics diagnostic pipeline for systems level immune health and therapeutic targeting in systemic autoimmunity (Principal Investigator; other institutions: CSIR-IGIB), CSIR, India, 330 lakhs, 2020-24. MLP135.

Publications

1. Liu, C.S.C., Mandal, T., Biswas, P., Hoque, M.A., Bandopadhyay, P., Sinha, B.P., Sarif, J., D'Rozario, R., Sinha, D.K., Sinha, B., Ganguly, D. (2024) Piezo1 mechanosensing regulates integrin-dependent chemotactic migration in human T cells. *Elife*. 12, RP91903.
2. Mehta, P., Chattopadhyay, P., Mohite, R., D'Rozario, R., Bandopadhyay, P., Sarif, J., Ray, Y., Ganguly, D., Pandey R. (2024) Suppressed transcript diversity and immune response in COVID-19 ICU patients: a longitudinal study. *Life Sci Alliance*. 7, e202302305.
3. Ghosh, A.R., Bandopadhyay, P., Sarkar, J., Khanna, S., Chaudhuri, T., Tantia, O., Chakrabarti, P., Ganguly D. (2023) Mitochondrial sourcing of interferogenic ligands and an autoantigen in human obesity-associated metaflammation. *Obesity*. 31, 2229-2234.
4. Talukdar, D., Bandopadhyay, P., Ray, Y., Paul, S.R., Sarif, J., D'Rozario, R., Lahiri, A., Das, S., Bhowmick, D., Chatterjee, S., Das, B.*, Ganguly D*. (2023) Association of gut microbial dysbiosis with disease severity, response to therapy and disease outcomes in Indian patients with COVID-19. *Gut Pathog*. 15, 22.
5. Sinha, B.P., Mehta, P., Hoque, M.A., Bandopadhyay, P., Nandi, A., Saha, I., Nandi Mitra, A., Mondal, A., Bhattacharjee, B., Chamilos, G., Pandey, R.*, Basu, K.*, Ganguly, D*. (2023) Deficient Phagocytosis in Circulating Monocytes from Patients with COVID-19-Associated Mucormycosis. *mBio*. 14, e0059023.

Patents

Agonism-Antagonism in Endosomal TLRs By Modulating Chemical Features In 8-Oxopurine: Process for Preparation And Application Thereof. Arindam Talukdar, Dipyaman Ganguly, Dipika Sarkar, Shrestha Pattanayak, Uddipta Ghosh Dastidar, Purbita Bandopadhyay, Bishnu Prasad Sinha, Shreya Roy, Jafar Sarif, Ranit DRozario, Trisha Ghosh, Rimica Das. Filing date: 07.03.24, India, 0030NF2024.

Invited Lectures

1. Advanced Immunology Workshop, Dept. of Rheumatology, Christian Medical College, Vellore, India, March, 2023.
2. Global Immunocourse, Indian Institute of Science, Bangalore, India, December, 2023. Indian Association for Cultivations of Science, Kolkata, India, January, 2024.
3. Annual Conference of Indian Rheumatology Association (West Bengal Chapter), Kolkata, February, 2024.

Conferences Attended

1. International Meet on Advanced Studies in Cell Signaling Network (CeSiN 2023), CSIR-Indian Institute of Chemical Biology, Kolkata, India, March 2023.
2. 50th Annual Conference of Indian Immunology Society, All India Institute of Medical Sciences, New Delhi, India, October 2023.
3. Annual Conferecne of the Association of Physicians in India (WB chapter), Kolkata, India. December, 2023: 8th ICANN conference, Indian Institute of Technology, Guwahati, India, November 2023.

Member of Society

1. Vice-president (East), Indian Immunology Society, (2022-2024)
2. Life member, Proteomics Society of India, (Since 2022)
3. Member, Technical Expert Committee (TEC), Drug and Vaccine Development, DBT, Govt. of India (2021-2024)
4. Member, Technical Expert Committee (TEC), International Co-operation Division, DST, Govt. of India (2022-2025)
5. Member, Senate, Academy of Scientific and Innovative Research, Ghaziabad, India.
6. Adjunct Faculty, Public Health Foundation of India, New Delhi, India.

Awards

1. Elected Fellow, Indian Academy of Sciences, Bangalore, India.
2. Shanti Swarup Bhatnagar Prize in Medical Sciences, Awarded by Council of Scientific and Industrial Research, New Delhi, 2022
3. Foundation Day Oration Medal from School of Tropical Medicine, Kolkata, India, 2024

Dr. Dipyaman Ganguly, Senior Principal Scientist

Group Members: Purbita Bandopadhyay, Project Assistant; Bishnu Prasad Sinha, ICMR SRF; Jafar Sarif, SRF; Ranit D'Rozario, SRF; Md. Asmaul Hoque, SRF; Shrestha Pattanayak, JRF; Suravi Mukherjee, Project Assistant; Shreya Roy, Project Assistant; Rituparna Jana, Project Assistant

Collaborators: Dr. Vanja Sisirak, CNRS ImmunoConcept, University of Bordeaux, Bordeaux, France; Prof. Arindam Talukdar, CSIR-Indian Institute of Chemical Biology, India; Prof. Sanghamitra Bandyopadhyay, Indian Statistical Institute, Kolkata, India; Prof. Amita Aggarwal, Dept. of Rheumatology and Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Education and Research, Lucknow, India; Prof. Rakesh Aggarwal, Dept. Of Gastroenterology, Jawaharlal Nehru Institute of Postgraduate Medical Education and Research, Puducherry, India; Dr. Bidisha Sinha, Department of Biological Sciences, Indian Institute of Science Education and Research, Kolkata, India; Prof. Patrick Blanco, CNRS ImmunoConcept, University of Bordeaux, Bordeaux, France; Dr. Roberto Lande, Istituto Superiore di Sanita, Rome, Italy; Dr. Fabrizio Conti, University Hospital, Rome, Italy; Prof. Parasar Ghosh, Dept. of Rheumatology, Institute of Postgraduate Medical Education and Research, Kolkata, India; Prof. Satinath Mukhopadhyay, Dept. of Endocrinology, Institute of Postgraduate Medical Education and Research, Kolkata, India; Dr. Yogiraj Ray, Department of Infectious Diseases, Institute of Postgraduate Medical Education and Research, Kolkata, India; Dr. Rajesh Pandey, CSIR-Institute of Genomics and Integrative Biology, India; Prof. Shantanu Sengupta, CSIR-Institute of Genomics and Integrative Biology, India; Dr. Swasti Raychaudhuri, CSIR-Center for Cell and Molecular Biology, Hyderabad, India; Dr. Hrishikesh Kumar, Institute of Neuroscience, Kolkata, India; Prof. Georgios Chamilos, IMBB FoRTH, University of Crete, Heraklion, Greece

Dr. Mrinal Kanti Ghosh and his group members

The DEAD-box protein p68 and β-catenin: the crucial regulators of FOXM1 gene expression in arbitrating colorectal cancer

Research Activities

Our laboratory is interested to: 1) study the role of ubiquitinase (*viz.,* CHIP, MDM2, XIAP, NEDD4) and deubiquitinases (*viz.,* USP7(HAUSP) responsible for maintaining cellular homeostatic balance, 2) understand the mode of action of RNA helicases (*viz.* p68) in oncogenesis, and 3) apply targeted drug delivery systems using nanoparticles in delivering drugs individually or in combination. Our research presents compelling evidence for the potentiation of colon carcinogenesis through FOXM1, elucidating its regulation by the master regulator DDX5 (p68) via coactivation of the canonical Wnt/β-catenin signaling pathway. The schematic diagram summarizes FOXM1 regulation by DDX5 (p68) through β-catenin coactivation and their occupancy on TCF/LEF sites of the FOXM1 promoter, enhancing transcription and subsequent impact on colon carcinogenesis hallmarks.

Cancer hallmarks including cellular proliferation, migration, clonogenic potential, apoptosis evasion, and metastasis challenge cellular homeostasis. Despite advances in detection and therapy, colorectal cancer (CRC) prognosis remains dismal. Understanding signaling cross-talks and molecular players driving initiation and progression is essential. FOXM1 is overexpressed in various cancers, influencing tumor initiation and progression, including as a potential CRC marker. However, limited reports exist on its gene regulation. Thus, elucidating FOXM1's mechanistic regulation can aid CRC clinical management.

DDX5 (p68), a multifunctional oncogenic regulator, was investigated for its role in FOXM1 regulation. Bioinformatic analyses (UALCAN, TCGA) revealed heightened DDX5 and FOXM1 expression in CRC. Immunohistochemistry in patient tissues confirmed strong DDX5 (p68)-FOXM1 correlation. Manipulating DDX5 (p68) expression in colon cancer cell lines modulated FOXM1 expression. Given DDX5 (p68)'s

association with Wnt signaling and β-catenin, we explored their relationship. Immunohistochemistry indicated strong β-catenin-FOXM1 correlation in CRC tissues. Wnt activation increased FOXM1 and Cyclin D1 expression. Manipulating β-catenin levels altered FOXM1 expression and downstream targets like Survivin. ChIP assay confirmed DDX5 (p68) and β-catenin occupancy on FOXM1 promoter TCF/LEF sites, affecting promoter activity. Functional assays supported the oncogenic potential of DDX5 (p68)-β-catenin-FOXM1 axis.

Thiostrepton, a FOXM1 inhibitor, and si-RNA attenuated DDX5 (p68)-induced FOXM1 expression, impacting cellular processes like proliferation, migration, and clonogenicity. RX-5902, targeting phosphorylated-p68 and β-catenin, shows promise in breast cancer clinical trials. DDX5 (p68) holds potential as an independent oncogenic biomarker for targeted therapy. Understanding the DDX5 (p68)-β-catenin-FOXM1 axis aids in CRC therapeutic development, including targeted inhibitors and personalized therapy based on individual expression profiles.

Future Research Plans

1. To elucidate the transcriptional and post-translational regulation of important molecular players involved in oncogenesis such as HAUSP, CHIP, DDX5, PML, and PTEN.
2. To develop an omics-based study (proteomics, transcriptomics) and employ the use of big data analysis techniques for successfully identifying novel factors involved in oncogenesis.
3. To test the therapeutic efficacy of natural compounds and delve into the roles of small molecules in the avenue of cancer therapeutics and focus upon the synergistic mode-of-action of anti-cancer agents.
4. To develop novel targeted drug delivery-based systems to curb tumorigenesis.

Publications

1. Shaw, R., Basu, M., Karmakar, S., Ghosh, M. K. (2024). MGMT in TMZ-based Glioma therapy: Multifaceted Insights and Clinical Trial Perspectives. *BBA Mol Cell Res.* 1871, 119673.
2. Ghosh, M. K., Roy, S. (2024). Chromosomal instability (CIN) triggers immune evasion and metastatic potential in cancer through rewired STING signalling. *Mol Biomed.* 5, (4).
3. Basu, B., Kal, S., Karmakar, S., Basu, M., Ghosh, M. K. (2024). E3 Ubiquitin Ligases in Lung Cancer: Emerging Insights and Therapeutic Opportunities. *Life Sci.* 336, 122333.
4. Saha, G., Roy, S., Basu, M., Ghosh, M. K. (2023). USP7 - A crucial regulator of Cancer Hallmarks. *BBA – Reviews on cancer* 1878, 188903.
5. Chakraborty, S., Karmakar, S., Basu, M., Kal, S., Ghosh, M. K. (2023). E3 Ubiquitin Ligase CHIP Drives Monoubiquitination-mediated Nuclear Import of Tumor Suppressor PTEN. *J Cell Sci.* 136, 260950.
6. Shaw, R., Karmakar, S., Basu, M., Ghosh, M. K. (2023). DDX5 (p68) orchestrates β-catenin, RelA and SP1 mediated MGMT gene expression in human colon cancer cells: Implication in TMZ chemoresistance. *BBA Gene Regulatory Mechanisms.* 1866, 194991.
7. Mukherjee S, et al., (2023). A small HDM2 antagonist peptide and a USP7 inhibitor synergistically inhibit the p53-HDM2-USP7 circuit. *Chem Biol & Drug Design.* 102, (1).
8. Tabassum, S., Basu, M., Ghosh, M. K. (2023). The DEAD-box protein p68 and β-catenin: the crucial regulators of FOXM1 gene expression in arbitrating colorectal cancer. *BBA Gene Regulatory Mechanisms.* 1866, 194933.
9. Sarkar, S., Karmakar, S., Basu, M., Ghosh, P., Ghosh, M. K. (2023). Neurological damages in COVID-19 patients: mechanisms and preventive interventions. *MedComm*. 4, e247,1-25.
10. Basu, B., Karmakar, S., Basu, M., Ghosh, M. K. (2023). USP7 imparts partial EMT state in colorectal cancer by stabilizing the RNA helicase DDX3X and augmenting Wnt/β-catenin signaling. *BBA Mol Cell Res.* 1870, 119446.
11. Kumar, S., Basu, M.,* Ghosh, P., Pal, U., Ghosh, M. K. (2023). COVID-19 therapeutics: Clinical application of repurposed drugs and futuristic strategies for target-based drug discovery. *Genes & Dis.* 10, 1402-1428.

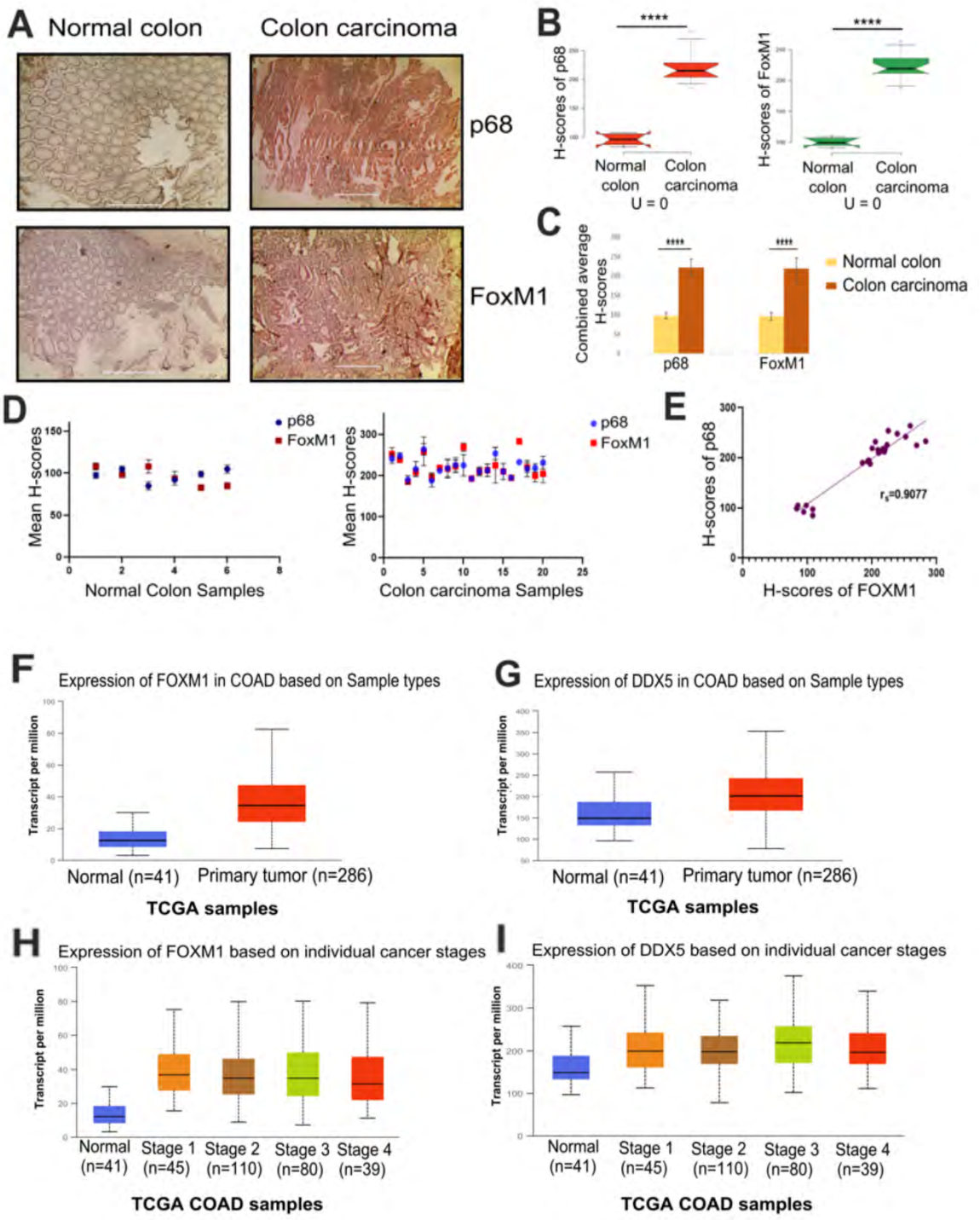


Figure 1: **Positive correlation between FOXM1 and p68 in human colon carcinoma tissues and Bioinformatic analysis of their expression profiles.* (a) Representative images from Immunohistochemical (IHC) staining of p68 and FOXM1 conducted in human normal colon and colon carcinoma tissue samples. The images were captured at 200× magnification. (b) The H-scores of p68 and FOXM1 were represented in the form of a Notched box plot in normal (*n *= 6) and colon carcinoma (*n *= 20) samples; H-scores were used for the calculation of Mann–Whitney U-values. (c) Comparative column graphs of the combined average H-scores of p68 and FOXM1. The mean (+/) s.d is epresented by error bars; the *p*-values were calculated using an independent, two-tailed Student's *t*-test, and *p < *0.0001 is signified as ****. (d) The mean H-scores of p68 and FOXM1 were compared with the help of scatter plots in normal and colon carcinoma tissue samples, respectively. (e) Spearman's rank correlation coefficient (rs) was depicted graphically by using the mean H-scores of p68 and FOXM1 from both normal and colon carcinoma tissues. (f & g), The expression levels of FOXM1 and DDX5 were bioinformatically assessed in COAD tissue samples with that of normal tissue samples. (h) and (i), representative study of FOXM1 and DDX5 expression levels through cancer stage-specific (I-IV) analysis of COAD tumor samples compared with normal tissue samples

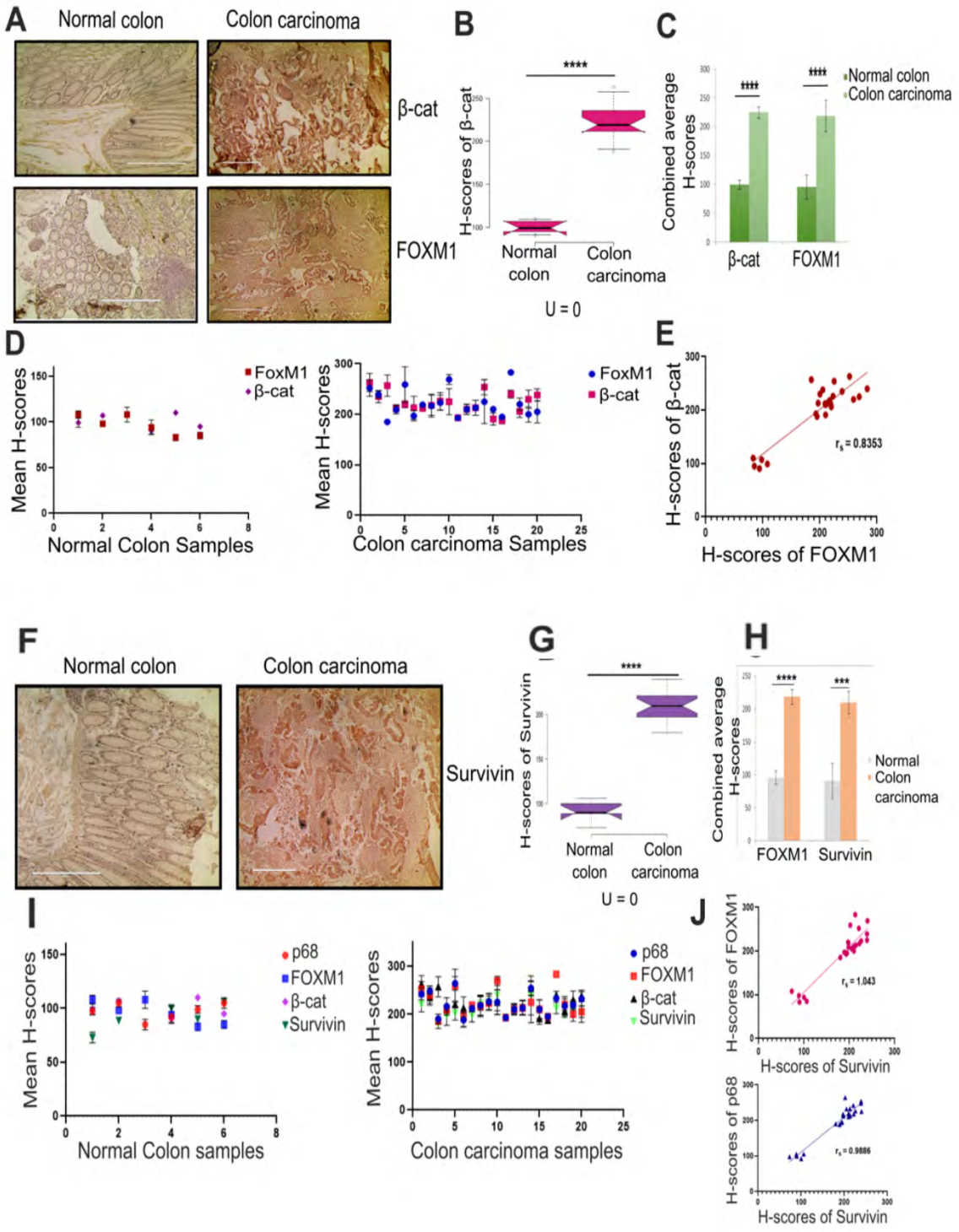


Figure 2: **Involvement of Wnt signaling and mediation of regulation of FOXM1 by β-catenin as well as p68-β-catenin synergism and their effects on downstream target genes of FOXM1.* (a) Representative Immunohistochemical (IHC) staining images of β-catenin and FOXM1 were conducted in human normal colon and colon carcinoma tissue samples. The images were captured at 200×magnification. (b) Representative Notched-box plots were obtained from the H-scores of β-catenin and FOXM1 in normal (*n *= 6) and colon carcinoma (*n*= 20) samples; H-scores were further used for the calculation of Mann–Whitney U-values. (c) Comparison between the combined average H-scores of β-catenin and FOXM1. The mean (+/) s.d is represented by error bars; the p-values were calculated using an independent, two-tailed Student's t-test, and p *< *0.0001 is signified as ****. (d) Depiction of scatter plots to compare the mean H-scores of β-catenin and FOXM1 in normal and colon carcinoma tissue samples, respectively. (e) Spearman's rank correlation coefficient (rs) was depicted graphically by using the mean H-scores of β-catenin and FOXM1 from both normal and colon carcinoma tissues. p68/ β-catenin synergism and their effects on downstream target genes of FOXM1. (f) Representative images obtained from Immunohistochemical (IHC) staining

Survivin in human normal colon and colon carcinoma tissue samples. The images were captured at 200× magnification. (g) Representative Notched-box plots were obtained from the H-scores of Survivin in normal (*n*= 6) and colon carcinoma (*n *= 20) samples; H-scores were used for the calculation of Mann–Whitney U- values. Comparison between the combined average H-scores of Survivin and FOXM1 in normal vs colon carcinoma samples. The mean (+/) s.d is represented by error bars; the *p*-values were calculated using an independent, two-tailed Student's *t*-test, and *p < *0.0001 is signified as ****. (h & i) Depiction of scatter plots to compare the mean H-scores of p68, β-catenin, FOXM1, and Survivin in normal and colon carcinoma tissue samples, respectively. (j) Spearman's rank correlation coefficient (rs) was depicted for the correlation between the mean H-scores of Survivin and FOXM1 along with the correlation between Survivin and p68 from both normal and colon carcinoma tissues.

Dr. Mrinal Kanti Ghosh, Chief Scientist
Group Members: Rajni Shaw, SRF; Shrabastee Chakraborty, SRF; Sunny Kumar, SRF; Subhojit Karmakar, SRF; Srija Roy, SRF; Sayani Ghosh, JRF; Mouli Chatterjee, JRF; Sabana Begam, JRF; Dr. Meeta Gera, WoS, ICMR; Dr. Sibani Sarkar, RA; Sourav Dey, PA
Collaborators: Dr. Suresh Bajoria, RTIICS (NH), Kolkata; Dr. Uttara Chatterjee, IPGMER & Park Clinic, Kolkata; Dr. Sandeep Chatterjee, Park Clinic, Kolkata

Dr. Shilpak Chatterjee and his group members

Mechanistic exploration of the role of sphingosine-1-phosphate receptor 1 (S1PR1) mediated signaling in regulating T cell functionality in tumor

Research Activities

Tumor-infiltrating CD8⁺ T cells exhibit high cell surface expression of S1PR1, leading to T cell dysfunctionality.

In this study, we aimed to determine if tumor-infiltrating CD8+ T cells exhibit elevated S1PR1 expression compared to peripheral T cells. We analyzed CD8+ T cells from 22 bladder tumor patients and found that tumor-infiltrating CD8+ T cells had increased S1PR1 expression compared to those from PBMCs (Fig. 1A). These intratumoral CD8+ T cells were functionally impaired, failing to produce effector cytokines (IFN-γ, TNF-α, GzmB) upon re-stimulation (Fig. 1B). We also evaluated CD8+ T cells from various pre-clinical tumor models (EL-4 lymphoma, B16-F10 melanoma, YUMM1.7 mouse melanoma) and found elevated S1PR1 expression on tumor-site CD8+ T cells compared to splenic CD8+ T cells (Fig. 1C-1E). Further analysis revealed that S1PR1 expression was confined to CD8+ T cells co-expressing PD1 and Tim3, indicative of a terminally exhausted phenotype (Fig. 1F-1H).

To understand the role of the S1P-S1PR1 axis in T cell functionality, we evaluated the expression of all five S1P receptors on T cells after activation in vitro. Real-Time quantitative PCR showed predominant S1PR1 expression on activated CD8+ T cells (Fig. 1I). Flow cytometry confirmed that S1PR1 expression increased steadily following TCR stimulation (Fig. 1J).

We then assessed the influence of S1P-S1PR1 signaling on CD8+ T cell functionality. Adding S1P during T cell activation significantly reduced GzmB, IFN-γ, and TNF-α production compared to vehicle-treated cells (Fig. 1K). S1P treatment also significantly reduced CD8+ T cell proliferation (Fig. 1L), consistent with reduced CD25 expression on

activated CD8+ T cells (Fig. 1M). Additionally, S1P-treated T cells exhibited higher apoptosis rates (Fig. 1N). These findings suggest that S1P-S1PR1 signaling impairs CD8+ T cell functionality and increases their susceptibility to apoptosis.

Transcriptomic analysis reveals S1P-induced CHOP activation in CD8+ T cells.

To investigate how S1P-S1PR1 signaling impacts CD8+ T cell functionality and metabolic fitness, we conducted bulk RNA-sequencing on vehicle and S1P-treated CD8+ T cells. Principal-component analysis showed that S1P-treated T cells were transcriptionally distinct from controls (Fig. 2A). Comparative transcriptomics revealed that the ER stress pathway was significantly enriched in S1P-treated CD8+ T cells (Fig. 2B). Notably, genes related to the PERK-mediated unfolded protein response, including Ddit3 (encoding CHOP), were highly enriched (Fig. 2C).

Protein analysis confirmed a ~2-fold upregulation of CHOP in S1P-treated CD8+ T cells (Fig. 2D). This upregulation was mediated by PERK activation, as inhibiting PERK abrogated CHOP activation (Fig. 2E). Knocking down S1pr1 with siRNA significantly reduced CHOP levels in S1P-treated CD8+ T cells compared to controls (Fig. 2F). These findings suggest that exogenous S1P activates the S1PR1 signaling axis, leading to CHOP upregulation through PERK activation.

S1PR1 inhibition improves T cell function and tumor control in vivo.

As we have shown that the S1P-S1PR1 axis promotes the T cell dysfunctionality at the tumor site, we argued that whether blocking this pathway would be able to improve the anti-tumor response of the T cells. To address this question, we used the YUMM1.7 melanoma tumor model. The mice were injected subcutaneously with the tumor, and once the tumor reached 100 mm^2 size, the S1PR1 specific inhibitor W146 (1mg/kg body weight) was injected at the tumor site, and tumor volume was measured. Interestingly, we observed that intratumoral injection of this drug significantly delayed tumor growth of YUMM1.7 melanoma (Fig 3A). In this experiment, we retrieved the T cells from the tumor site from both the vehicle-treated and W146-treated Yumm1.7 Melanoma tumor-bearing mice and checked the expression of S1PR1, CHOP, p-P38 and different effector molecules produced by tumor-infiltrating $CD8^+$ T cells. We observed that W146 treatment reduces the expression of both CHOP and p-P38 along with S1PR1 (Fig 3B, 3C & 3D) and partially restores the IFN-γ, GZM-B, and TNF-α as compared to vehicle-treated TILs (Fig 3E). Our data indicate that the S1P-S1PR1 axis can act as an important druggable target to improve the immunotherapeutic response of the T cells in tumor.

Future Research Plans

1. Chemogenetic screening for small molecule inhibitors: Conducting a chemogenetic screen to identify and validate novel small molecule inhibitors against S1PR1 represents a critical avenue for future research. Developing effective inhibitors could significantly enhance the precision and efficacy of immunotherapy strategies targeting the S1P-S1PR1 signaling axis, ultimately improving anti-tumor T cell responses.
2. Clinical translation and therapeutic development: As the study underscores the potential significance of inhibiting S1PR1 for improving the therapeutic efficacy of anti-tumor T cells, the next steps could involve translating these findings into clinical applications. Developing and testing therapeutic interventions targeting the S1P-S1PR1 axis in relevant preclinical models and eventually in clinical trials could pave the way for novel immunotherapeutic strategies in cancer treatment.

Extramural / CSIR Funding

1. Role of endoplasmic reticulum (ER) stress induced UPR signaling in regulating the metabolic fitness and functionality of $CD8^+$ T cells in cancer, India Alliance DBT Wellcome, 2020-2024, 359.11 lakhs, IA/I/19/1/504277
2. Mechanistic exploration of the role of shingosine-1-phosphate receptor 1 (S1PR1) in regulating the functional fate of tumor infiltrating CD8 T cells, SERB, India, 2020-2023, 46.54 lakhs, CRG/2019/001334
3. Indian Brest Cancer Genome Atlas, CSIR, Hq, 2021-2026, 4990.00 lakhs, HCP-43

Publications

1. Kar, A., Ghosh, P., Gautam, A., Chowdhury, S., Basak, D., Sarkar, I., Bhoumik, A., Barman, S., Chakraborty, P., Mukhopadhyay, A., Mehrotra, S., Ganesan, S. K., Paul, S., Chatterjee, S. (2024) CD38-RyR2 axis-mediated signaling impedes $CD8^+$ T cell response to anti-PD1 therapy in cancer. *Proc Natl Acad Sci USA*. 121, e2315989121.

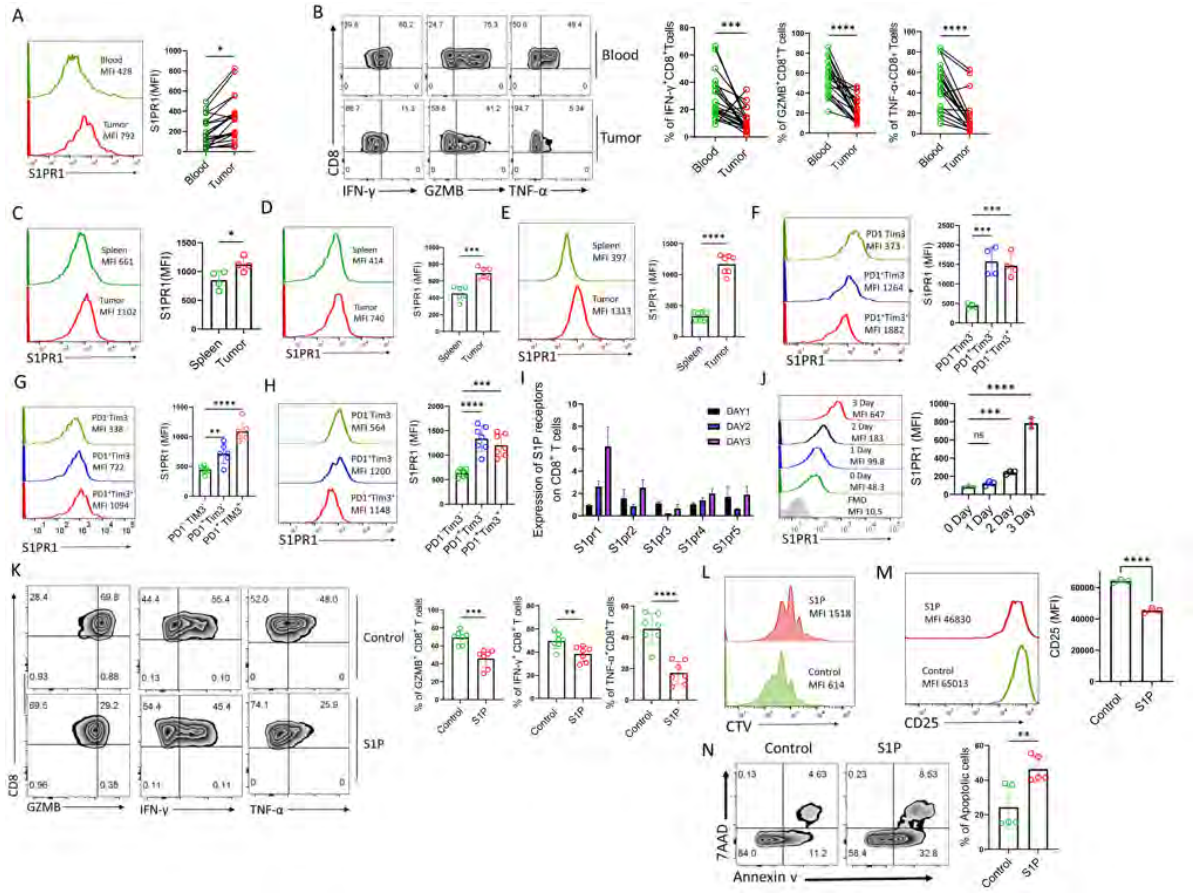


Figure 1: Tumor-infiltrating CD8⁺ T cells have increased expression of S1PR1. (A) Flow cytometry analysis of S1PR1 expression in CD8⁺ T cell from tumor tissue and PBMC obtained from bladder cancer patients (N=22). The adjacent scatter plot represents the cumulative data of mean florescence intensity (MFI) of S1PR1. (B) Cytokine production was checked in TILs isolated from bladder tumor and peripheral blood by flow cytometry. Adjacent plot represents cumulative data. (C-E) Flow cytometry analysis of S1PR1 in TILs and splenic CD8⁺ T cells isolated from EL-4 (C), B16-F10Melanoma (D), YUMM1.7 Melanoma (E). (F-H) S1PR1 expression in PD1⁺Tim3⁺, PD1⁺Tim3⁻, PD1⁻Tim3⁻CD8⁺ TILs isolated from EL4 (F), B16-F10 Melanoma (G), YUMM1.7 Melanoma (H) respectively. (I) Real-time PCR analysis of five S1P receptors (S1PR1-S1PR5) in activated CD8⁺ T cells. (J) S1PR1 expression in activated T cells by flow cytometry. (K) In activated CD8⁺ T cells different cytokines were analyzed in control and S1P-treated cells by flow cytometry. (L-N) Flow cytometry analysis of cell proliferation by CTV (L), CD25 (M), and apoptosis by Annexin/7AAD staining (N) in S1P treated and vehicle-treated CD8⁺ T cells. * P<0.05; **<0.01; ***, P<0.005; ****, P<0.0001.

2. Basak, D., Mondal, S., Srivastava, S. K., Sarkar, D., Sarkar, I., Basu, S., Bhoumik, A., Chowdhury, S., Pal, D. K., Chatterjee, S. (2023) Intratumoral PD1⁺CD38⁺Tim3⁺ CD8⁺ T cells in pre-BCG tumor tissues are associated with poor responsiveness to BCG immunotherapy in patients with non-muscle invasive bladder cancer. *Cells (MDPI)*. 12, 1939.
3. Talukdar, D., Bandopadhyay, P., Ray, Y., Paul, S. R., Sarif, J., D'Rozario, R., Lahiri, A., Das, S., Bhowmick, D.,Chatterjee, S., Das, B., Ganguly, D. (2023) Association of gut microbial dysbiosis with disease severity, response to therapy and disease outcomes in Indian patients with COVID-19. *Gut Pathog.* 15, 22

Patents

Small Molecules For Adoptive T-Cell Therapy (Act) Through Activation Of The mTOR Signalling Pathway, Process For Preparation Thereof, 18/05/2023, 202311034981.

Invited Lectures

1. Immunometabolism: A Target for Improving Cancer Immunotherapy. Adamas University, Kolkata. Metabolomics in Drug Discovery, 29th August 2023.
2. T Cell Exhaustion: Reversal and Clinical Implications for Cell Therapy Use. CAR T Cell

Therapy Centre (CTCTC), ACTREC, Navi Mumbai. 2nd SACT event, Series of Advancements in Cell Therapy, 29-30 September 2023.

3. Immunometabolism and CAR T cell therapy. NCCS, Pune. 5th Annual Conference of Immuno-Oncology Society of India: "I-OSICON 2024", 12-14 January, 2024.

Conferences Attended

1. 2nd SACT event, Series of Advancements in Cell Therapy, 29-30 September 2023.
2. 50th Annual Conference of Indian Immunology Socity: “IMMUNOCON-50”, 5-8 October, 2023.
3. 5th Annual Conference of Immuno-Oncology Society of India: "I-OSICON 2024", 12-14 January, 2024.

Member of Society

Member, Technical Expert Committee (TEC), Cancer Disease Biology Program, DBT, Govt. of India (2022-2025)

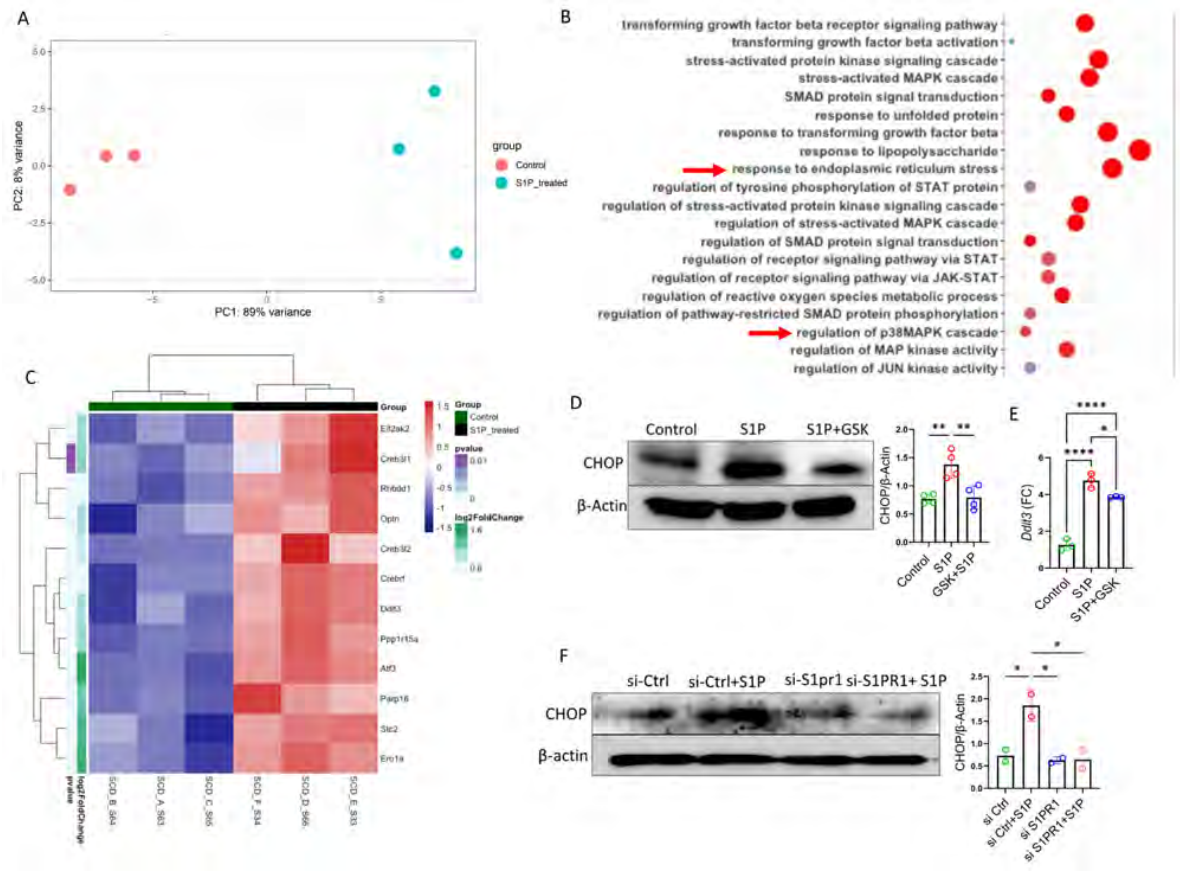


Figure 2: Distinct transcriptional profile of S1P-treated CD8+ T cells. (A) PCA plot depicting the distribution of the gene profile of each sample from two groups. (B) Pathway enrichment analysis of top 20 pathways. (C) Heatmap showing the expression of differentially regulated genes. (D) Expression of CHOP in control, S1P treated, and GSK2656157 pretreated S1P treated CD8+ T cells by western blot. (E) qPCR analysis of Ddit3 (CHOP) expression in CD8+ T cells. (F) CHOP expression was checked in the following groups: CD8+ T cells transfected with control siRNA and treated in the presence and absence of S1P, and CD8+ T cells transfected with S1Pr1 siRNA and treated in the presence and absence of S1P. * P<0.05; **<0.01; ***, P<0.005; ****, P<0.0001.

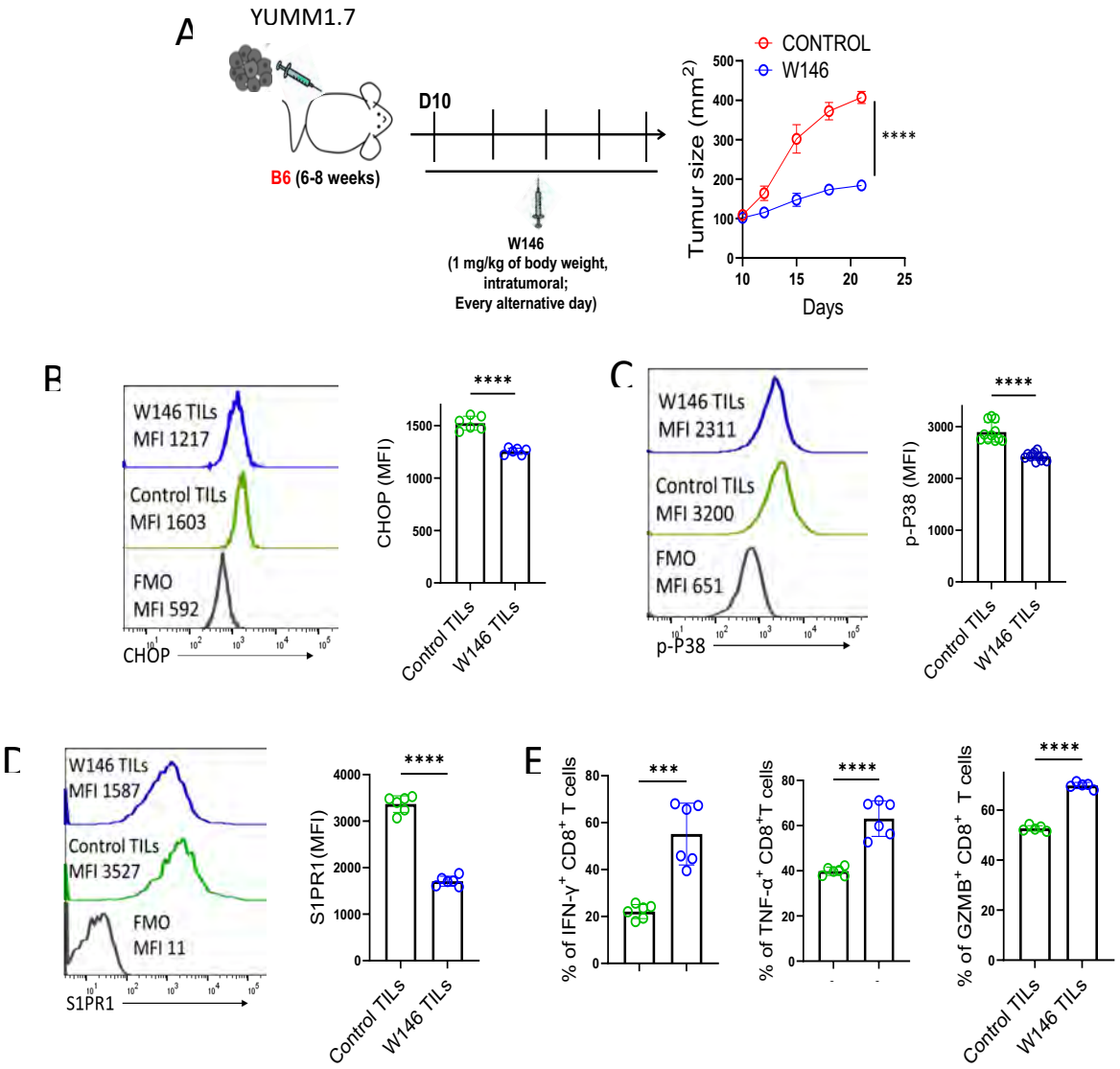


Figure 3: S1PR1 inhibition improves T cell function and tumor control in vivo. (A-E) B6 mice (n=6) were subcutaneously established with YUMM1.7 melanoma tumor and treated either with vehicle control or W146 (S1PR1 antagonist) and tumor growth was measured. (A) An illustration of the experimental strategy (left panel) and assessment of tumor growth at different time points is presented. (B-E) $CD8^+$ T cells retrieved from tumor site were assessed for (B) expression of CHOP, (C) p-P38MAPK, (D) S1PR1 levels (E) production of intracellular cytokines. * P<0.05; **<0.01; ***, P<0.005; ****, P<0.0001.

Dr. Shilpak Chatterjee, Principal Scientist
Group Members: Anwesha Kar, CSIR-SRF; Debashree Basak, CSIR-SRF; Ishita Sarkar, CSIR-SRF; Puspendu Ghosh, CSIR-SRF; Arpita Bhoumik, CSIR-Senior Resaerch Associate
Collaborators: Dr. Arindam Talukdar, CSIR-IICB, Kolkata; Dr. Sandip Paul, JISIASR, Kolkata; Dr. Shantanu Sengupta, CSIR-IGIB, New Delhi; Dr. Soumen Basak, NII, New Delhi; Dr. Shikhar Mehrotra, MUSC, USA; Dr. Ramanuj Mukherjee, CNCI, Kolkata

Dr. Siddik Sarkar and his group members

Developing biological based therapeutics (biologics) for the treatment of cancer including breast and ovary

Research Activities

Cancer is a dynamic disease and further added miseries due to inter- and intra- cellular heterogeneity. The heterogeneity in spatial locations of different populations of cells help us in identifying the involvement of infiltrating T cell in cancer prognosis. In recent past immunotherapy specifically immune-checkpoint inhibition has emerged as one of the most potent treatment options in melanoma and liquid malignancy (leukemia), but success is limited in solid tumor malignancy. In our laboratory, we are focusing on developing next generation immunotherapeutic that could target the immune surveillance pathways, immune check points, and activate the immune system in general and T cells or NK cells in particular, eventually leading to cancer cell killing in solid tumors. Cancer cells escape immune surveillance not only by upregulating immune check points, but also by downregulating MHC/ HLA molecules and hence antigen presentation pathways are inhibited. In this regard, we are developing chimeric antigen receptor T/ NK (CAR-T/ CAR-NK) targeting neo-antigens or cancer surface markers that induce cancer cell killing independent of MHC expression. To further enhance the infiltration of immune cells and selective killing of cancer cells we are developing Armed oncolytic adenovirus. The overall objective of the laboratory is to find and identify biomarkers that could be eventually targeted by developing different types of biologics. These biologics would effectively kill the cancer cells and increase the overall survival of cancer patients pertaining to solid tumor malignancy of breast and ovary. In nutshell, the ongoing research activities are: 1) developmen of effective bi-specific CAR-T based therapy for breast and ovarian cancer, 2) development of chimeric bifunctional immunobodies as next generation anticancer therapeutics, and 3) developmen of armed oncolytic Adenovirus carrying suicidal gene recombinant carboxylesterase. We have already manufactured bispecific CAR-T cells targeting mesothelin and PDL1. It has been observed both in 2D and 3D cell cuture system that thsese CAR-T cells can effectively lysed the ovarian cancer cells more specifically the cancer cells overexpressing mesothelin.

Future Research Plans

1. We will expand CAR-T cells and evaluate the efficacy of CAR-T cells in NSG/NCG-X mouse model.
2. CAR-T memory cell and exhaustion markers will be studied.

3. We have made biologicals cyto-ab (IL-2-α-PDL1-CH1-IgG1-Fc) which has received novelty confirmation based on URDIP search report and patent filing paper work is on-going. These biological will be manufactured in GMP grade CHO-S cells.

Extramural / CSIR Funding

1. Mutation-aggregation Profiling of Amyotrophic Lateral Sclerosis (ALS) Patients in West Bengal. Tenure: Jan 2024-Jan 2027, Special Secretary, Science and Technology & Biotechnology, WB. 65.7 lakhs, STBT-11012(99)/12/2023-ST SEC.
2. Genomic Surveillance program for SARS-CoV-2: Consortium of India and Sri Lanka Funding Agency: The Wellcome Trust, UK, Tenure: Jan 2022-10 April 2024, 45 lakhs, 223547/Z/21/Z.

Publications

Sarkar, P., Banerjee, S., Saha, S. A., Mitra, P., Sarkar, S. (2023) Genome surveillance of SARS-CoV-2 variants and their role in pathogenesis focusing on second wave of COVID-19 in India. *Sci Rep* 13, 10.1038/s41598-023-30815

Invited Lectures

1. The molecular prognostic score, a classifier for risk stratification of high-grade serous ovarian cancer. “International Conference on Cancer Biology: Molecular Mechanisms, Genomics and Novel Therapeutics”, Department of Biotechnology, Indian Institute of Technology Madras, 14-16 September 2023.
2. Gene editing and advancement of CAR T therapy: CAR-T, a cell and gene therapy in the treatment of solid tumor malignancy. 5th Annual Congress of Immuno-Oncology Society of India, National Centre for Cell Science Pune.

Conferences Attended

1. International Conference on Cancer Biology: Molecular Mechanisms, Genomics and Novel Therapeutics. Department of Biotechnology, Indian Institute of Technology Madras. 14-16 September 2023.
2. 5th Annual Congress of Immuno-Oncology Society of India, National Centre for Cell Science Pune. 12-14 January 2024

Member of Society

Member of the Society of Biological Sciences (SBC) (2018- onwards)

Dr. Siddik Sarkar, Senior Scientist
Group Members: Sarbar Ali saha, CSIR-SRF; Abhishek Swarnakar, DBT-JRF; Arnab Chakrabarty, UGC-JRF; Victor Roy, CSIR-JRF; Avipsa Dey, Project-JRF; Somoshree Sengupta, DBT-RA
Collaborators: Dr. Pralay Mitra, IIT Kharagpur; Dr. Mahitosh Mandal, IIT Kharagpur; Dr. Sanchita Goswami, University of Kolkata; Dr. Biswaroop Basu, CNCI Kolkata

Cell Biology and Physiology Division

The Cell Biology and Physiology division deals with different research domains of modern biology with an aim towards the understanding of basic as well as clinical aspects of disorders that includes cardiometabolic disorders, neurological disorders, lung disorder, reproductive disorders and cancer. The investigators associated with this division are interested in systems biology and cellular biology, investigating the functions of subcellular organelles and intracellular signaling events in normal as well as in pathophysiological conditions. The research endeavours are uptaken with a strong and persistent outlook towards development of novel therapeutic targets, diagnostics and therapeutic leads.

Dr. Bijesh P. and his group members

Targeting One-Carbon Metabolism Mediated Lung Epithelial Cell Regeneration for the Treatment of COPD

Research Activities

Although the role of one-carbon metabolism (1C) in developing cells/tissues is well elucidated, its role in adult non-proliferative tissues is yet to be well elucidated. The 1C metabolism involves an array of metabolic pathways, including methionine and folate cycles. The methyl groups are transferred in 1C metabolism and are involved in synthesizing purines and pyrimidines, homeostasis of amino acids such as glycine, serine, and methionine, and epigenetics. Mitochondrial 1C metabolism is an important area, especially concerning geriatric diseases. They are known to support the synthesis of the energy molecules creatine and choline. Another role of 1C metabolism is maintaining homeostasis of nucleotides and amino acids (Figure 1).

We have observed significantly higher expression of the folate transporter gene, FOLR1, in the lung compared to other organs of the body. In the lung, the epithelial cells express FOLR1 compared to other cell types. Although the alveolar epithelial type 2 cells (AEC2) act as lung stem cells. We have observed significant expression of FOLR1 in the AEC2.

We speculate that 1C metabolism has a role in maintaining normal epithelial lung function as well as protecting the cells from inflammatory disorders. Physiological changes in 1C metabolism in normal and disease conditions should be studied. The ongoing work aims to elucidate the role of folates and one-carbon metabolism in the physiology of the lung. Our primary focus is on 1C metabolism in progressive lung disorders such as idiopathic pulmonary fibrosis (IPF) and chronic obstructive pulmonary disease (COPD).

The ongoing research questions in our laboratory are to determine the role of one-carbon metabolism in the development and progression of progressive lung epithelial-related disorders and to identify upstream regulatory proteins of one-carbon metabolism in the lung epithelial cells.

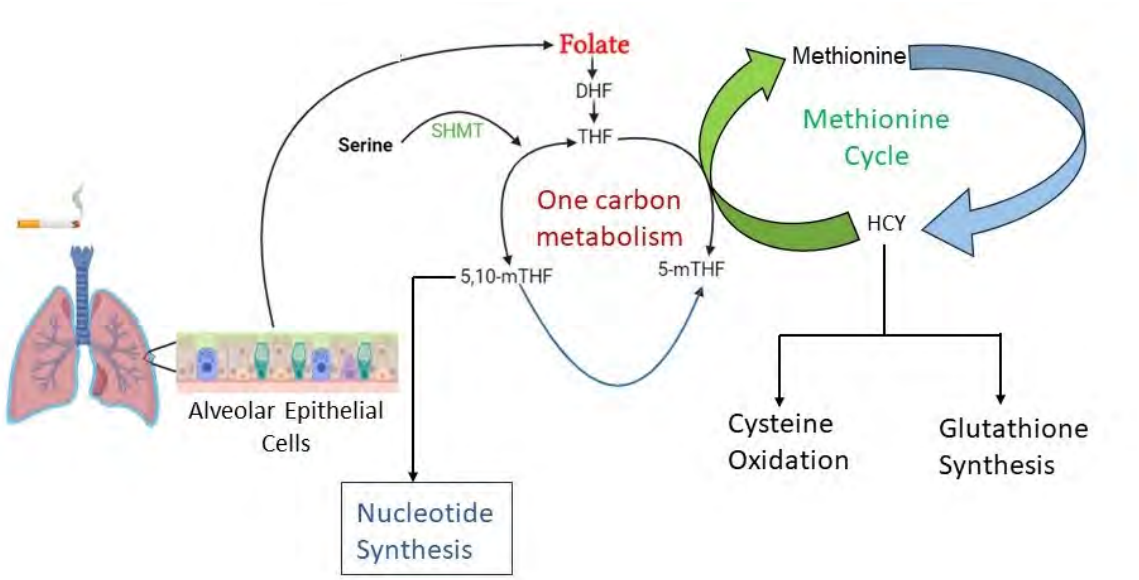


Figure 1: Importance of one-carbon metabolism in cellular homoeostasis. One carbon metabolism can be targeted for regenerating lung alveolar structure as it is highly active in the alveolar epithelial type 2 cells.

Future Research Plans

Our laboratory aims to utilize the regulatory proteins of one-carbon metabolism as targets for the treatment of progressive lung disorders. We are in the process of identifying critical upstream regulatory proteins and small molecules that can affect their function. These regulatory molecules will then be screened for their potential in alleviating progressive lung disorders utilizing suitable in vitro and in vivo models.

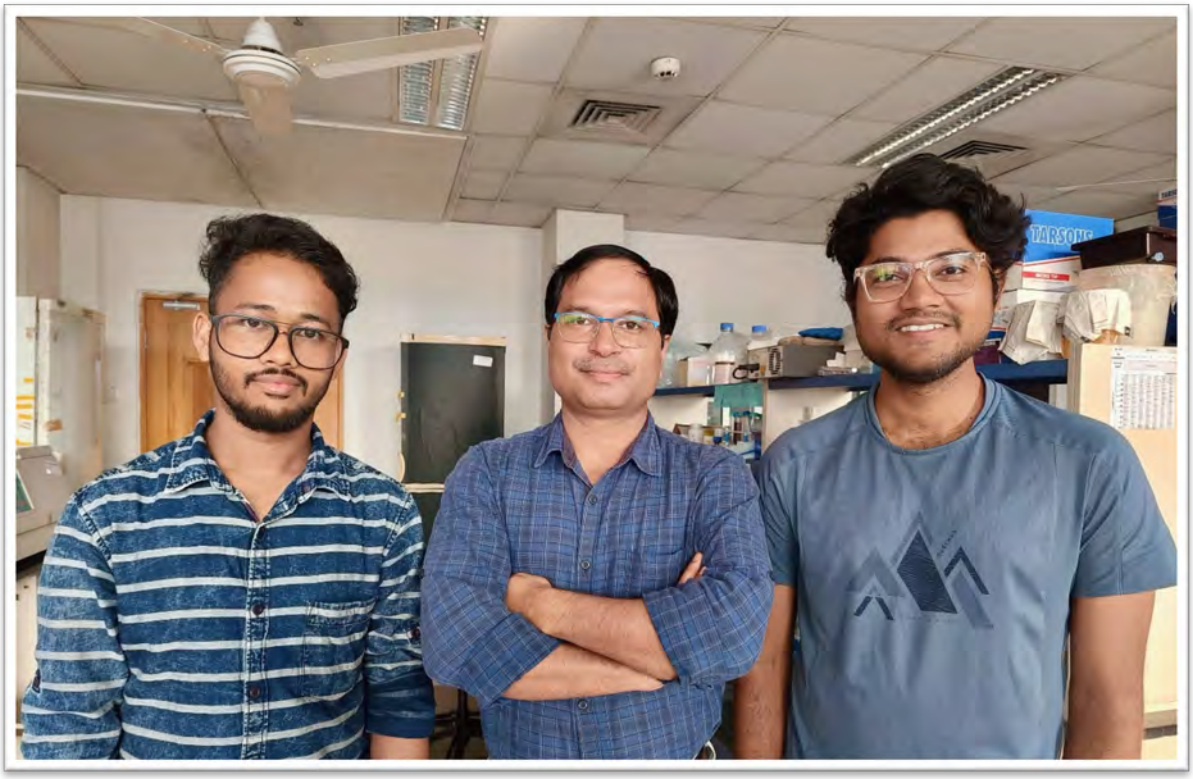
Extramural / CSIR Funding

Targeting FOLR1 for treating progressive inflammatory lung disorders such as COPD. SERB Department of Science & Technology (DST), 2023-2025, Rs 30.57 Lakhs, Startup Research Grant (SRG/2023/000091).

Patents

- Dihydrofolate for Hypoglycemic Activity, Vikas Singh Chauhan, Bijesh Puthusseri, Ajana Pathikkal, Ulaganathan Mabalirajan, Atmaja Karmakar, Divya Peethambaran, Application filing date: 31/05/2023, US Patent Application No. 18/326,450
- Encapsulated dihydrofolate formulation for dietary supplementation as effective nutraceutical supplement and method of preparation thereof, Bijesh Puthusseri, Vikas Singh Chauhan, Ajana Pathikkal, Ulaganathan Mabalirajan, Sunita Das, Atmaja Karmakar, Divya Peethambaran, Provisional application filing date: 26/03/2024, PCT 202411023759.

Dr. Bijesh P., Scientist
Group Members: Sunita Das, UGC-JRF; Anjali P., UGC-JRF; Amrita Gond, UGC-JRF; Ananyo Kumar Ghosh, UGC-JRF
Collaborators: Dr. Vikas Singh Chauhan, PhD, CSIR-Central Food Technological Research Institute, Mysuru, Karnataka.



Dr. Md. Jahangir Alam and his group members

To understand the crosstalk between cardiovascular diseases and metabolic diseases and to explore the roles of extracellular vesicles in this interaction

Research Activities

Atherosclerotic cardiovascular disease remains a leading cause of vascular disease worldwide. It can cause acute coronary syndromes (heart attacks) characterized by myocardial infarction or stable angina pectoris. Components of metabolic syndrome (MetS), i.e. Hyperglycemia, Obesity, dyslipidemia, hypertriglyceridemia and hypertension, are the major risk factors for atherogenesis and other cardio-metabolic diseases (CMDs) such as cardiovascular disease and diabetes. Many of these risk factors participate in the activation of inflammatory pathways thereby altering the function of the cells of the endothelium that drives atherosclerosis. Moreover, an inflammatory state in other tissues, like liver tissue, can aggravate atherogenesis in distant parts of the body, such as arteries. Existing studies suggest that there is a complex association between MetS and atherosclerosis. Therefore, understanding the factors associated with the MetS-athero-inflammation axis will help to reduce the CVD burden in human subjects with cardiovascular disease.

In view of this scenario, my research interest is to identify the key early molecular events contributing to the development of chronic diseases such as coronary artery disease (CAD) and non-alcoholic fatty liver disease (NAFLD).

To study the change in the proteome signature of liver-derived exosomes in the progression of atherosclerotic CVDs.

Small extracellular vesicles (sEVs or exosomes) play essential roles in pathophysiology, such as CVDs, by communicating with target cells through their biological cargo. Although there exists a close association between the liver and the cardiovascular system, the mechanisms linking liver-derived sEVs and atherosclerosis remain incompletely elucidated.

We have isolated extracellular vesicles from macrophage-conditioned media and human plasma by an ultracentrifugation-based method. Dynamic light scattering and cryo-electron microscopy confirmed the shape and size of the exosomes. The western blotting of exosome-specific markers CD63 and TSG101 in human plasma showed the presence

of exosomes. LC-MS of the conditioned media showed a proteome difference between control and cholesterol treatment. We have started the experiment on ApoE$^{-/-}$ mice to find the change in exosome proteome during atherosclerosis.

Evaluation of the role of Plasmalogens on hepatic steatosis-induced Atherosclerosis.

Plasmalogens are the key structural components of the cell membrane and act as endogenous antioxidants and are primarily synthesized in the liver. Emerging evidence suggests that the reduction of circulating plasmalogen is associated with hepatic steatosis and coronary artery disease. However, the mechanistic understanding of plasmalogens in these diseases is not well understood. We checked the effectiveness of plasmalogens on hepatic steatosis and hepatic steatosis-induced atherosclerosis parameters in vitro, as well as their underlying mechanism. Our preliminary data suggests that feeding rats HFCD diet-induced NAFLD (non-alcoholic fatty liver disease) symptoms and lipidomics analysis of the liver showed a significant decrease in the levels of plasmenyl ethanolamine (PlsEtns). The administration of plasmalogens could offer an effective therapeutic approach to prevent atherosclerosis progression and lower the risk of cardiovascular disease, especially in cases of NAFLD.

Understanding the role of Calicin in atherosclerosis progression.

A previous study in human patients with STEMI indicates a significant alteration in the expression level of a novel protein, calicin. Calicin was originally identified as a novel actin-binding protein found in the acrosome of spermatozoa that helps in the migration & motility of sperm and maintains the nuclear structure. Since its role in atherosclerosis progression is not known, we aimed to elucidate its role in smooth muscle cell remodelling and calcification of the plaques. We checked the RNA expression of calicin by real-time PCR and protein expression by confocal microscopy in the cholesterol-loaded macrophage and liver cell lines. Our data showed that cholesterol increases the expression of calicin both at RNA and protein levels. Moreover, data mining of the IntAct database showed that calicin has binary molecular interactions with four proteins that have roles in mitochondrial quality control and are implicated in CVDs. An increase in the levels of calicin by cholesterol treatment indicates its possible role in atherosclerosis progression. The physical interactions of calicin with the proteins suggest its potential involvement in CVDs. The structural properties of calicin warrant a detailed study to find novel interactors and their signalling function.

Future Research Plans

1. Lipidomics and metabolomics of liver-derived exosomes in the context of NAFLD and atherosclerosis. To validate novel proteins of extracellular vesicle-derived proteins, which were differentially expressed in CAD, and elucidate the molecular mechanism thereof.
2. To check the co-expression and interaction of calicin with other proteins to reveal the signalling pathway related to inflammation, calcification and smooth muscle cell migration during atherosclerosis.
3. Further validation of the plasmalogens in a mice model (ApoE knock out) of atherosclerosis. To find the effect of PEDS1 (an enzyme that converts Alkyl ether lipid to respective plasmalogens) overexpression on hepatic steatosis and to develop an agonist for the same.

Extramural / CSIR funding

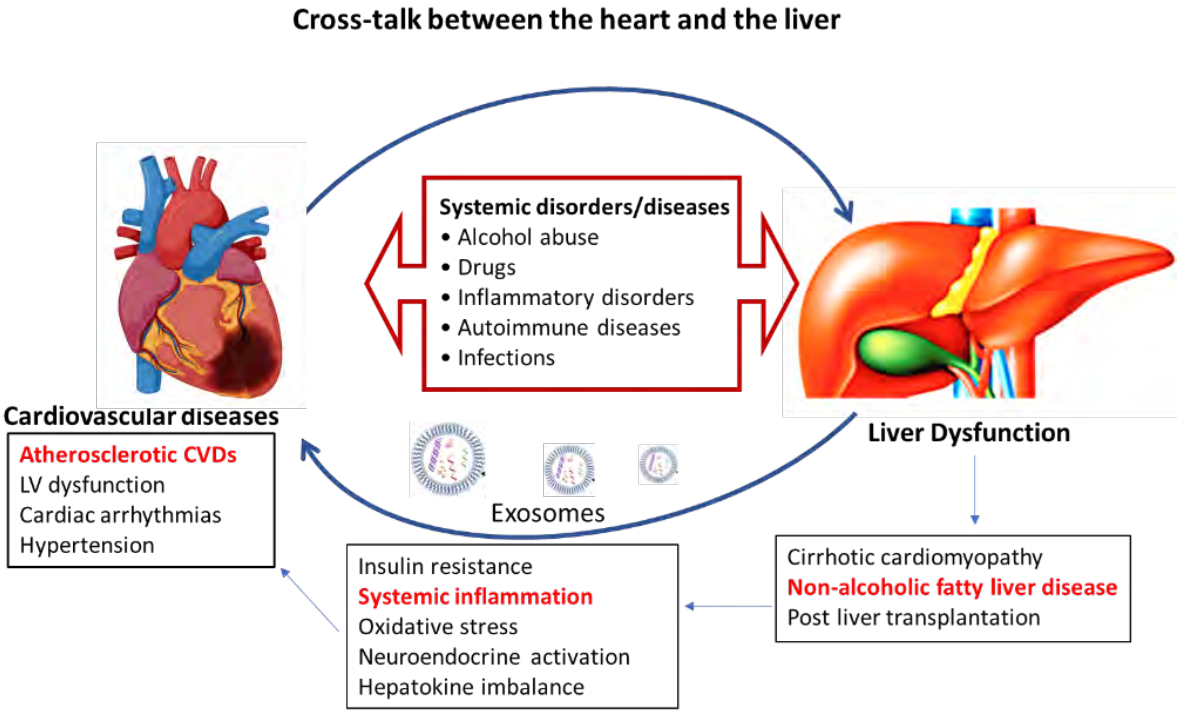
Deciphering the crosstalk between hepatic steatosis and Atherosclerosis: Modulating the AEBP1-PPARγ axis in maintaining cholesterol Homeostasis. R& Seed Fund, CSIR, 2024-25, 23.7 Lakhs, RDS000002.

Publications

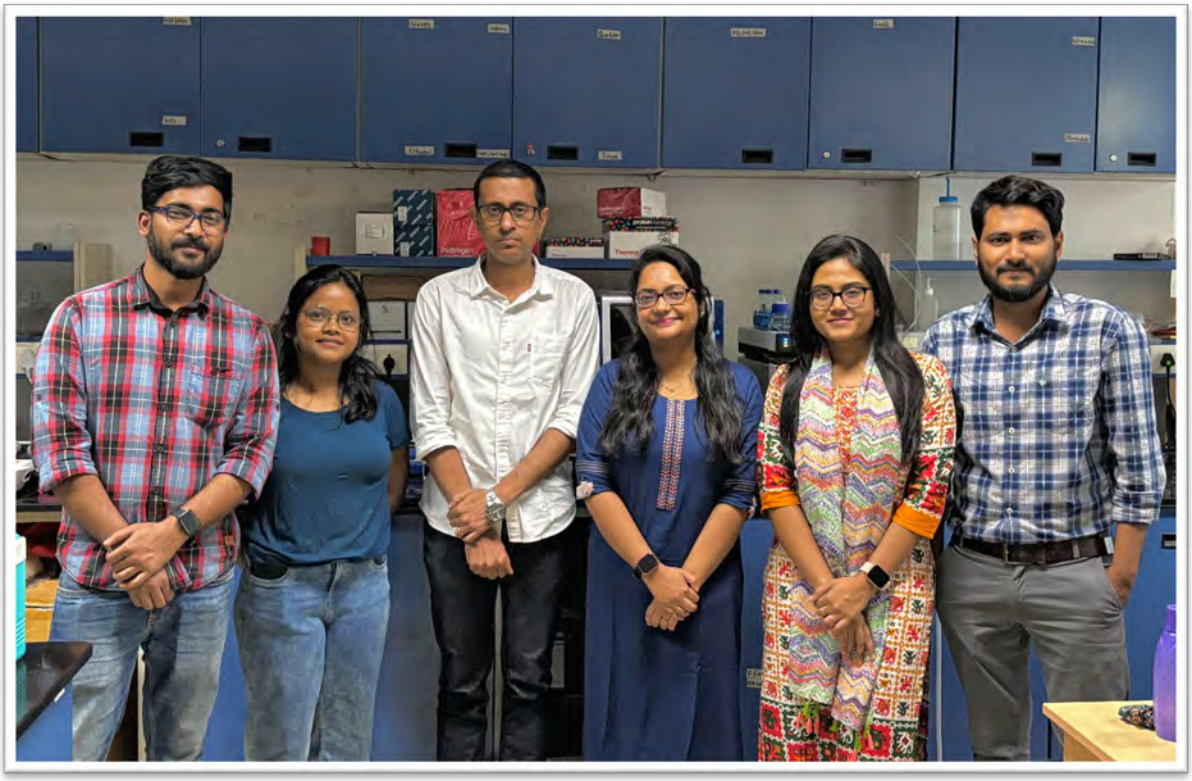
1. Navya, M., Alam, M. J., Maulik, S. K., and Banerjee, S. K. (2023) The Role of Platelets in Non-Alcoholic Fatty Liver Disease: From Pathophysiology to Therapeutics. *Prostaglandins & Other Lipid Mediators*, 106766.
2. Shreya, S., Alam, M. J., Anupriya, A., Jaiswal, S., Rani, V., and Jain, B. P. (2023) Lipotoxicity, ER Stress, and Cardiovascular Disease: Current Understanding and Future Directions. *Cardiovascular & Hematological Agents in Medicinal Chemistry*. 22, 1-17
3. Tiwari, V., Alam, M. J., Bhatia, M., Navya, M., and Banerjee, S. K. (2024) The structure and function of lamin A/C: Special focus on cardiomyopathy and therapeutic interventions. *Life Sciences*, 122489.

Member of Society

Life member, International Society of Heart Research (Indian Section), Department of Pharmacology, All India Institute of Medical Sciences, New Delhi-110029, India.



Dr. Md. Jahangir Alam, Scientist
Group Members: Arkya Roy, UGC-JRF; Gopal Dolai, UGC-JRF
Collaborators: Dhabalesar Patra, PhD, Structural Biology & Bioinformatics Division, CSIR-IICB, Kolkata; Ramu Adela, PhD, Department of Pharmacy Practice, NIPER-Guahati



Dr. Joy Chakraborty and his group members

Identification of a dietary phytochemical with Monoamine oxidase inhibitory properties: Implications in Parkinson's disease-associated behavioral deficits in a mice model

Research Activities

Parkinson's disease (PD) is one of the most prevalent age-related neurodegenerative disorders. Behavioral complexities worsen over time due to progressive dopaminergic (DArgic) neuronal loss at substantia nigra region of brain. Available treatments typically aim to increase dopamine (DA) levels at striatum. DA is degraded by Monoamine oxidase (MAO), thus dietary phytochemicals with MAO inhibitory properties can contribute to elevate DA levels and reduce the ailments. Characterization of naturally occurring dietary MAO inhibitors is inadequate. Based on available knowledge, we selected different classes of molecules and conducted a screening process to assess their potential as MAO inhibitors. The compounds mostly derived from food sources, broadly belonging to triterpenoids (ursane, oleanane and hopane), alkaloid, polyphenolics, monoterpenoids, alkylbenzene, phenylpropanoid and aromatic alcohol classes. Among all the molecules, highest level of MAO inhibition is offered by α-viniferin, a resveratrol trimer. Cell viability, mitochondrial morphology and reactive oxygen species (ROS) generation remained unaltered by 50 μM α-viniferin treatment in-vitro. Toxicity studies in Drosophila showed unchanged gross neuronal morphology, ROS level, motor activity or long-term survival. α-Viniferin inhibited MAO in mice brain and elevated striatal DA levels. PD-related akinesia and cataleptic behavior were attenuated by α-viniferin due to increase in striatal DA. Our study implies that α-viniferin can be used as an adjunct phytotherapeutic agent for mitigating PD-related behavioral deterioration.

Future research plans

MAO is one of the key sites where ROS is generated. MAO-mediated ROS generation and mitochondrial functioning is a complex relationship. Excess ROS can compromise mitochondrial membrane potential and thus the functioning of the organelle. However, isolated reports also suggest that MAO-mediated ROS can contribute to the electron transport chain. Additionally, increased MAO levels can influence mitochondrial quality control by regulating autophagy. The balance might trample when MAO

substrates (such as DA) are aberrantly high. One of the options to manage this problem is the use of antioxidants. However, antioxidants come with several limitations; like reduction of ROS levels below the required basal levels and the difficulty to maintain an effective concentration at physiological conditions. In case of PD, this scenario is highly relevant. To compensate the lower levels of DA due to progressive DArgic neuronal loss during PD, L-DOPA is prescribed to increase DA synthesis. Whether this increased amount of DA per neuron can accelerate neurodegeneration in PD is a matter of controversy. However, alternatives which can reduce this MAO substrate mediated strain on DArgic neurons include DA receptor agonists and inhibitors of DA degradation. Synthetic DA receptor agonists have limited utility. The dose to restore behavioral deficiencies may vary due to altered receptor sensitivity or receptor unavailability at the proper sites. On top of that, DA receptor agonists fail to comprehend phasic DA release mediated response.

These issues highlight the worth of MAO inhibitors for synergistic therapy development and treat PD-related behavioral complicacies. Outcomes from the clinical trials of MAO B inhibitors (e.g., selegiline and rasagiline) also advocate that incorporating MAO inhibitors in the treatment regime can delay the need of L-DOPA therapy and thus may extend the treatment efficacy. Although there is a substantial amount of literature that supports the disease-modifying effect of selegiline when consumed in the early days of PD, interestingly some discrete reports from clinical trials also question its influence on life expectancy. These synthetic inhibitors are also related to hypertensive crises. Considering these aspects, we point out that naturally occurring compounds that are used in traditional medicine to modify neurological disorders are highly under-explored, although they have huge potential to elicit the same effects as mentioned for synthetic MAO inhibitors.

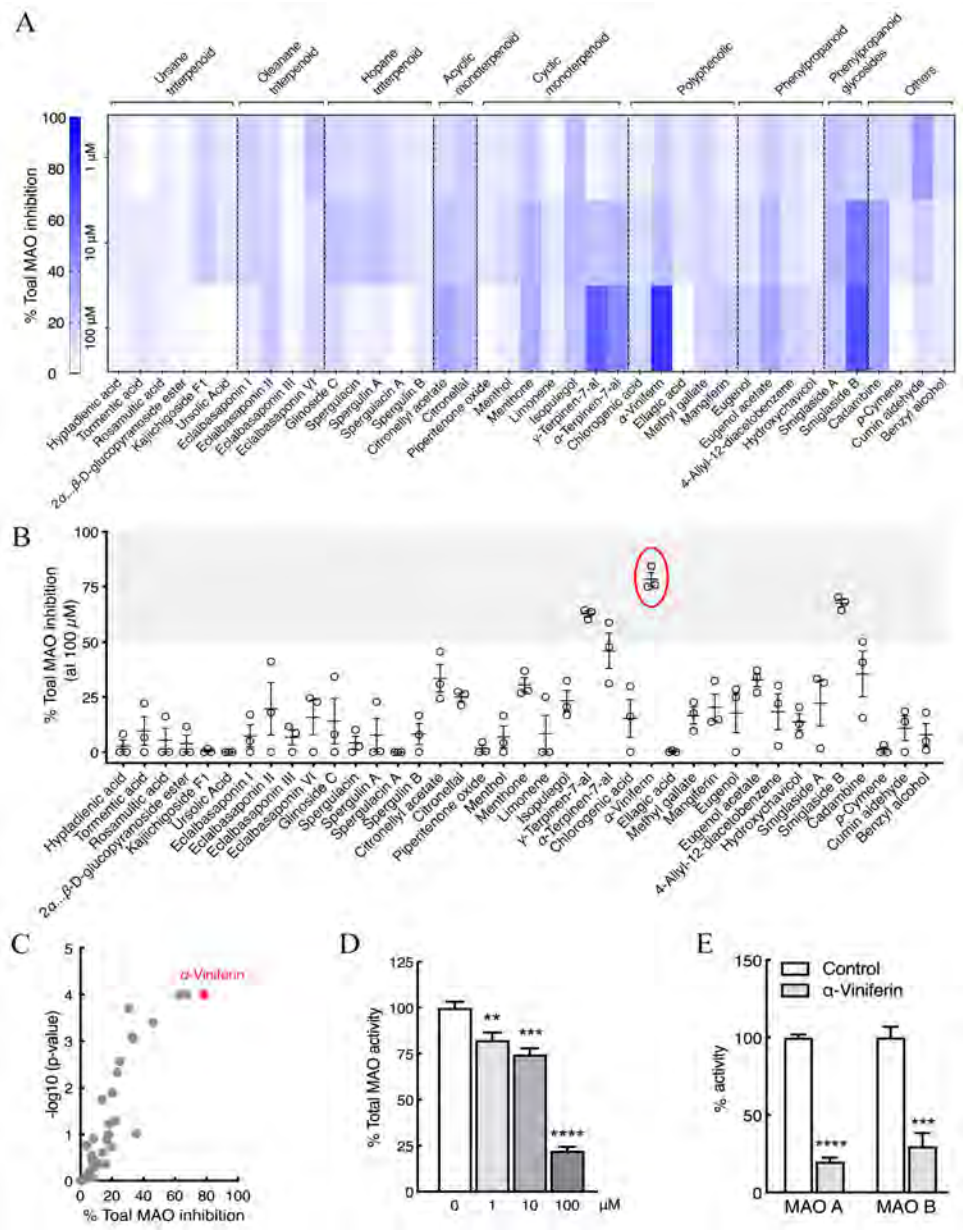
α-Viniferin is found to be the most promising MAO inhibitordemonstrating no cytotoxic effects. It carries the therapeutic potential to improve behavioral deficits in PD by regulating relevant neurotransmitter levels at striatum. We will further direct our research to find out whether α-viniferin or plants containing α-viniferin can be used as an adjuvant therapy in the form of functional foods or nutraceutical agents, where neuro-motor incoordination is prevalent due to aberrations in MAO-influenced neurotransmitter levels.

Extramural / CSIR Funding

1. Impact of Voltage-dependent anion-selective channel 1 (VDAC1) protein on mitochondrial shaping and dynamics. Funding agency: Department of Biotechnology (DBT), 2023-2026. 4798330.0. (BT/PR45354/MED/122/315/2022).
2. Phytopharmaceutical development of Sesquiterpene coumarin enriched fraction of Ferula assa-foetida gum against Parkinson's disease. Funding agency: Council of Scientific & Industrial Research (phytopharma mission III). 2024-2027. 17800000.0, (MMP075201).

Publications

1. Mondal, R., Banerjee, C., Nandy, S., Roy, M., and Chakraborty, J. (2023) Calcineurin inhibition protects against dopamine toxicity and attenuates behavioral decline in a Parkinson's disease model. *Cell Biosci* 13, 140.
2. Banerjee, C., Barman, R., Darshani, P., Pillai, M., Ahuja, S., Mondal, R., Pragadheesh, V. S., Chakraborty, J., and Kumar, D. (2024) alpha-Viniferin, a dietary phytochemical, inhibits Monoamine oxidase and alleviates Parkinson's disease associated behavioral deficits in a mice model. *Neurochem Int* 174, 105698.



Library of compounds screened for Monoamine oxidase (MAO) activity assay identifies *α*-viniferin as a potent inhibitor. (A)Heat map represents percentage mean inhibition of total MAO activity by mentioned compounds at 1, 10, and 100 µM dose. N = 3. (B) Scatter plot illustrates mean inhibition of total MAO activity by tested molecules at 100 µM dose, with the highlighted area indicating molecules exhibiting ≥50% inhibition. Mean ± SEM, N = 3. (C) Volcano plot represents percentage total MAO inhibition (x-axis) versus significance (y-axis) of all compounds screened for MAO assay at 100 µM concentration. (D) Bar graph demonstrates dose dependent total MAO inhibition by *α*-viniferin. N=3, One way ANOVA followed by Dunnet's post hoc test.,**p ≤ 0.01, ***p≤ 0.001, ****p ≤ 0.0001. (E)Bar graphs demonstrate MAO A or B specific inhibition by *α*-viniferin at 100 µM concentration. N=3, student's t test, ***p≤ 0.001, ****p≤0.0001.

Dr. Joy Chakraborty, Senior Scientist
Group members: Moumita Roy, CSIR-SRF; Rupsha Mondal, CSIR-SRF; Chayan Banrejee, UGC-SRF; Aishi Majumder, UGC-JRF; Sumangal Nandy, DBT- Project associate
Collaborators: Dr. Deepak Kumar, PhD, CSIR Indian Institute of Chemical Biology, Kolkata, India; Dr. Partha Chakraborty, PhD, CSIR Indian Institute of Chemical Biology, Kolkata, India; Dr. Krishnananda Chattopadhyay, PhD, CSIR Indian Institute of Chemical Biology, Kolkata, India; Dr. Dipyaman Ganguly, PhD, CSIR Indian Institute of Chemical Biology, Kolkata, India.

Dr. Partha Chakrabarti and his group members

Impact of gut microbiome derived metabolites on non-alcoholic fatty liver disease' (NAFLD)

Research Activities

The term 'Non-alcoholic fatty liver disease' (NAFLD) was first coined around the 1980s and within a span of 33 years, the global prevalence rate has risen to whopping 30%. Considering the etiopathogenesis, among the gamut of reversible and non-reversible pathogenic drivers, gut dysbiosis plays a crucial role. Despite the advancement in understanding the mechanistic perspective of disease pathogenesis, due to highly variable disease progression rate and varied clinical manifestations, sketchy knowledge is available for the development of effective treatment strategies. As gut microbiota derived metabolites are known to interact with host cells for regulating physiological homeostasis, we wanted to seek the 'drugs from the bugs' to pave new preventive as well as therapeutic avenues. Immune cell infiltration and lobular inflammation in the background of steatosis are the cardinal features of nonalcoholic steatohepatitis (NASH). An array of gut microbiota derived metabolites including short-chain fatty acids (SCFA) multifariously modulates NASH pathogenesis. In this study we aim to decipher the molecular basis for the favorable impact of sodium butyrate (NaBu), a microbiota-derived SCFA, on the immunometabolic homeostasis in NASH.

NASH was developed in wild type C57Bl/6 mice fed with methionine choline deficient (MCD) diet. Immunomodulatory effects of NaBu administered either by oral gavage or through drinking water were determined by histology, immunohistochemistry, flow cytometry, gene expression and serum biomarkers. Liver macrophages (LM), bone marrow derived macrophage (BMDM) and RAW264.7 cells were analyzed for anti-inflammatory effects of NaBu by immunofluorescence microscopy, qPCR and immunoblotting. NaBu dependent gene expressions were determined by RNA sequencing and promoter engagement of canonical NF-κB subunit p65 by chromatin immunoprecipitation (ChIP) sequencing. We show that NaBu imparts a robust anti-inflammatory effect in lipopolysaccharide (LPS) stimulated or classically activated M1 polarized macrophages and in diet induced NASH model. Mechanistically, NaBu enhanced acetylation of p65 along with its differential recruitment to the

proinflammatory gene promoters independent of its nuclear translocation. NaBu also quelled LPS mediated catabolism and phagocytosis of macrophages, exhibited a differential secretome which consequently resulted in skewing towards a M2 like prohealing phenotype and induced death of proinflammatory macrophages to abrogate metaflammation *in vitro* and *in vivo*.

In summary, NaBu potently suppresses inflammatory insults in NASH through differential chromatin recruitment of acetylated p65, suppressing proinflammatory and augmenting anti-inflammatory gene expressions and inducing apoptosis of proinflammatory LM in NASH livers. Thus NaBu could be a potential therapeutic and preventive agent in mitigating NASH (Figure 1).

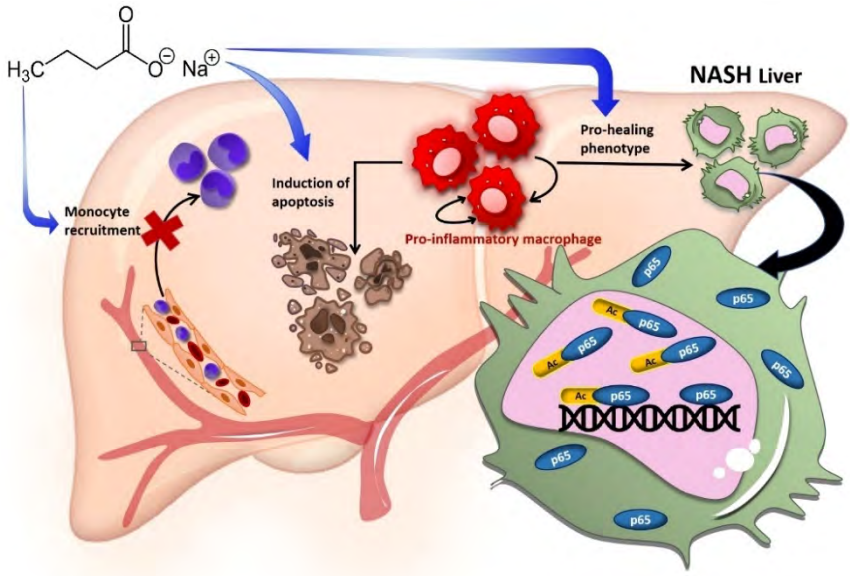


Figure 1. Schematic of the mechanism of NaBu in amelioration of NASH. NaBu ameliorated inflammatory insults of NASH by inhibiting pro-inflammatory macrophage infiltration, modulating polarization status as well as by inducing apoptosis of pro-inflammatory macrophages (blue arrows). The molecular mechanism of mitigated inflammatory response is hyperacetylation of p65 and its differential recruitment to proinflammatory gene promoters.

Future research plans

1. Elucidate other liver-derived molecular factors that could affect the pancreatic beta cell physiology.
2. Assess the role of gut microbiota derived metabolites in the progression of NAFLD.
3. Determine the role of ubiquitin-proteasome system in the pathogenesis of NAFLD.

Extramural / CSIR Funding

1. Adipose tissue-β cell axis in the pathophysiology of Non-obese Type 2 Diabetes: Role of Adipokines. ICMR, 2021-24. 57.4 lakh (5/4/5-6/Diab./2021-NCD-III)
2. Understanding the regulatory role of co-activator binding protein PIMT in the pancreatic β-cells of diabetic animals and T3c diabetic (chronic pancreatitis) humans. Funding agency: SERB, Department of Science & Technology (DST), 2021-24, 12.9 lakh, (CRG/2021/000689/IBS)
3. Non-alcoholic Fatty Liver Disease (NAFLD): Novel Pathogenetic mechanism and therapeutic development. CSIR, 2020-25, 499 lakh, MLP138.
4. Phenome India-CSIR Health Cohort Knowledgebase. CSIR, 2022-27, 9896.09 Lakh, HCP47.

Publications

1. Edwin RK, Acharya LP, Maity SK, Chakrabarti P, Tantia O, Joshi MB, Satyamoorthy K, Parsa KVL, Misra P. (2024) TGS1/PIMT knockdown reduces lipid accumulation in adipocytes, limits body weight gain and promotes insulin sensitivity in mice. *Biochim Biophys Acta Mol Basis Dis*. 1870,166896.
2. Challa NL, Sarkar A, Satyamoorthy K, Babu PP, Chakrabarti P, Parsa KVL, Misra P. (2024) TGS1/PIMT regulates pro-inflammatory macrophage mediated paracrine insulin resistance: Crosstalk between macrophages and skeletal muscle cells. *Biochim Biophys Acta Mol Basis Dis*. 1870,166878.

3. Sarkar, D., Chowdhury, S., Goon, S., Sen, A., Dastidar, U. G., Mondal, M.A., Chakrabarti, P., Talukdar, A. (2023) Discovery and Development of Quinazolinones and Quinazolinediones for Ameliorating Nonalcoholic Fatty Liver Disease (NAFLD) by Modulating COP1-ATGL Axis. *J Med Chem*. 66, 16728-16761.
4. Ghosh AR, Bandopadhyay P, Sarkar J, Khanna S, Chaudhuri T, Tantia O, Chakrabarti P, Ganguly D. (2023) Mitochondrial sourcing of interferogenic ligands and an autoantigen in human obesity-associated metaflammation. *Obesity (Silver Spring)*. 31, 2229-2234
5. Bandyopadhyay D, Basu S, Mukherjee I, Chakrabarti S, Chakrabarti P, Mukherjee K, Bhattacharyya SN. (2023) Accelerated Export of Dicer1 from Lipid-Challenged Hepatocytes Buffers Cellular miRNA-122 Levels and Prevents Cell Death. *J Biol Chem*. 299, 104999.
6. Sarkar A, Mitra P, Lahiri A, Das T, Sarkar J, Paul S, Chakrabarti P. (2023) Butyrate limits inflammatory macrophage niche in NASH. *Cell Death Dis*. 14, 332.
7. Sharma R, Maity SK, Chakrabarti P, Katika MR, Kapettu S, Parsa KVL, Misra P. (2023) PIMT Controls Insulin Synthesis and Secretion through PDX1. *Int J Mol Sci.* 24, 8084.

Patents

1. Protacs for ask1 protein degradation: preparation and use thereof. Arindam Talukdar, Himadri Sekhar Sarkar, Partha Chakrabarti, Israful Hoque, Abhishek Sen, Uddipta Ghosh Dastidar, Anindita Dey, Filing date: 18/05/2023, 202311034982 IN
2. Non-cytotoxic quinoline derivatives selectively targeting the mTORC1 pathway and decreasing the total lipid accumulation in hepatocytes for the treatment of fatty liver disease (NAFLD). Subhadeep Palit, Tanusree Das, Bhim Majhi, Partha Chakrabarti, Sanjay Dutta, 7/03/2024, 202411017222 IN

Book Chapters

Sarkar, J., and Chakrabarti, P. (2023) Metabolic Syndrome: From Mechanisms to Interventions, 1st Ed, Elsevier, New York.

Invited Lectures

1. Heterogeneity in Type 2 Diabetes. Society of Biological Chemists, Kolkata Chapter, 12.4.2023
2. Bais and noise in Medicine: Case of Diabetes. Ramakrishna Mission Institute of Culture, Kolkata, 11.5.2023
3. Proteotoxicity in Liver Diseases. Amity University, Kolkata, 9.11.2023

Member of Society

Committee member, Programme Advisory Committee on Biomedical Health Science (PAC-BHS), SERB, Government of India (2022-2025).

Dr. Partha Chakrabarti, Senior Principal Scientist

Group Members: Saheli Chowdhury, UGC-SRF; Ankita Sarkar, UGC-SRF; Pratiti Mandal, DST-INSPIRE fellow; Tanusree Das, CSIR-SRF; Abhishek Sen, ICMR-SRF; Sujay K. Maity, ICMR-SRF; Arijita Basu, ICMR project RA

Collaborators: Abhijit Chowdhury, MD, DM, Gastroenterology and Hepatology, Institute of Postgraguate Medical Education and Research, Kolkata, India;Sujoy Ghosh, MD, DM, Endocrinology, Institute of Postgraguate Medical Education and Research, Kolkata, India; Om Tantia, MS, FRCS, ILS hospital, Kolkata, India; Sandip Paul, PhD, JIS Institute of Advanced Studies and Research, Kolkata, India; Parimal Misra, PhD, Dr Reddy's Institute of Life Science, Hyderabad, India;Arindam Talukdar, PhD, CSIR-IICB, Kolkata, India; Sanjay Dutta, PhD, CSIR-IICB, Kolkata, India.

Dr. Prem Prakash Tripathi and his group members

Hippocampal neurodegeneration induces transient endogenous regeneration and long-term exhaustionof the neurogenic niche

Research Activities

The hippocampal dentate gyrus, responds to diverse pathological stimuli throughneurogenesis. This phenomenon, observed following brain injury or neurodegenera-tion, is postulated to contribute to neuronal repair and functional recovery, therebypresenting an avenue for endogenous neuronal restoration. This study investigatedthe extent of regenerative response in hippocampal neurogenesis by leveraging thewell-established kainic acid-induced status epilepticus model in vivo. In our study, we observed the activation and proliferation of neuronal progenitors or neural stemcell (NSC) and their subsequent migration to the injury sites following the seizure. Atthe injury sites, new neurons (Tuj1+BrdU+ and NeuN+BrdU+) have been generatedindicating regenerative and reparative roles of the progenitor cells. We furtherdetected whether this transient neurogenic burst, which might be a responsetowards an attempt to repair the brain, is associated with persistent long-termexhaustion of the dentate progenitor cells and impairment of adult neurogenesismarked by downregulation of Ki67, HoPX, and Sox2 with BrdU+ cell in the later partof life. Our studies suggest that the adult brain has the constitutive endogenousregenerative potential for brain repair to restore the damaged neurons, meanwhile,in the long term, it accelerates the depletion of the finite NSC pool in thehippocampal neurogenic niche by changing its proliferative and neurogenic capacity.A thorough understanding of the impact of modulating adult neurogenesis willeventually be required to design novel therapeutics to stimulate or assist brain repairwhile simultaneously preventing the adverse effects of early robust neurogenesis onthe proliferative potential of endogenous neuronal progenitors.

We investigated the adverse effects of the chemiconvulsant, kainic acid, a glutamate agonist, on the hippocampus and its sub-fields in adult mice. KA was administered to assess the persistence of neuronal death in hippocampal pyramidal layers post status-epilepticus (SE) induction. Apoptotic DNA fragmentation was detected through TUNEL-positive

staining. Our findings revealed that KA-induced excitotoxicity resulted in selective cell death through apoptosis in the pyramidal neuronal layers of the CA3 and CA1 subfields of the hippocampal regions.

We aimed to evaluate the proliferation of dentate neuronal to examine the response of neural progenitor/precursor cells within the neurogenic niche to excitotoxicity-induced neurodegeneration. Adult young mice experiencing seizures were administered BrdU injections once every 24 hours for consecutive 3 and 7 days, respectively, on the 3rd and 5th day of post-KA treatment. The day after the final BrdU injections, mice were perfused, and their brains were isolated for further analysis. Immunostaining was conducted using the BrdU antibody to visualize labeled cells (BrdU birth dating technique). Our analysis aligns with prior findings, indicating that SE substantially enhances cellular proliferation in the DG following SE.

Upon detecting neurodegeneration within the CA3 and CA1 subfields, the robust activation of SGZ neuronal precursors prompts proliferation and subsequent differentiation into diverse neuronal progenitors of neurogenic lineages. Nevertheless, the question of whether these nascent progenitors migrate to the injury sites remains unanswered. To elucidate this, we conducted simultaneous investigations into the presence of these new cells in both CA3 and CA1. Initially, we probed the presence of BrdU+ cells at the injury sites post-SE, revealing a significant prevalence of new cells in both CA3.

To ascertain the ultimate fate of IPCs born early after SE, we executed a BrdU pulse-labeling experiment on the third day, administering it intraperitoneally six times with two-hour intervals between each dose, after the SE induction. This allowed us to subsequently track the survival and maturation of these neurons at the 45-day mark post-SE. The coronal sections from mice sacrificed at this time point revealed a higher number of BrdU+ profiles compared to the age-matched control group within the DG. This discernible increase suggests that the neuronal progenitors emerging post-SE not only persevered but also underwent further differentiation to yield nascent neurons. By co-labeling BrdU with TuJ1 and NeuN, we performed a rigorous quantitative assessment of neuroblasts and mature neurons generated after SE. Our analysis showed a statistically significant increase in new neurons within the DG.

In line with our hypothesis, the initial and vigorous activation of Type 1 neuronal precursors after SE is expected to trigger a prolonged depletion of the neuronal progenitor populace within the neurogenic niche of the DG over the long term. Accordingly, our initial investigation centred on the expression of three pivotal neurogenic activity markers—Ki67, HoPX, and Sox2—following 240 days of post-KA treatment. Strikingly, a notable reduction across all markers was evident within the DG of KA-treated mice in comparison to their age-matched control counterparts. Furthermore, we evaluated the prolonged impact of SE on neurogenic efficacy, specifically focusing on the fate and survival of neurons generated from intermediate progenitor cells (IPCs). Subsequently, we tracked their survival and maturation after 45 days (at 240 days). Upon co-labeling BrdU with NeuN to examine the newly generated neurons in the DG, a notable decrease in newly generated neurons was evident.

To comprehensively assess the long-term impact of SE on the dentate neurogenic niche, we examined the expression of various early neurogenic markers from day 10 to day 240 following SE. An age-related decline in the expression of proliferative markers, Ki67 and PCNA, was detected within the DG from day 10 to day 240 after SE. Notably, in control mice, no significant distinction in Ki67 expression emerged between the two distinct age groups. However, a marked difference in Ki67 expression was evident between 10 days and 240 days in KA-treated mice. Collectively, quantitative comparisons between PBS and KA at day 240 unveiled a substantial decline in all neurogenic markers. Cumulatively, these findings underscore that early-life SE accelerates the depletion of the dentate neural progenitor pool compared to age-related physiological decreases. Furthermore, it strongly impairs the neuroproliferative efficacy of the neurogenic niche to a much greater extent than the normative age-related decline.

Future Research Plans

In future, we aim to investigate the extent of alteration of the hippocampal neurogenic niche following seizure induction by kainic acid, emphasizing the morphological responses of the various cell types associated with the neurogenic pathway. We want to study the activation-dependent conversion of radial neural stem cells (HopX+GFAP+) to reactive astrocytes, associated with a transition to a more gliogenic fate (S100β+GFAP+) than neurogenic, meanwhile undermining adult neurogenesis. This study may suggest the induction of aberrant neurogenesis following disruption of neurogenic niche after seizure that we may establish with series of cognitive test

such as recognition, spatial memory and mood disorders along with any alterations of the hippocampal synaptic plasticity in adult mice.

Extramural / CSIR Funding

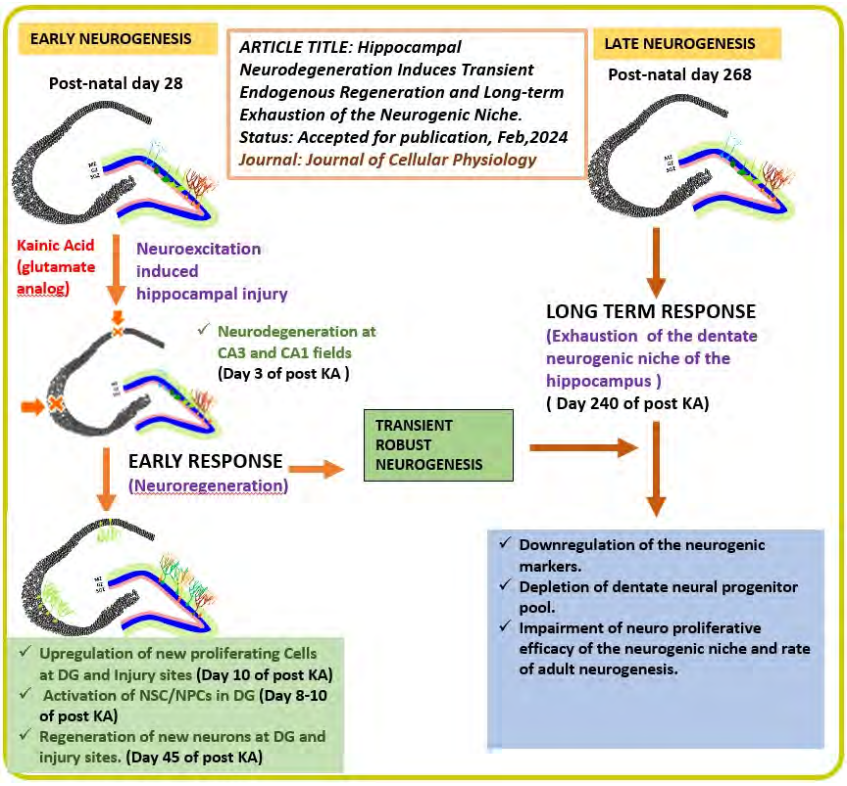
Functional dissection of Jmjd3 during embryonic and adult hippocampal neurogenesis, SERB, Department of Science & Technology (DST), 2021-24, 44.22 lakhs, (CRG/2021/003564)

Publications

1. Dey, J., Chandra, S., Gupta, J., Tripathi, P. P.* (2024) Hippocampal neurodegeneration induces transient endogenous regeneration and long-term exhaustion of the neurogenic niche. *J Cell Physiol*. e31249.
2. Begum, F., Srivastava, A. K., Tripathi, P. P.*, Ray, U.* (2023) A substrate for a cell free in vitro assay system to screen drugs targeting trypsin like protease-based cleavage of SARS-CoV-2 spike glycoprotein and viral entry. *Journal of Medical Virology*, e28796.

Patents

A recombinant construct for screening drugs against SARS-CoV-2 spike protein. Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava, filing date 04/05/2023, PCT/IN2022/050949



Kainic acid-induced status epilepticus activates neuronal progenitors and NSCs in the early hippocampal neurogenesis, generating new neurons at injury sites. However, this transient neurogenic burst leads to long-term depletion of progenitor cells, impairing adult neurogenesis

Dr. Prem Prakash Tripathi, Senior Scientist
Group Members: Jhilik Dey, UGC-SRF; Sreyashi Chandra, CSIR-SRF; Rahul Mallick, CSIR-SRF; Aniket Dey, CSIR-JRF
Collaborators: Jalaj Gupta, PhD, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India; Amit Srivastava, PhD, CSIR- Indian Institute of Chemical Biology, Kolkata, India; Upasana Ray, PhD, CSIR-Indian Institute of Chemical Biology, Kolkata, India.

Dr. Ratanti Sarkhel

Analysis of Methionine sulfoxide reductase A (MsrA)-Malate Synthase (MS) interaction in *Salmonella Typhimurium* and identification of hot spot of the interactome

Research Activities

Designing primers for MsrA and MS and proceeding for cloning and expression of these genes.

Future Research Plans

- Identification of critical methionine (Met) residues in malate synthase of *Salmonella* Typhimurium which get preferentially oxidized and repaired by methionine sulfoxide reductase A (MsrA) repair system
- Construction of malate synthase variants by mutation of critical Met residues and study their effect on conformation and activity
- Analysis of MsrA- MS interaction and identify the hotspots
- Design specific hotspot based inhibitor of the interactome

Publications

Sarkhel, R., Priyadarsini, S., & Mahawar, M. (2024) Nutrient limitation and oxidative stress induce the promoter of acetate operon in *Salmonella* Typhimurium. *Archives of Microbiology*. 206, 1-7.

Book Chapter

Paul, S., Chakraborty, S., Biswas, P., Mandal, A. K., Sadhukhan, T and Sarkhel, R. (2024) Vet – View, 1ST Edition, Astral International Pvt Ltd, India.

Conferences Attended

V11 Annual Convention Of SVBBI and International Symposium on, "Multiomics to one health: Challenges and way forward in biomedical research" held at ICAR- Indian Veterinary Research Institute, Bareilly, December 14- 15, 2023.

Member Of Society

Society of Veterinary Biochemists and Biotechnologists of India (SVBBI), Bhubaneshwar, India, Life membership

Awards

Best oral presentation award, V11 Annual Convention Of SVBBI, held at ICAR- Indian Veterinary Research Institute, Bareilly (Dec 14- 15, 2023).

Dr. Rupasri Ain and her group members

Cellular and molecular rendezvous at the maternal-fetal interface: Implication in placental pathophysiology

Research Activities

We are interested in how early trophoblast development is regulated by miRNAs, transcription factors, and specific cellular signaling events to ensure normal development. We also investigate how trophoblast-derived factors modulate vascular smooth muscle cells (VSMC) to impart phenotypic changes required for normal pregnancy progression. We use the tools and concepts of molecular biology, cell and developmental biology, genetics, and microscopy to further our understanding of trophoblast stem cell differentiation, angiogenesis, and placental development.

Moonlighting of Cellular Prion protein in vascular smooth muscle cell fate: Surveilled by trophoblast cells.

Uterine spiral artery remodelling (uSAR) is a hallmark of haemochorial placentation. Compromised uSAR leads to adverse pregnancy outcomes. Salient developmental events involved in uSAR are active areas of research and include (a) trophendothelial cell invasion into the spiral arteries, selected demise of endothelial cells; (b) de-differentiation of vascular smooth muscle cells (VSMC); and (c) migration and/or death of VSMCs surrounding spiral arteries. Here we demonstrated that cellular prion (PRNP) is expressed in the rat metrial gland, the entry point of spiral arteries with the highest expression on E16.5, the day at which trophoblast invasion peaks. PRNP is expressed in VSMCs that drift away from the arterial wall. RNA interference of Prnp functionally restricted migration and invasion of rat VSMCs. Furthermore, PRNP interacted with two migration-promoting factors, focal adhesion kinase (FAK) and platelet-derived growth factor receptor-β (PDGFR-β), forming a ter-molecular complex in both the metrial gland and A7r5 cells. The presence of multiple putative binding site of odd skipped related-1 (OSR1) transcription factor on the Prnp promoter was observed using in silico promoter analysis. Ectopic overexpression of OSR1 increased, and knockdown of OSR1

decreased expression of PRNP in VSMCs. Co-culture of VSMCs with rat primary trophoblast cells decreased the levels of OSR1 and PRNP. Interestingly, PRNP knockdown led to apoptotic death in ~9% of VSMCs and activated extrinsic apoptotic pathways. PRNP interacts with TRAIL-receptor DR4 and protects VSMCs from TRAIL-mediated apoptosis. These results highlight the biological functions of PRNP in VSMC cell-fate determination during uteroplacental development, an important determinant of healthy pregnancy outcome.

Molecular Orchestration of Epithelial Mesenchymal Transition During Trophoblast and Placental Development.

Trophectoderm cells of the blastocyst are the precursor of the placenta that is comprised of trophoblast, endothelial and smooth muscle cells. Since trophoectoderm cells are epithelial in nature, epithelial mesenchymal transition (EMT) of trophoblast stem (TS) cells might play pivotal role in placental morphogenesis. However, the molecular regulation of EMT during placental development and trophoblast differentiation still remained elusive. In this report, we sought to identify the molecular signature that regulates EMT during placental development and TS cell differentiation in mice. On E7.5 onwards the TS cells, located in the ectoplacental cone (EPC), rapidly divide and differentiate leading to formation of placenta proper. Using a real time PCR based array of functional EMT transcriptome with RNA from mouse implantation sites (IS) on E7.5 and E9.5, it was observed that there was an overall reduction of EMT gene expression in the IS as gestation progressed from E7.5 to E9.5 albeit the levels of EMT gene expression were substantial on both days. Further validation of array results using real time PCR and western blot analysis showed significant decrease in EMT-associated genes that included (a) transcription factors (Snai2, Zeb1, Stat3 and Foxc2), (b) extracellular matrix and cell adhesion related genes (Bmp1, Itga5, Vcan and Col3A1), (c) migration and motility- associated genes (Vim, Msn and FN1) and (d) differentiation and development related genes (Wnt5b, Jag1 and Cleaved Notch-1) on E9.5. To understand whether EMT is an ongoing process during placentation, the EMT-associated signatures genes, prevalent on E 7.5 and 9.5, were analysed on E12.5, E14.5 and E17.5 of mouse placenta. Interestingly, expression of these EMT-signature proteins were significantly higher at E12.5 though substantial expressions was observed in placenta with progression of gestation from mid- to late. To evaluate whether TS cells have the potential to undergo EMT ex vivo, TS cells were subjected to EMT induction, which was confirmed using morphological analysis and marker gene expression. Induction of EMT in TS cells showed similar gene expression profile of placental EMT. These results have broad biological implications, as inadequate mesenchymal transition leading to improper trophoblast-vasculogenic mimicry leads to placental pathophysiology and pregnancy failure.

Future Research Plans

Cell fate determination and differentiation accompany an exquisite molecular orchestra that is still an active area of research. Trophoblast cells, recognized as parenchymal cells of the placenta, execute most placental functions, indispensable for successful pregnancy. They differentiate from multipotent trophoblast stem (TS) cells during development. Despite being recognized as the developmental counterpart of embryonic stem (ES) cells in the context of placental development, many facets of regulation of trophoblast development remained elusive. In rodents and primates, specialized populations of trophoblast cells of the placenta invade the uterine stroma and establish relationships with uterine blood vessels supplying the placenta. Two populations of invading trophoblast cells can be identified: (i) interstitial and (ii) endovascular. Interstitial trophoblast cells penetrate through the uterine stroma and are often situated in perivascular locations, whereas endovascular trophoblast cells enter uterine blood vessels, where they replace endothelial cells. It has been proposed that “trophoblastic vascular colonization” is an effective mechanism for removing maternal vasomotor control and thus dramatically augmenting the delivery of maternal resources to the placenta. This hallmark developmental event in effect, creates flaccid, low-resistance blood vessels, known as spiral artery remodelling, and is fundamental for the optimal delivery of nutrients to the fetus. Our future goal is to dissect the mechanism of spiral artery remodelling, regulation of TS cell differentiation by non-coding RNAs, Regulation of VSMC plasticity by trophoblast cells etc.

Extramural / CSIR Funding

1. Regulation of trophoblast development and placental pathophysiology by long non-coding RNA. SERB-POWER, 2021-24, 51 lakhs, (SPG/2020/000334).
2. Hippo dynamics is a critical regulator of

trophoblast stem cell self-renewal and differentiation. ICMR, 2020-23, 43.59 lakhs, (2020-3442/SCR/ADHOC-BMS)

3. Molecular regulation of spiral artery remodeling. DBT, 2019-23, 68.98 lakhs, (BT/PR30860/MED/97/407/2018).

Publications

1. Paul, M., Ain, R. (2024) Evaluation of Molecular Interactions and Cellular Dynamics at the Maternal-Fetal Interface during Placental Morphogenesis. *Methods in Molecular Biology*. 2728, 45-76.
2. Bose, R., Jana, S.S., Ain, R. (2023) Cellular Prion protein moonlights vascular smooth muscle cell fate: Surveilled by trophoblast cells. *Journal of Cellular Physiology.* 238(12):2794-2811.
3. Jena, S.K., Das, S., Chakraborty, S., Ain, R. (2023) Molecular determinants of epithelial mesenchymal transition in mouse placenta and trophoblast stem cell. *Scientific Reports*. 13(1):10978.

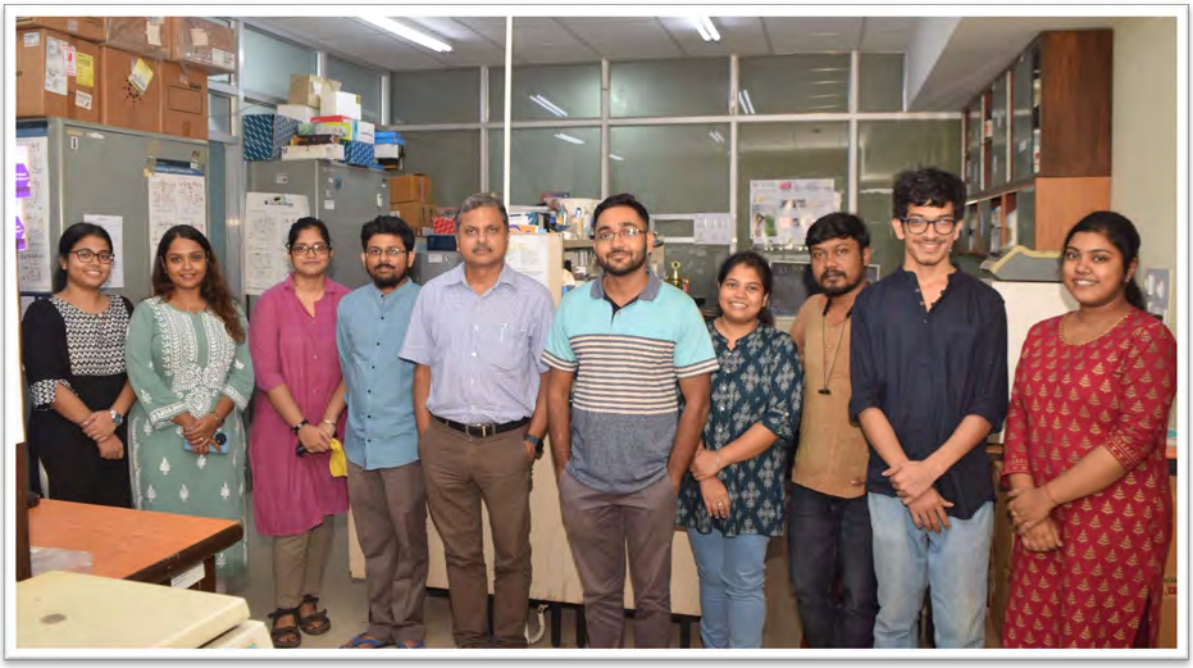
Invited Lectures

1. Genesis of trophendothelial cells and trophoblast-directed functions of vascular smooth muscle cells: Implications in placental biology. RGCB, Kerala. RGCB Conferenece, 20-23 September 2023.
2. Invasive trophoblast cells: Guardian of cell-cell communication in placental morphogenesis. ACTREC, Navi Mumbai. 46th Annual Meeting of Indian Society of Cell Biology, 10-12 January 2024.
3. Decoding cell-cell communication during spiral artery remodeling. CSIR-IICT, Hyderabad. 34th Annual meeting of Indian Society for the Study of Reproduction and Fertility. 23-25 February 2024.
4. MicroRNAs in trophoblast development and placental disorder. Visva-Bharati University, Santiniketan. National seminar on recent advances in Animal Science, 7-8 March 2024.

Awards

Prof. N.R. Moudgal Memorial Oration Award, Awarded by Indian Society for the Study of Reproduction and Fertility, Hyderabad, 2024.

Dr. Rupasri Ain, Chief Scientist
Group Members: Rumela Bose, CSIR-SRF; Shipra Jena, UGC-SRF; Tamal Gope, CSIR-SRF; Swarnali Dey, UGC-SRF; Madhubanti Ghosh, CSIR-SRF; Priyanka Das, UGC-SRF; Poulomi Sarkar, CSIR-JRF; Debankur Pal, CSIR-JRF; Sourav Ganguly, ICMR- Project Assistant; Shreya Deb, SERB- Research assistant; Baitali Guha, DBT-Research Assistant



Dr. Sib Shankar Roy and his group members

Comprehending the molecular mechanisms and pathophysiological aspects of cancer metabolism

Research Activities

The discovery of metabolic reprogramming in cancer cells dates back to the 1920s when the Warburg effect was first reported by Otto Warburg. However, only over the past few years, the rise of onco-metabolism has fundamentally reformed the field of oncology research. Both intrinsic and extrinsic factors may concurrently contribute to influence cellular bio-energetics. Oncogenic mutations have been reported to play a significant role in altering several signalling networks, eventually contributing to metabolic reprogramming. Transcription factors often act as a bridge between different external stimuli and cellular responses and thereby can influence oncogenic outcomes. Among these important oncogenic transcription factors is the proto-oncoprotein Ets1, hailing from the Ets family of Transcription Factors. By regulating several aspects of cancer, including angiogenesis, metastasis, resistance to chemotherapy, etc., Ets1 plays a distinctive role in oncogenesis. Several TME-derived factors including diverse kinds of growth factors, cytokines, and metabolites assist the developing tumour cells to gain numerous survival advantages leading towards cancer progression. This necessitates identifying the regulatory role displayed by these TME-derived factors in cancer progression by modulating the functional dynamics of transcription factors. Our current research thus aims to comprehend how Ets1 regulates glycolytic genes and the consequences that follow for the metabolic state of cancer cells in response to a key TME-derived signal such as the Epidermal Growth Factor. An additional dynamic and challenging component in the pathogenesis of cancer is the relevance of structural and functional alterations in mitochondria, the primary site of bioenergetic modulations within the cellular system. Hence, our research work also focuses towards identifying the role of ETS1 in regulating the mitochondrial dynamics in the context of cancer progression. Modulating the function of transcription factors like ETS1 through leveraging the knowledge of its interacting partners could be a promising therapeutic approach towards cancer remission. The transcriptional activity of ETS1 is reportedly suppressed by DAXX (Death Domain Associated Protein 6)/EAP (Ets1 Associated Protein) via protein-protein interactions. Therefore, a detailed study was conducted to unveil the intricacies of ETS1-DAXX interactions in mediating diverse aspects of carcinogenesis.

Accumulating pieces of evidence indicate that the alterations in lipid metabolism have immense

importance during the development of carcinogenic features. Lipogenesis as well as the Fatty Acid Oxidation are crucial components of de-regulated lipid metabolism. In this context, our research is directed towards unravelling the possible interactions of adipocytes and cancer cells as well as the detailed mechanism of SREBP1 and CPT1-mediated oncogenic advancement. One of the most effective strategies for managing cancer is metabolic targeting, and nutrient transporters as well as ion exchangers are frequently referred to be the "Achilles' heel of cancer." In this light, studying the solute carrier family of proteins that are involved in nutrient or metabolite transfer in cancer cells is of immense importance. Mitochondrial neutral amino acid transporters as well as monocarboxylate transporters are being extensively studied in the laboratory to develop novel pharmacological intervention strategies. Our aims and objectives are:

- To comprehend the implications of mitochondrial structure-function aberrations on metabolic fate of cancer cells and associated oncogenesis
- To explore the role and regulation of Ets1 oncogenic transcription factor in oncogenesis
- To explore the implications of cellular transporters on tumorigenesis and identification of potential therapeutic targets for therapeutic intervention
- To develop and synthesize novel PARP-inhibitors: innovations in chemical entities and generic formulations for treating breast and ovarian cancer

Deciphering the implications of mitochondrial structure-function aberrations on metabolic fate of cancer cells and associated oncogenesis:

ETS1, an oncogenic transcription factor, induces mitochondrial dysfunction in ovarian cancer by upregulating Drp1, leading to mitochondrial fragmentation. This fragmentation reduces the mitochondrial load and decreases the expression of ATP synthase, an essential component of mitochondrial OXPHOS, impairing cellular respiration. As a result, cancer cells shift their energy reliance on aerobic glycolysis, a process known as the Warburg effect. Our study shows that pharmacological or molecular inhibition of Drp1 can significantly curtail ETS1-associated epithelial-mesenchymal transition (EMT) and metastasis in ovarian cancer. In parallel, SREBP1, another key factor in cancer metabolism, promotes de novo lipogenesis, crucial for tumor growth. Often dysregulated, SREBP1 enhances ovarian cancer cell proliferation by modulating not just lipogenesis but also glycolysis, mitochondrial functions, and fatty acid metabolism. Inhibtion of SREBP1 disrupts its nuclear localization and signaling, effectively hampering cancer cell proliferation and migration, consequently highlighting its potential as a therapeutic target in cancer treatments. Furthermore, during tumor development, cancer cells are known to significantly overexpress CPT1A, a key enzyme in fatty acid oxidation (FAO) that supports adaptation to the tumor microenvironment derived cues like TGFβ1. Targeting CPT1A with siRNA and Etomoxir reduces migration, invasion, and impacts EMT genes, to ultimately cause suppression of TGFβ1-induced EMT, underscoring the therapeutic potential of disrupting this metabolic pathway in cancer management. These studies underscore the intricate link between metabolic pathways and cancer progression, with a particular emphasis on how mitochondrial functionality influences oncogenesis, presenting new avenues for targeted cancer therapy.

To understand the functionality and regulation of Ets1 oncoprotein in ovarian cancer progression:

Our investigations aimed at understanding the role of Epidermal Growth Factor (EGF) and its capacity to drive cancer cell aggressiveness in Epithelial ovarian cancer (EOC). ETS1 upregulation was observed in response to EGFR-ERK1/2 signaling pathway activation, consequently increasing the glycolytic rate, lactate production, and overall invasiveness of the cancer cells. Further, a comprehensive transcriptomics analysis and subsequent validation via qRT-PCR revealed the glycolytic reliance of EGF treated cells to be a consequence of direct trasncritional regulation of key glycolytic genes and transporters by ETS1. Additionally, the interaction between ETS1 and DAXX in ovarian cancer underscores the therapeutic potential of targeting protein-protein interactions. DAXX suppresses the transcriptional activity of ETS1, impacting EMT phenotypes. This interaction is confirmed through various experimental approaches, suggesting that modulating DAXX expression could alter ETS1 activity and affect cancer progression. It highlights a critical avenue for developing new cancer treatments.

Investigating the role of transporters in cancer development and potential therapeutic opportunities:

Dynamic metabolite and nutrient transport are crucial for cellular survival and cancer progression. Malignant cells exploit transporters like MCTs to

modulate their metabolic landscape and enhance aggressiveness. In this study, *in silico* analysis of ovarian cancer datasets revealed high levels of MCT4 and MCT1 mRNA. MCT4 has been subsequently found to be associated with poor prognosis and is linked to oncogenic functionalities such as adhesion and migration. Molecular and pharmacological targeting of MCT4 resulted in reduced EMT and invasion. Additionally, the cancer-specific transporter SLC1A5_var, distinct from its plasma membrane counterpart, facilitates glutamine uptake under hypoxia to enhance ATP production and chemoresistance, making it a promising target for personalized therapy. Our research focuses on defining its structure for the development of specific inhibitors to curb tumor growth.

Design and Synthesis of Novel PARP Inhibitors: New Chemical Entities and Generic Drug Processes for Breast and Ovarian Cancer Treatment:

In this multi-CSIR lab project we aim to develop less toxic and more affordable PARP inhibitors for breast and ovarian cancer, addressing a critical need in India's cancer research as part of the "Fit India movement." This initiative will facilitate the creation of patentable new molecules to treat TNBC and ovarian cancer. Following the outlined rationale, various assays were conducted to identify the most effective and efficient system. After standardizing the assay system, we began screening new chemical entities synthesized by the scientists of our chemistry division. We employed a thorough methodology to screen different compounds. Besides, we are currently involved in screening compounds developed by Prof. P. Jaisankar, which are derivatives of Olaparib modified to function as PROTACs. PROTACs, or Proteolysis Targeting Chimeras, represent an advanced technology in drug discovery that aims to develop novel therapeutics by targeting disease-associated proteins. These bifunctional molecules consist of one ligand that binds to a target protein and another that recruits an E3 ubiquitin ligase enzyme. This interaction forms a ternary complex that leads to the ubiquitination and subsequent proteasomal degradation of the target protein. PROTACs offer significant advantages over traditional inhibitors, such as higher potency, increased selectivity, and the ability to target proteins previously deemed "undruggable." Further, the PARPi-induved hematological toxicity issues were addressed in collaboration with our clinical collaborator. In a small cohort, it was found that intermittent dosing of Rucaparib, reduces hematological toxicity significantly, without affecting the efficacy. Studies on mechanism behind the toxicity and the possible solution are being studied.

Future Research Plans

Worldwide, cancer remains the second most prevalent cause of morbidity and mortality. Metabolic plasticity allows the cancer cells to adapt and survive even under hostile nutrient-deprived conditions. Several pioneering works in the field of onco-metabolism have emphasised on the implication of metabolic blockers as an alternative strategy to neutralize the limitations of standard chemotherapeutic regimes. Two-fold inhibition of Glycolysis as well as lactate transport using nominal concentrations of the respective blockers was found to revoke the invasiveness of the ovarian cancer cells. Likewise, alternative approaches to target the major factors in fatty acid metabolism were also discovered to be similarly efficient. In this line, combinatorial approaches could also be employed while keeping in mind the associated cytotoxicity. Generally, the synergistic effects of two compounds help in dosage reduction and check the cytotoxicity not compromising the effectiveness.

Extramural/ CSIR Funding

Headquarter coordinated project (HCP-40), entitled “PAN CSIR cancer research program making cancer care affordable empowering women’s health: focusing on breast and gynaecological cancers of Indian relevance”. Council of Scientific and Industrial Research (CSIR), 2021-2026. (8/26/HCP-40/2021-TMD-IND INT).

Publications

1. Ghosh, D., Pakhira, S., Ghosh, D.D., Roychoudhury, S. and Roy, S.S., 2023. Ets1 facilitates EMT/invasion through Drp1-mediated mitochondrial fragmentation in ovarian cancer. *Iscience*, *26*, 107537.
2. Chatterjee, P., Bhowmik, D. and Roy, S.S., 2023. A systemic analysis of monocarboxylate transporters in ovarian cancer and possible therapeutic interventions. *Channels*, *17*, 2273008.
3. De, K., Prasad, P., Sinha, S., Mukhopadhyay, S. and Roy, S.S., 2023. Synthesis, Characterization, and Biological Evaluation of Radiolabeled Glutamine Conjugated Polymeric Nanoparticles: A Simple Approach for Tumor Imaging. *ACS Applied Bio Materials*, *6*, 2172-2183.

Invited Lectures

1. Translational Cancer Research: Bridging the Gap between Bench and Bedside, held at SRMIST, Chennai, International Conference on New Horizons in Bioengineering: Fostering Academia-Industry Partnership ICB-24, February 14-15, 2024.
2. Metabolic adaptations in tumour cells, Department of Zoology, Visva Bharati, Santiniketan, National Seminar on "Recent Advances in Animal Science", March 07-08, 2024.
3. Metabolic and Bio-energetic Adaptations in Cancer Cells, BITS, Pilani, Goa, 92nd Annual Meeting, Society of Biological Chemists SBC(I), December 18-20, 2023.
4. Metabolic and Bioenergetic Adaptations in Gynaecological Cancer Cells, Adamas University, Kolkata, Bio-Next-2023, held at, during 4-6 October, 2023.
5. Oncogene-mediated mitochondrial alterations through imbalance of its fission-fusion dynamics, National Institute of Technology Rourkela (NIT-R), 3rd International Conference on Frontiers in Biological Sciences (InCoFIBS-2023), October 5-7, 2023.

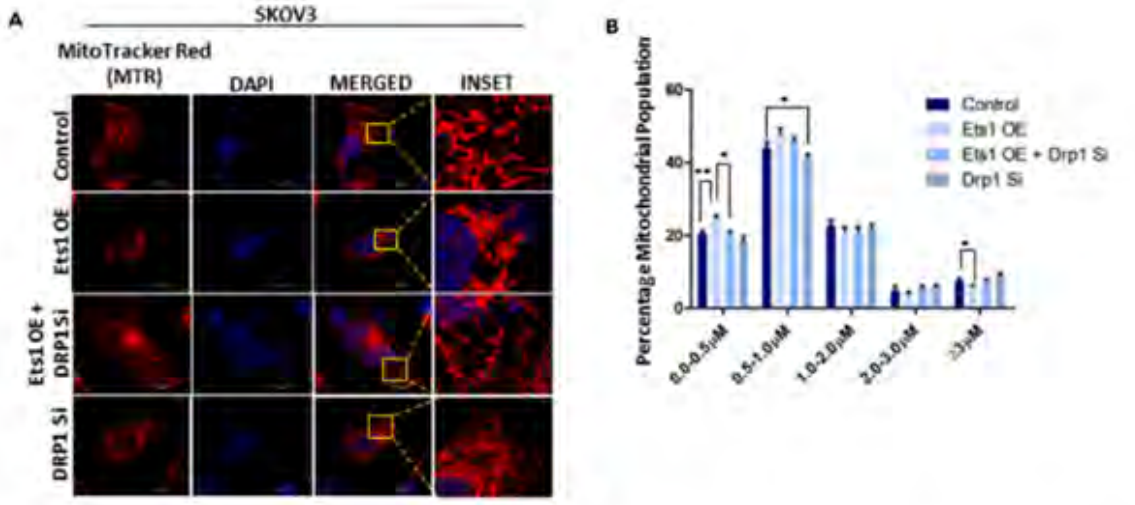


Figure 1: MTR-based confocal imaging for understanding mitochondrial fragmentation on Drp1 inhibition through siRNA-mediated silencing (A.) is done for SKOV3 cells (n=3). (B) Mitochondrial size estimation on Drp1 silencing in SKOV3 cells is done using LASX software and represented as histogram. (*p < 0.05, **p < 0.01, ***p < 0.001).

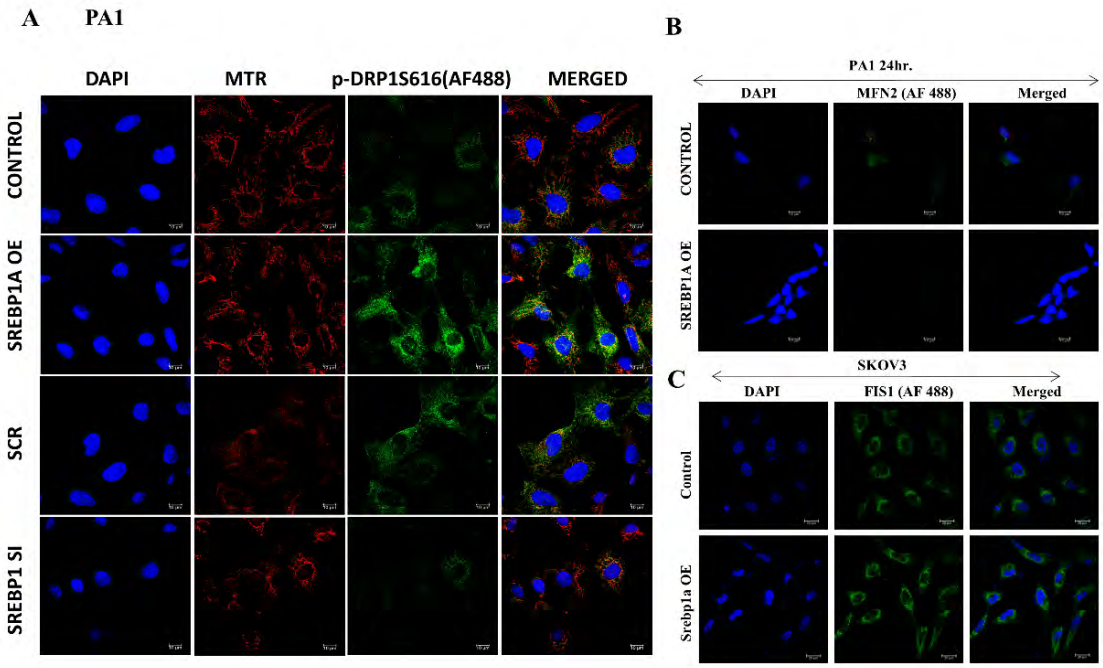


Fig. 2 Srebp1 promotes mitochondrial dysfunction; A)Confocal microscopic image of mitochondria stained with MitoTracker™ Red CMXRos in PA1 cells, B) Confocal image of MFN2 stained with Alexa Fluor 488 green upon Srebp1 over expression in PA1 cell, C) Confocal image of FIS1 stained with Alexa Flour 488 green upon Srebp1 over expression in SKOV3 cell.

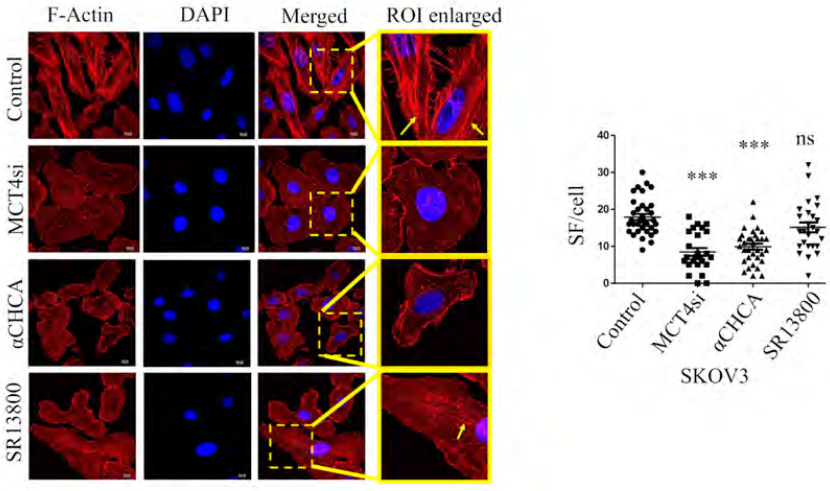


Figure 3: Reduction of high intensity stress fiber formation upon MCT4 inhibition in ovarian cancer cells. Microscopic images showing differences in high intensity Stress-Fiber (SF) formation upon MCT blocking in different groups like Control, MCT4si, α-CHCA and MCT1/2 blocker SR13800 in SKOV3 cells. Arrows indicate the stress fibers (Scale bar 10µm). *p<0.05, **p<0.01, ***p<0.001, ns= non-significant.

Dr. Sib Shankar Roy, Chief Scientist

Group Members: Priti Chatterjee, CSIR-SRF; Prasenjit Das, UGC-SRF; Deepshikha Ghosh, csir Project Associate II; Sk Eashayan Tanbir, CSIR-SRF; Suman Pakhira, CSIR-SRF; Bidisha Mukherjee, NTRFSRF; Debabrata Laik, UGC-JRF; Subhadeep Kundu, CSIR-JRF; Udit Dey, UGC-JRF; Pallabi Debnath, Project Associate

Collaborator(s): Dr. Satinath Mukhopadhyay, SSKM Hospital, Kolkata, India; Dr. Ashima Mukherjee, KolGOTrg, Kolkata, India; Dr. Saikat Chakraborty, PhD, CSIR-IICB, Kolkata, India; Dr. Deepak Kumar, PhD, CSIR-IICB, Kolkata, India; Dr. P Jaisankar, PhD, CSIR-IICB, Kolkata, India

Dr. Subhas C. Biswas and his group members

Alzheimer's disease: Targetting neuroinflammation for therapeutic solutions

Research Activities

Neurodegenerative diseases (NDs) are characterized by progressive dysfunction of synapses, neurons, glial cells, and their networks. NDs represent a growing healthcare concern worldwide because of the increasing elderly population. Unfortunately, the exact cause of these diseases is still unknown, and there are not always many treatment options available to combat them. The loss of synapses and neuronal cells underlie the pathophysiology of all NDs, including Alzheimer's disease (AD).

The multi-factorial aetiology of AD strongly suggests an integrated role of neurons and glia in pathobiology of the disease. Astrocytes, the most abundant of the glial cells, undergo cellular, biochemical, molecular, and functional changes during the pathogenesis of neurodegenerative diseases including AD termed as reactive astrogliosis. Reactive astrocytes are rich reservoirs of cytokines which may exert both beneficial and detrimental impacts on neuronal health. However, the role of individual astrocyte-secreted cytokines and their molecular mechanisms in relation to neuronal health is poorly understood, despite their increasing recognition as potential molecules for therapeutic targeting. We have identified that tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) as a neuroprotective cytokine in AD models. In an ongoing study, we are determining the underlying key molecular mechanisms of TIMP-1 on neuroprotection, synaptic plasticity, and cognitive recovery in AD.

Our study revealed the underlying key molecular mechanisms of TIMP-1, an astroglia-derived, Aβ-responsive anti-inflammatory cytokine have effects on neuroprotection, synaptic plasticity and cognitive recovery in AD. We are intrigued to find that endogenous TIMP-1 levels are strikingly diminished in the hippocampus of a transgenic model of AD, the 5xFAD mouse, compared to WT mice across age. Interestingly, intra-cerebroventricular injection of exogenous TIMP-1 in this mouse model not only improved their long-term hippocampus-dependent contextual memory (explicit memory), but also rescued fear memories (implicit memory). While TIMP-1 ensured neuronal viability by regulating two prominent, yet intertwined, cell-death pathways – apoptosis and autophagy by binding to its cognate receptor CD63, it also improved synaptic integrity and function – the direct cellular correlates of cognitive recovery. The latter effect may be attributed to an enhanced expression of BDNF and BDNF-associated signaling especially at synapses, following TIMP-1 injection to 5xFAD mice.

In 5xFAD mice, we detected higher endogenous TIMP-1 level at eary age as early as 7 day and lower endogenous TIMP-1 levels than in WT mice at adulthood, the earliest being at 2 months, coinciding with an inherent early Aβ accumulation in this model. Possibly, the early secretion of TIMP-1 in response to Aβ is an attempt by the astrocytes to protect and repair neuronal damage due to the insult but in case of a prolonged presence of Aβ, as in aging 5xFAD mice, TIMP-1-mediated neuroprotection is lost due to the downregulation of TIMP-1 by an unknown mechanism. Interestingly, a study has shown that transcriptomes of neurons derived from human induced pluripotent stem cells generated from skin fibroblasts of AD patients carrying a mutation in the *PSEN1* gene show downregulation of *Timp-1* gene, emphasizing TIMP-1's neuroprotective significance and alluding to a possible connection with AD-associated genes.

We show that TIMP-1 can activate Akt pathway. We demonstrate that CD63 is the specific receptor responsible for TIMP-1-driven Akt activation in Aβ-treated primary neurons. TIMP-1 via CD63 induces Akt signaling in many different cell types. CD63 is probably the most important binding partner for intracellular TIMP-1 signaling as opposed to other competitive interactors, especially when TIMP-1 is in excess and unbound like the exogenous addition in our study. While we do not completely disregard a possible effect of TIMP-1 injection on MMP activities in 5xFAD mice or a subsequent contribution towards the beneficial effects mediated by TIMP-1, we predict that the MMP-independent role of TIMP-1, as a signaling molecule, majorly contributes to the long-term effects of TIMP-1 in our model system *in vivo*. Since AD is a proteopathic disease where autophagy and apoptosis cooperate in mediating neurotoxicity and Akt is a common upstream regulatory kinase for both apoptosis and autophagy, TIMP-1 likely mediates neuroprotection by stimulating this common regulatory point (phosphorylating Akt) for the interconnected cell death pathways in our AD models. Nevertheless, regulation of both apoptosis and autophagy has direct implications in cognitive functioning which have not been explored here.

Progressive changes in synaptic structure and function often precede the actual neuronal loss and memory deficits in AD. We find that TIMP-1 not only ensures overall neuronal viability, but also protects synaptic structures. It improves pre- and post-synaptic protein levels as well as spine density and size in 5xFAD mice compared to untreated ones. The actin cytoskeleton plays a pivotal role in spine dynamics, both from structural and functional perspectives. Notably, loss of F-actin occurs selectively at synapses at very early ages in a mouse model of AD (APPswe/PS1ΔE9), well ahead of the onset of pathological hallmarks and memory deficits in this model. We show that the F/G actin ratio was significantly increased in hippocampal synapses with TIMP-1 treatment in 5xFAD mice as opposed to untreated 5xFAD animals. Our observations suggest that TIMP-1 has an important role in regulating synaptic dynamics. However, not all the synaptic markers are sensitive to TIMP-1 treatment in 5xFAD mice which is consistent with previous reports on differential responses of synaptic proteins in AD brain. Moreover, we did not explore whether the final synaptic recovery promoted by TIMP-1 directly prevented neuronal death or whether there are two independent mechanisms at play. Nevertheless, our work draws attention towards the beneficial roles of an astrocyte-secreted factor, TIMP-1 on synaptic structure and function in neurodegenerative diseases, beyond the body of evidence of several critical physiological effects of astrocyte-secreted proteins on synapses.

Reduced release of BDNF in brain and the circulation are key determinants of pathological conditions in brain including AD. We detected significantly diminished levels of BDNF and BDNF-mediated signaling at hippocampal synapses in 5xFAD mice. TIMP-1 not only strongly elevates BDNF levels in 5xFAD mice, but also enhances BDNF/TrkB-directed downstream Akt and ERK signaling pathways at these synapses. Our observations strengthen the ameliorative role of TIMP-1 specifically at synapses as demonstrated by its ability to induce the expression of a well-recognized synaptically crucial neurotrophin.

A key finding of our study is the ability of TIMP-1 to enhance Long Term Potentiation (LTP) in the 5xFAD mouse hippocampus. Previous studies have mostly shown cytokine-driven LTP suppression, constituting cytokine-driven neuroinflammation, as a contributing event in AD; here we demonstrate a cytokine-mediated beneficial upregulation of LTP in an AD model. Interestingly, TIMP-1 *albeit* via extracellular MMP-9 inhibition, is required for both LTP maintenance and late-phase LTP inhibition, the latter seen as a strategy to impede non-target late-phase LTP induction and to ensure consolidation of ongoing plasticity. We show that TIMP-1 contributes to early-phase LTP induction as a cell-signaling molecule triggering intracellular pathways. However, whether TIMP-1 has a local effect at synapses as a part of astrocyte-neuron communication is an open question.

In conclusion, TIMP-1 emerges as a multifunctional cytokine released by reactive astrocytes at early stages in AD which not only protects neurons against apoptosis and autophagic deregulation but has a direct implication on several regulators of synaptic plasticity. This explains the mechanistic basis of TIMP-1-mediated cognitive recovery in 5xFAD mice. Three major revelations are (1) the notable extent of BDNF induction observed upon exogenous TIMP-1 injection to 6-month-old 5xFAD mice that have greatly reduced levels of endogenous TIMP-1, (2) the prominent induction of TIMP-1-driven LTP in 5xFAD mice and (3) the action of TIMP-1 as a regulatory hub for multiple interconnected pathways impacting neuronal properties (Figure 1). These findings broadly indicate that a specific astrocyte-secreted cytokine can impact cell functions at different levels which may be seen as a biological strategy undertaken by astrocytes to ensure flexibility to adapt to changes in homeostasis in neurodegenerative diseases including AD.

Future Research Plans

1. To study the role of astrocyte origin anti-inflammatory cytokines as neuroprotective and nootropic molecules in models of AD.
2. Studying microgliosis, their secretory profiles and role in AD pathogenesis.
3. Targeting abberant autophagy to reverse neurodegeneration and amelioration of behaviour in AD mice.
4. Detection of disease specific signatures in AD models and clinical samples.

Publications

Sarkar, S., Gharami, K., Paidi, RK., Srikumar, BN., Biswas, SC. (2023) An astrocyte-derived cytokine TIMP-1 restores synaptic plasticity in an Alzheimer's disease model. *bioRxiv.*

Invited Lectures

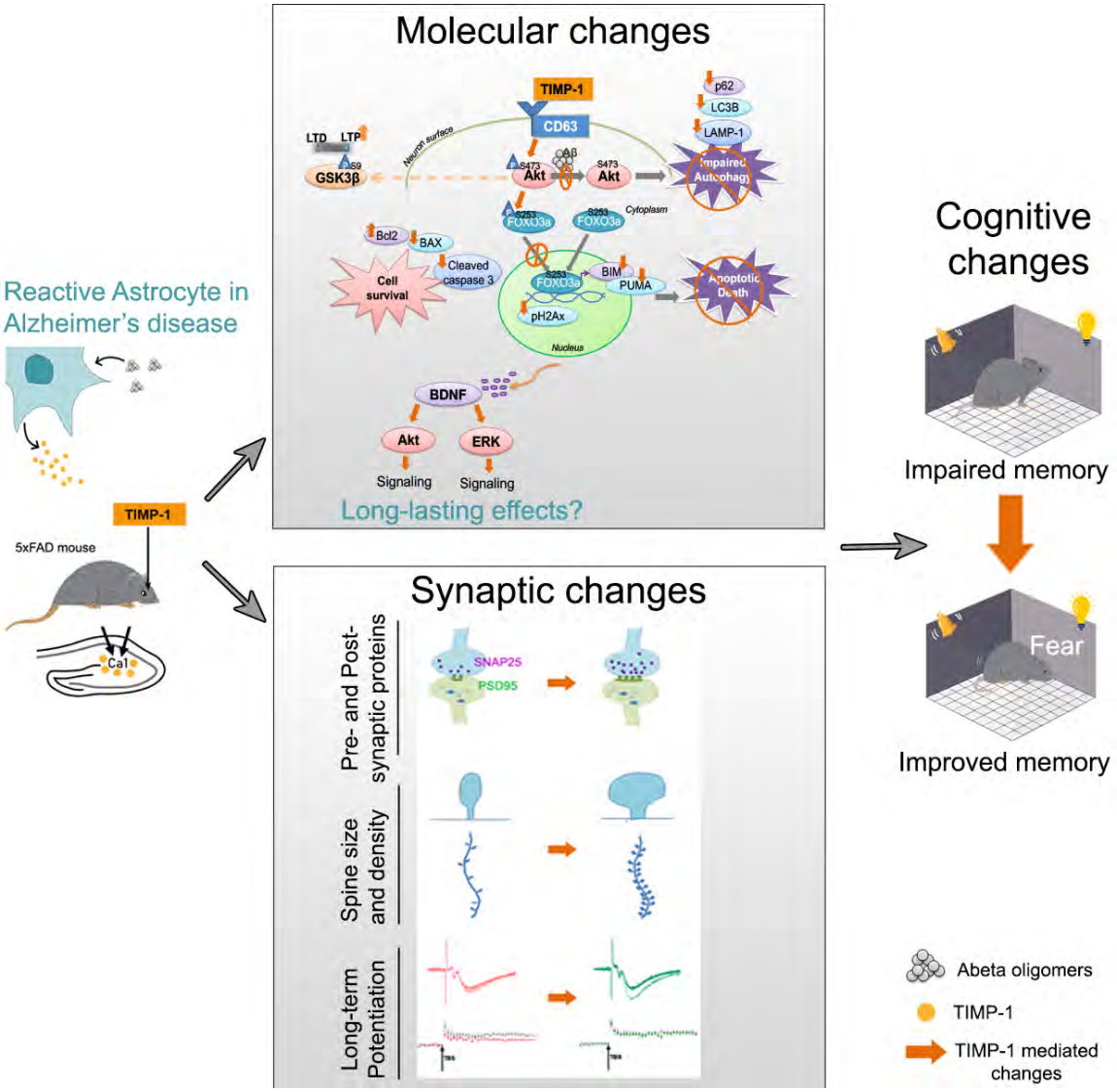
1. Neuroprotective potential of reactive astrocytes in Alzheimer's disease. Kalimpong. Bio-analytical Methods and Applications (BAW)-2024, Frontiers in Disease Biology Conference, 27th-30th March, 2024.
2. Alzheimer's disease: early response of astrocytes to amyloid-β. North Eastern Hill University, Shillong, Meghalaya, 37th Annual Meeting of Society of Neurochemistry, India (SNCI), 14th-16th September, 2023.
3. Mechanistic insights and therapeutic implication of astrocyte secreted cytokines in Alzheimer's disease. Jiwaji University, Gwalior, XLI Annual Meeting of the Indian Academy of Neurosciences and International Conference on Brain: Chemistry to Cognition. 4-6 October, 2023.

Conferences Attended

1. BAW-2024, Frontiers in Disease Biology Conference, Sinclairs Retreat, Kalimpong. 27th-30th March, 2024
2. 37th Annual Meeting of Society of Neurochemistry, India (SNCI), North Eastern Hill University, Shillong, Meghalaya. 14th-16th September, 2023
3. XLI Annual Meeting of the Indian Academy of Neurosciences and International Conference on BRAIN: CHEMISTRY TO COGNITION. Jiwaji University, Gwalior. 4-6 October, 2023.

Member of Society

1. Secretary, Executive Committee (EC), Neuroupdate Kolkata, Kolkata (2017 – 2025).
2. General Secretary, Executive Committee (EC), Indian Academy of Neurosciences, Lucknow (2023 – 2025).



Dr. Subhas C. Biswas, Chief Scientist

Group Members: RA: Kusumika Garami, RA, DST Women Scientist; Anoy Das, UGC-SRF; Sukanya Sarkar, DST INSPIRE-SRF; Soumita Goswami, UGC-SRF; Diptesh Roy, CSIR-SRF; Naqiya Ambareen, CSIR-SRF; Angshuman Murmu, UGC-JRF; Ananya Mondal, UGC-JRF; Nimai Gorai, UGC-JRF

Collaborators: Prof. P. K. Gangopadhyay, KPC MC&H, 1F, Raja S C Mullick Road, Kolkata, India; Dr. Atanu Biswas, Bangur Institute of neurosciences, 52/1A, SN Pandit Road, Kolkata, India; Dr. K. C. Ghosh,Calcutta National Medical College & Hospital, Kolkata, India; Dr. Joy Chakraborty, PhD, Cell Biology & Physiology, CSIR-IICB, Kokata, India; Dr. Nakul C. Maity, Structural Biology and Bioinformatics division, CSIR-IICB, Kokata, India; Dr. Asim Paul, Structural Biology and Bioinformatics division, Structural Biology and Bioinformatics division; Dr. Biswadip Banerjee, Organic and Medicinal Chemistry division, Structural Biology and Bioinformatics division

Dr. U. Mabalirajan and his group members

Deciphering the molecular mechanisms and therapeutic targets in emphysema, COPD, and pulmonary fibrosis: The roles of Smar-1, Rad50, RXRγ, and CAR-T cell strategies

Research Activities

Idiopathic pulmonary fibrosis (IPF) is a chronic lung disease with a very poor prognosis as it has a 2.5 to 5 years mean survival after proper diagnosis. Even nintedanib and pirfenidone cannot halt the progression, though they slow the progression of IPF. Hence, there is a need to understand the novel pathophysiology. Phospholipase A2 (PLA2) could be the ideal candidate to study in IPF, as they have a role in both inflammation and fibrosis. In the present study, we have shown the expression profile of various secretory Phospholipase A2 (PLA2) isoforms by analyzing publicly available transcriptome data of single cells from the lungs of healthy individuals and IPF patients. Among 11 members of sPLA2, PLA2G2A is found to be increased in the fibroblasts and mesothelial cells while PLA2G5 is found to be increased in the fibroblasts of IPF patients. We identified a subset of fibroblasts expressing high PLA2G2A with moderate expression of PLA2G5 and which are specific to IPF only; we named it as PLA2G2A+ IPF fibroblast. Pathway analysis revealed that these PLA2G2A+ IPF fibroblast have upregulation of both inflammatory and fibrosis-related pathways like the TGF-β signaling pathway, IL-17 signaling, the arachidonic acid metabolism pathway and ECM-receptor interaction. In addition to this, we found elevated levels of sPLA2-IIA in plasma samples of IPF patients in our cohort. PLA2G3, PLA2G10 and PLA2G12B are found in to be increased in certain epithelial cells of IPF patients. Thus, these findings indicate that these five isoforms have a disease-dominant role along with innate immune roles as these isoforms are found predominantly in structural cells of IPF patients. Further, we have targeted sPLA2 in mice model of bleomycin-induced lung fibrosis by pBPB, a known sPLA2 inhibitor. pBPB treatment attenuated lung fibrosis induced by bleomycin along with a reduction in TGF-β and deposition of extracellular matrix in lung. Thus, these findings indicate that these sPLA2 isoforms especially PLA2G2A may serve as a therapeutic target in lung fibrosis.

While a pro-asthmatic role of Th2 locus control region that is located in intronic regions of Rad50 is known, we had identified novel role of role of Rad50 protein in asthma pathogenesis. We found that RAD50 is predominantly expressed in bronchial epithelia and reduced in asthmatic conditions.

Mimicking this reduction in naïve mice using Rad50 siRNA leads to epithelial barrier disruption. This airway epithelial maintenance seems to be a moonlighting function of Rad50 as Rad50 deficiency mediated features were not associated with DNA damage.

In addition, we had found another novel role of Rad50 in COPD pathogenesis. On the one hand Rad50 was found to be reduced in lung of human COPD patients and on the other hand, Rad50 knockdown is linked with sterile airway injury with drastic neutrophilia without much neutrophil elastase activity and however when these knockdown mice are challenged with ovalbumin with allergic airway inflammation caused severe emphysema like changes in lung along with increased mortality. Microarray (Rad50 siRNA treated mice) findings indicated that most of the genes are upregulated are linked to neutrophil recruitment. Importantly, the top 50 genes, there were genes that are very much linked to early neutrotime or genes that are importantly present in secondary granules like Ngp, Ifitm6, Ly6g and Camp. These indicate that Rad50 knockdown condition is linked to depriming of neutrophils in the lung whereas these neutrophil seems to be primed to enter into the systemic circulation to spread inflammation to systemic levels to cause multiorgan like dysfuntion to cause deaths in these mice. We are further investigating this in depth as this is very much crucial to avoid fatal COPD condition.

Future Research Plans

1. We want to determine how RXRgamma is involved in hyperplasia of pulmonary neuroendocrine cells in lungs followed by its relation with alveolar repair in COPD condition.
2. We want to determine how SMAR-1 is involved in pathogenesis of idiopathic pulmonary fibrosis.
3. We want to prepare the formulation of Standardised Sonneratia apetala with Dr. Jaisankar and Dr,Arun bandyopadhyay
4. We want to prepare the water soluble form novel benzoxazinone derivative, PD-05, potent human neutrophil elastase inhibitor to test its activity in neutrophil elastase dominant lung diseses (*Dr. Jaisankar and Dr, Arun bandyopadhyay)*
5. Using the clues obtained from our lab, we will be heading towards identification of epithelial protective agents for incorporation in existing therapeutic regimens in asthma and COPD.

Extramural / CSIR Funding

1. Modern innovative solutions for Environmental/ Occupational Lung Health challenges using Clinical and Pre-clinical strategies (Mission Lung), CSIR, 2020-25, 169 lakh, (MLP-137).
2. The steroid sensitizing role of RXR-gamma, a nuclear receptor, in the pathogenesis of emphysema, DST-SERB, 2021-2024, 35 Lakhs (GAP432).
3. Development of Genetically Engineered 'Off-the-shelf' and Inducible CAR-T Cells for Cancer Therapeutics, DBT Multi-institutional, 2023-2026, 55 Lakhs, (GAP448).
4. Enhancing the Nutritional Quality and Bioavailability of Nutrients in Processed Products of Millet through Microbial and Physiochemical Interventions and their Popularization for the Socioeconomic Development of Tribes/Vulnerable Group, ICAR- Multi-institutional, 2022-2025, 20.5 Lakhs, (GAP451).

Publications

1. Sengupta, S., Abhinav, N., Singh, S., Dutta, J., Mabalirajan, U., Kaliyamurthy, K., Mukherjee, P. K., Jaisankar, P., & Bandyopadhyay, A. (2022). Standardised *Sonneratia apetala* Buch.-Ham. fruit extract inhibits human neutrophil elastase and attenuates elastase-induced lung injury in mice. *Frontiers in pharmacology*, 13, 1011216.
2. Sengupta, S., Reddy, J. R., Rajesh, N., Jaiswal, A., Mabalirajan, U., Palakodety, R. K., Mukherjee, P., & Bandyopadhyay, A. (2022). Novel benzoxazinone derivative as potent human neutrophil elastase inhibitor: Potential implications in lung injury. *European journal of pharmacology*, 931, 175187.
3. Jaiswal, A., Rehman, R., Dutta, J., Singh, S., Ray, A., Shridhar, M., Jaisankar, J., Bhatt, M., Khandelwal, D., Sahoo, B., Ram, A., & Mabalirajan, U. (2023). Cellular Distribution of Secreted Phospholipase A2 in Lungs of IPF Patients and Its Inhibition in Bleomycin-Induced Pulmonary Fibrosis in Mice. *Cells*, 12, 1044.
4. Mahesh, P. A., Moitra, S., Mabalirajan, U., Garg, M., Malamardi, S., Vedanthan, P. K., Christopher, D. J., Agrawal, A., & Krishna, M. T. (2023). Allergic diseases in India - Prevalence, risk factors and current challenges. *Clinical and experimental allergy: journal of the British Society for Allergy and Clinical Immunology*, 53, 276–294.

5. Singh, S., Dutta, J., Ray, A., Karmakar, A., & Mabalirajan, U. (2023). Airway Epithelium: A Neglected but Crucial Cell Type in Asthma Pathobiology. *Diagnostics (Basel, Switzerland)*, 13, 808.
6. Soumya Sinha Roy, S. S., Sagar, S., Faizan, M., Chaudhary, N., Singh, V., Singh, P., Gheware, A., Sharma, K., Azmi, I., Singh, V. P., Kharya, G., Mabalirajan, U., Agrawal, A., Ahmad, T. (2023) Obesity impairs cardiolipin-dependent mitophagy and therapeutic intercellular mitochondrial transfer ability of mesenchymal stem cells" Cell Death Dis, 14, 324.

Dr. U. Mabalirajan, Principal Scientist
Group Members: Ashish Jaiswal, UGC-SRF; Joytri Dutta, UGC-SRF; Sabita Singh, UGC-SRF; Archita Ray, CSIR-SRF; Atmaja Karmakar, CSIR-SRF
Collaborators: Dr. Arun Bandypadhyay, PhD, CSIR Indian Institute of Chemical Biology, Kolkata, India; Dr. P. Jaisankar, PhD, CSIR Indian Institute of Chemical Biology, Kolkata, India; Dr. Parthasarathi Bhattacharyya, Institute of Pulmocare & Research, Kolkata, India; Dr Anigra Dasgupta, BR Singh Hospital, Sealdah, Kolkata, India; Dr. Mahesh, MD, Chest Clinic, JSS medical College, JSS University, Mysore.

Infectious Diseases and Immunology Division

Faculties, fellows and technical staffs of Infectious Diseases and Immunology Division of CSIR-IICB are actively involved in various research endeavours encompassing basic and application-based sciences related to the prevention and control of various infectious diseases. These include protozoan diseases like leishmaniasis and malaria as well as viral diseases like coronavirus, dengue, chikungunya, hepatitis B virus, neurotrophic viruses like herpes and enteric viruses like rotavirus. Research is ongoing towards understanding the “dengue-COVID-19 conundrum”-how SARS-CoV-2 and dengue virus are co-evolving in the face of their own immunity and the mutual “cross-reactivity”, observed between these viruses. This division has established the platform for further in-depth research into virus association with kala-azar, an original discovery from CSIR-IICB. The other interest lies in wound healing pharmacophores (nucleoside analogues and drug loaded nanoparticles) which are currently gaining a lot of importance with the emergence and increasing abundance of muti-drug resistant pathogenic bacteria globally.

Dr. Chandrima Shaha

Host-pathogen interactions: protozoal evasion of host defense and implications in disease pathogenesis

Research Activities

The complex interaction between the host and the pathogen is important to constantly study and analyze the evolution of these processes to understand diseases. The evasion strategies used by protozoal parasites like the trypanosomatids involve the modulation of host components that make up the large arsenal of host defense mechanisms. This ever-evolving study area needs to be constantly worked upon and analyzed for a holistic understanding of neglected tropical diseases. An analysis of the host pathogen interaction of the *Leishmania* parasite has been carried out. With this as background, an analysis of possible drugs that can be proposed for leishmaniasis was also moderated. The idea was to figure out a target in the parasite that could be easily marked by drugs.

Presently, in the field of drug discovery, mitochondria are acknowledged as significant pharmacological targets due to their vital role in energy regulation, which renders cells fatally damaged. Any interference with energy homeostasis would be ideal targets based on which mitochondria-targeted drugs have been developed for a variety of human diseases. The Kinetoplastids, have only one large mitochondrion spreading throughout the cell body unlike mammalian cells, which have hundreds or thousands of mitochondria. The mitochondrial respiratory chain of parasites shows greater diversity in the electron transport complexes (ETC) than their hosts making them good targets for therapy. Existing drugs in use like the amphotericin B, miltefosine, pentamidine and antimonials interfere with membrane permeability resulting in the collapse of the mitochondrial membrane potential.

Literature on a few plant-based substances that can target the mitochondria was investigated as potential anti-leishmanials as some of them are already in use as anti-parasitic drugs. Two anti-malarial drugs artemisinin and chloroquine show strong anti-leishmanial activity both *in vitro* and *in vivo* in animals and can target the mitochondria. Quinolones, coumarins and quercetin are additional compounds that may be taken into consideration as anti-leishmanial medications since they are effective in

eliminating parasites in animal models of the disease and also interfere with mitochondrial functioning. Analysis of multiple studies give a clear indication that the primary site of artemisinin action in the parasite is the mitochondria and with its anti-leishmanial efficacy could be considered for therapy against leishmaniasis. Chloroquine was the drug of choice for malaria till new antimalarials like artemisinin, mefloquine and pyrimethamine were developed. Since then, chloroquine and its derivatives have been repurposed for HIV, systemic lupus erythematosus, rheumatoid arthritis, and several other diseases. An analysis of literature shows that chloroquine with its potential to disrupt the electron transport chain can be tested as an anti-leishmanial. Coumarins are a naturally occurring class of phenolic compounds of the benzopyrone family with a wide variety of structures with coumarin 7 as the privileged scaffold. Coumarins also affect the mitochondria but there is a need to identify the ETC complex component that coumarins affect as coumarins could be considered as potential anti-leishmanials. Quinoline alkaloids are secondary metabolites found in plants are also produced by some bacterial species. Quinoline alkaloids have a wide range of biological activities including activity against cancer, malaria, inflammation and viruses. This compound showed superior efficacy *in vivo* as well in infected BALB/c mice and hamsters and interfered with mitochondrial function indicating this as a potential compound that can be tested for therapeutic purposes. Hence, several of the compounds have been suggested for testing as anti-leishmanial agents and the advantage is that some of them are already in use in humans and can be repurposed.

Future Research Plans

Attempts to make vaccine formulations for leishmaniasis have been a major challenge due to the host's very complex immune response. An additional challenge is the delivery of drugs to the disease-causing form of the parasites lodged inside host macrophages and this is an area of intensive research. In the backdrop of such problems with increasing incidences of leishmaniasis, the major goal continues to be the development of new drugs or repurposing of existing medications developed for other diseases. The following topics will be analyzed,

1. Possible new drugs from plant sources
2. Promising molecules as anti-leishmanials from synthetic compounds.
3. An analysis of immunological changes post-infection and correlation to drug response.
4. Analysis of the major challenges for vaccination against Kala-azar

Extramural/CSIR funding

National Academy of Sciences funding for JC Bose Distinguished Chair Professorship.

Invited Lectures

1. Why the history of science is important. On the occasion of remembering Prof. Shyamadas Mikherjee, Jadavpore University, Aug 2, 2023.
2. Our cells to our rescue: the revolution in cell sciences. 6th G.N. Ramachandran Lecture. S.N. Bose National Centre for Basic Sciences. Kolkata. Sept 1, 2023.
3. Avoiding death by the invader and the host: the challenge and its relevance to diseases. Lecture Series on Frontiers in Science and Engineering. National Academy of Sciences India - Delhi Chapter, Science Foundation, Deen Dayal Upadhyaya College, November 2, 2023
4. Journey of a scientist, Indian Association for the Cultivation of Science, January 3, 2024.
5. A journey, on the international Day of Women and Girls at IICB, 16th February, 2024.

Conferences Attended

1. Frontiers in Science and Engineering. National Academy of Sciences India - Delhi Chapter, Science Foundation, Deen Dayal Upadhyaya College, November 2-4, 2023.
2. 11th Academic Advisory Council and the 12th Leadership Conclave meetings at IIT Gandhinagar, January 8 and 9, 2024.
3. Women in STEM meeting for the launch of SWATI at INSA, February 11, 2024.

Member of Committees

1. Chair, SEC of Rashtriya Vigyan Puraskar
2. Chair, Om Prakash Bhasin Award for Biotechnology
3. Member, Promotion Assessment Committee, Indian Institute of Science, Bangalore.
4. Member, Member, Science and Engineering Research Board, DST- Empowered Committee
5. Member, Governing Council, Indian Association of Cultivation of Science, Kolkata
6. Member, Governing Council, National Institute of Plant Genome Research. NDelhi
7. Member, Jury, Sun Pharma Awards
8. Member, Director Selections, Bose Institute, Kolkata.

9. Member, Alumni Award Selection Committee, IIT Gandhinagar.
10. Member, Advisory Committee of Lakshmipat Singhania-IIM Lucknow National Leadership Awards 2023.
11. Member, Council, West Bengal Academy of Science and Technology.
12. Member, Academic Advisory Council, IIT Gandhinagar.
13. Member, Leadership Conclave, IIT Gandhinagar
14. Member, Academic Advisory Committee, IIT Gandhinagar.
15. Member, International Conference on Metabolic Disorder. August 19, 2023.
16. Member, Launch of "SWATI" the national portal for Women in STEMM, February 11, 2024

Awards

1. Award of 6th G.N. Ramachandran Lecture. S.N. Bose National Centre for Basic Sciences, September, 2023.
2. Republic TV recognition on the occasion of India Women's summit, New Delhi, February 8, 2024.

Dr. Nahid Ali and her group members

Multifaceted role and management of leishmaniasis and cancer

Research Activities

In recent years, great advances have been made in bioinformatics and biotechnology approaches to validate protein kinases (PKs) as potential drug targets and diagnostic markers. The leishmanial kinome consists of 175–195 PKs, depending on the species, and represents roughly 2% of the encoded proteins. PKs in *Leishmania* regulate essential functions of the cell, including cell cycle progression, differentiation, and virulence, and thus their inhibition is anticipated to be disease-modifying. The PKs, which include the Aurora Kinase (LdAIRK) and *Leishmania*-activated C-kinase antigen (LACK), are highly conserved among the species and stages of the *Leishmania* parasite. LdAIRK and LACK, with molecular weights of 36 and 34 kDa, respectively, belong to the mitotic serine/threonine kinase family and are known to be mediators of the cell division cycle and differentiation in *Leishmania* parasites. Their sero-diagnostic potential was accessed through enzyme-linked immunosorbent assay (ELISA) and a dipstick format using Indian and Brazilian visceral leishmaniasis (VL) patients' sera and Indian VL urine and post-kala-azar dermal leishmaniasis (PKDL) samples. LACK antigen demonstrated 100% sensitivity with Indian and Brazilian VL sera and specificity of 97.87% and 95% with sera from both endemic countries, respectively. Additionally, LACK, showed 100% sensitivity and specificity with urine samples of patients and endemic and nonendemic healthy controls and other diseases, respectively. Further, with LdAIRK, a sensitivity of 98.73% and 97.5% and a specificity of 100% and 84.21% with the serum IgG antibodies of VL patients in India and Brazil, was observed respectively. Additionally, LdAIRK demonstrated 100% sensitivity and 95.83% specificity for the non-invasive diagnosis of VL using urine samples from Indian patients. Notably, a sensitivity of 93.75% towards sera and 81.82% towards urine from patients with Indian PKDL as compared to healthy controls was also observed. The reactivity of LdAIRK and LACK with follow-up patients' samples showed point-of-cure (POC) potential with declining positivity post six months' treatment. Finally, a prototype of lateral flow test (LFT) format with LdAIRK antigen showed good affinity with human VL samples.

We explored the effects of 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)-based liposomes with different charges (neutral, anionic, and cationic) on mouse bone-marrow-derived dendritic cells (DCs), which play a crucial role in connecting innate and adaptive immunity. Our investigation focused on how these liposomes influenced DC uptake,

immunostimulation, and intracellular processing. We found that the liposomes could induce phenotypic maturation of DCs by increasing the expression of costimulatory molecules (CD40 and CD86) and stimulating the production of cytokines like tumor necrosis factor-α, interleukin-12, and nitric oxide. Notably, combining monophosphoryl lipid A (MPLA) with cationic liposomes further enhanced the expression of costimulatory molecules and cytokine production, with a preference for positively charged liposomes in activating DCs. Using pH-sensitive dye analysis and pathway inhibition assays, we discovered that cationic liposomes were taken up more efficiently by DCs via endocytosis and transported to neutral compartments for processing, whereas anionic and neutral liposomes tended to accumulate in acidic compartments. These findings underscore the potential of cationic DSPC liposomes as superior vehicles for vaccine delivery, especially for preferentially activating DCs, compared to neutral and negatively charged liposomes.

Subunit recombinant vaccines are highly valued for their safety in vaccination. Recognizing the crucial role of T-cell immunity in combating visceral leishmaniasis (VL), our team is developing a new vaccine formulation containing three potent antigens—gp63, EF1-α, and CPC—enhanced with T-cell epitopes. To overcome limitations of protein-based vaccines, we are utilizing cationic liposomal delivery systems, specifically MPLA-bearing liposomes. Our current research involves comparing a chimeric epitope-enriched fusion antigen with a combination of recombinant antigens, both encapsulated in MPLA-bearing cationic liposomes. Our goal is to evaluate their ability to provide complete protection against virulent *Leishmania donovani* infection in BALB/c mice and hamsters. We are particularly interested in examining the generation of CD4+ and CD8+ T cells, cytokine production, and the longevity of protective immunity following disease resolution.

The *Leishmania* homologue of activated C kinase (LACK) is a 34 kDa protein conserved across different *Leishmania* species and life stages, and it plays essential roles in cellular processes critical for leishmanial infection. The specific expansion of LACK-reactive T cells suggests its potential as a vaccine target. To assess the vaccine effectiveness of LACK against *L. donovani,* a native 34-kDa LACK protein was purified from *L. donovani* promastigotes and identified as the LACK antigen. Its efficacy was then compared with that of a protective antigen, gp63, when both were encapsulated in identical cationic DSPC liposomes. Further investigation into the vaccine potential of *L. donovani* LACK in its recombinant form is underway. This involves cloning, purifying, and expressing the antigen, followed by studying its immunogenicity and vaccine efficacy in a mouse model of visceral leishmaniasis (VL).

Under the Global Challenges Research Fund (GCRF)-supported project titled "Repurposing of clinical drugs for anti-leishmaniasis therapy," we investigated the potential of repurposed clinical drugs for treating leishmaniasis. Specifically, we explored the effects of clofazimine, loratadine, and cyproheptadine—medications already approved for treating leprosy and allergies—on inhibiting the TcAAAP069 permease and demonstrating trypanocidal activity against all stages of *Trypanosoma cruzi*. Given that the *T. cruzi* proline transporter shares an orthologous gene with *Leishmania*, we evaluated the impact of each drug encapsulated in PC-SA liposome on *L. donovani* promastigotes and amastigotes in vitro.

In a collaborative project between India and the UK funded by GCRF-EPSRC, titled "Patient-centric supramolecular formulations of new anti-leishmanial drugs for Indian Communities," we investigated the in-vitro efficacy of 20 newly synthesized chemical compounds on *Leishmania* promastigotes. Among these compounds, five were identified for further evaluation. These selected compounds, along with their liposomal formulations, were tested on intracellular amastigotes. Following these in-vitro studies, two promising drugs were advanced to assess their efficacy in vivo using BALB/c mice.

Our lab has been researching cationic liposomes for three decades, particularly focusing on their role in drug delivery and their unique ability to modulate the immune response. Recently, we've made significant progress in utilizing liposomes to address immune suppression in cancer. Our cationic liposomes, especially PC-SA, have shown promise in delivering drugs to target sites while also possessing immune-modulating capabilities. In studies with B16F10 melanoma, we found that PC-SA liposomes alone or in combination with doxorubicin effectively reduced immunosuppressive cytokines like IL-10 and TGF-β. This was achieved by controlling the expression of Stat-3, a key driver of immune suppression. Moreover, we discovered that PS asymmetry, a characteristic of cancer cells, plays a crucial role in immune evasion by cancer cells. By targeting PS and PD-L1 simultaneously with a modified cationic immunoliposome, we achieved significant tumor inhibition without the toxicity associated with traditional therapies. This formulation also allowed

for the incorporation of low doses of doxorubicin, leading to complete tumor clearance in mice. Additionally, we addressed the challenge of mutant p53, a barrier to cancer therapy, by developing a novel peptide entrapped in cationic liposomes targeting PS. This approach prevented mutant p53 from acquiring drug resistance and showed promise in overcoming bioavailability issues associated with the free peptide. In summary, our research demonstrates the potential of cationic liposomes as versatile platforms for targeted drug delivery and immune modulation in cancer therapy, offering hope for more effective and less toxic treatment options in the future.

Publications

1. Das S, Mukherjee S, Ali, N. 2023. Purification of immune-active macrophage super enhancers by chemical cross-linked chromatin immune precipitation. *STAR Protocol*. 2023 Jan 11;4(1):102004. doi: 10.1016/j.xpro.2022.102004.
2. Kamran M, Bhattacharjee R, Das S, Mukherjee S, Ali, N. 2023. The paradigm of intracellular parasite survival and drug resistance in leishmanial parasite through genome plasticity and epigenetics: Current insights and future perspective. *Frontiers in Cellular and Infection Microbiology-Parasite and Host*.13:1001973.
3. De M, Sukla S, Bharatiya S, Keshri S, Roy DG, Roy S, Dutta D, Saha S, Ejazi SA, Ravichandiran V, Ali, N, Chatterjee M, Chinnaswamy S. 2024. IFN-λ3 is induced by *Leishmania donovani* and can inhibit parasite growth in cell line models but not in the mouse model, while it shows a significant association with leishmaniasis in humans. *Infection and Immunity*. 2024 Feb 13;92(2):e0050423. doi: 10.1128/iai.00504-23.
4. Maji, M., Ghosh, S., Didwania, N., and Ali, N. 2024. Liposomes differentially charged stimulate dendritic cells with varying effects on uptake and processing when used alone or in combination with an adjuvant. *ACS Omega.*2024(Accepted and in press).

Book Chapters

Das, A., Ali, N. Emerging Concepts in *Leishmania* Vaccine Adjuvants in Challenges and Solutions in Visceral Leishmaniasis by A. Selvapandiyan, R. Singh, N. Puri, N. K. Ganguly, Springer Nature Singapore Pvt Ltd.ISBN 978-981-99-6999-9.

Patents

Ali, N, Didwania N, Ejazi SA, Sabur A, Kamran, M, “Liposomal formulation for the treatment of Visceral Leishmaniasis Inventors”. Application Number: 202311028946 Filing Date: 20/04/2023

Dr. Nahid Ali, J. C. Bose fellow, INSA Emeritus scientist

Group Members: Ms. Nicky Didwania, Senior Project Associate (JCB); Ms. Sneha Ghosh, Senior Research Fellow (ICMR); Mr. Anirban Bhattacharyya, Senior Research Fellow (ICMR); Mr. Soumik Kayal, Scientific Administrative Assistant (JCB)

Dr. Pijush K. Das

Addressing key components of macrophage defense signaling targeted by Leishmania parasites for successful survival towards developing robust anti-leishmanial with drug delivery systems

Research Activities

The work is centered on studying macrophage biology using visceral leishmaniasis as a model macrophage disease. The key question we try to address is how macrophage signaling pathways that produce robust defense molecules are hijacked by Leishmania parasites and therefore have tremendous potential for developing therapeutic targets, in general, for macrophage-associated diseases. We showed that the Leishmania parasite exploits some negative regulators of macrophage defense including inhibition of activation of the inflammasome, induction of NF-κB by upregulating A20 and UCP2 (J Immunol 2011, 2012, 2014; FASEB J 2014, 2017; Eur J Immunol 2011a, 2015; J Biol Chem 2014; Cell Death Differ 2016) and upregulation of PD-1 involving FOXO-1 and SIRT1 (Clin Transln Immunol 2017: J Cell Sci 2019; Int J Biochem Cell Biol 2014). Inhibitors of these negative regulators therefore have huge potential for developing anti-leishmanials and for that matter any anti-macrophage-residing microbes (Eur J Immunol 2011b; Int J Biochem Cell Biol 2017; Antimicrob Agents Chemother 2015; J Antimicrobial Chemother 2021). Now we have unraveled the complete cascade of signaling events how the PD-1 pathway fine-tunes the pro-inflammatory responses in macrophages and showed that PD-1 negatively regulates macrophage immune activation by turning off JNK and STAT1 signaling and Leishmania exploits this (Cell Immunol 2023). Regarding inflammasome activation, we also published Protocols for inflammasome study for the benefit of relevant researchers (Springer Publications 2024). Furthermore, we considered recent progress in translating these research areas into therapeutic strategies aimed at combating macrophage-associated diseases. Invasion of macrophages by a variety of intracellular pathogens induces early

oxidative burst to eliminate the infection and heme oxygenase-1 (HO-1) plays a very critical role. The immunomodulatory effects of HO-1 can drive both beneficial and detrimental consequences in host immunity against infectious agents by limiting infection-induced inflammation and tissue pathology. We published a review that aims to address the role and regulation of HO-1 and the signaling pathways modulated by it toward gaining a comprehensive knowledge of this critical regulator of macrophage defense (Nova Science Publishers 2023). The intricate interplay between parasitic infections and the apoptotic pathway underscores the vital role of apoptosis in host-parasite interactions, serving as both a defense mechanism for the host and a survival strategy for parasites. Understanding the molecular mechanisms of apoptosis and its modulation by parasites opens avenues for therapeutic interventions, including targeted antiparasitic drugs and tailored strategies. We also published a comprehensive review to summarize the role of apoptosis in parasite infections (Springer Nature publications, in press).

Future Research Plans

A comprehensive review of the literature of my career-long extensive work on how macrophage signaling pathways that produce robust defense molecules are hijacked by macrophage-associated pathogens like Leishmania, which might lead to developing potential therapeutic leads.

Publications

1. Roy, S., Gupta, A.K., Banerjee, M., Das, P.K. and Ukil, A. (2023) PD-1 negatively regulates macrophage immune activation by turning off JNK and STAT1 signaling: Exploited by Leishmania for its intra-macrophage survival. *Cellular Immunol.* 391-392,104758.
2. Saha, S., Das, P.K. and Ukil, A. (2023) Heme Oxygenase 1: A potential drug target with multiple functions, Chapter 7, Advances in Health and Medicine, pages 149-164, Lowell T. Duncan (Ed), Nova Science Publishers, New York, USA.
3. Biswas, A., Bhattacharjee, A. and Das, P.K. (2024) Modulation and determination of the status of inflammasomes in Leishmania-infected macrophages in Immune Homeostasis pp 137–146, Part of the book series: Methods in Molecular Biology ((MIMB, volume 2782) Springer publications.
4. Das, T., Roy, S., Das, P.K. and Ukil, A. (2024) Role of Apoptosis in Parasitic infections: Therapeutic targets and strategies in Apoptosis and Human Health: Understanding Mechanistic and Therapeutic Potential (Book Series) Springer Nature publications, USA. (In press).

Member of Committees

1. Member of Sectional Committee VI (General Biology) of INSA for 2021-2024
2. Member of Life Sciences discipline of CSIR-NET
3. Member of the CSIR SRF/RA committee in Biochemistry, Biophysics, Microbiology and Immunology (Life Science/12)
4. Member of the Award Selection Committee of SBC

Dr. Rupak Bhadra and his group member

Stringent response regulator DksA, c-di-GMP signaling and virulence regulation in the cholera pathogen *Vibrio cholerae*

Research Activites

The stringent response in bacteria is a complex regulatory mechanism which involves numerous genes and regulators. We have already shown that nutritional deficiency mediated stringent response gene regulatory circuit in the cholera pathogen *Vibrio cholerae* involves multiple genes like *relA*, *spoT*, *relV*, *gppA* and *dksA.* Interestingly, deletion of the *dksA* gene, which encodes the stringent response regulatory protein DksA in *V. cholerae*, leads to decrease in motility, haemagglutinin protease (HAP) and cholera toxin production, which are important virulence factors of *V. cholerae*. In fact, studies from other laboratories also indicate that DksA indeed plays crucial roles in regulating major regulators of *V. cholerae*, which most likely converge in maintaining the intracellular concentration of the quorum sensing master regulator HapR. We did extensive complementation analysis of Δ*dksA* mutants, which supports that DksA opposes biofilm formation and tries to keep intracellular signalling molecule 3', 5' cyclic diguanylic acid (c-di-GMP) levels low and this may be due to positive regulation of the quorum sensing master regulator HapR by the DksA protein. Based on this analysis we hypothesized that the phenotypes exhibited by the Δ*dksA* mutant are due to increase in levels of intracellular small signalling molecule c-di-GMP. Furthermore, it has recently been reported that c-di-GMP controls motility of *V. cholerae* via the positive regulatory protein TfoY (encoded by *tfoY* gene) through LonA protease (encoded by the *lonA* gene). In fact, LonA degrades the motility promoting protein TfoY. Thus, it appears that the LonA protease serves as a negative regulator of motility in *V. cholerae*. Our experimental data indicate that the *V. cholerae* Δ*dksA*Δ*lonA* double mutant strain CΔdksAΔlonA is hypermotile compared to the control strains C6709 (wild-type), CΔdksA (Δ*dksA*), and CΔlonA (Δ*lonA*). Thus, it may be argued that in *V. cholerae* Δ*dksA* cells there is a rise in intracellular c-di-GMP level, which leads to rapid degradation of the TfoY through LonA protease leading to hypomotility of Δ*dksA* cells. However, further genetic evidences are needed to confirm this observation. Based on this experimental data it has been concluded that deletion of the *lonA* gene in *V. cholerae* under Δ*dksA* genetic background probably leads to significant accumulation of TfoY protein in the double mutant CΔdksAΔlonA, which ultimately rescued Δ*dksA* cells from hypomotility to hypermotility phenotype. Another evidence that the DksA regulator controls intracellular c-di-GMP level obtained by overexpression of the *vieA* gene, which encodes c-di-GMP degrading phosphodiesterase (PDE)

enzyme of *V. cholerae* cloned under the arabinose inducible promoter P_{BAD} of the expression vector pBAD24 in Δ*dksA* mutant leading to rectification of its motility defect. We have also constructed three recombinant plasmids carrying mutant alleles of the *vieA* gene (deleted part of the C-terminal coding region), called pPD1.6, pPD1.2 and pPD768. When each of these clones was introduced in the *V. cholerae* Δ*dksA* (CΔdksA strain) mutant cells and each of these mutant strains examined separately for motility, it was found that the function of VieA (PDE) has probably been attenuated due to partial deletion from its C-terminal end. These results further support that the DksA regulator of *V. cholerae* most likely regulates the intracellular level of c-di-GMP level through regulation of PDE, which needs further confirmation. Lastly, we attempted to determine the intracellular c-di-GMP concentration by ^{32}P labelling followed by detection by two-dimensional thin layer chromatography. It has been observed that there is indeed an increase in intracellular c-di-GMP in *V. cholerae* Δ*dksA* mutant cells compared to the wild-type strain C6709. Further work is needed to confirm the results obtained in this direction.

Future Research Plans

Since the quorum sensing master regulator HapR is down regulated in Δ*dksA* strain and HapR is a strong negative regulator of biofilm formation in *V. cholerae*, therefore, it will be of interest to determine the ability of biofilm formation by Δ*dksA* cells. The principal regulators of *V. cholerae* biofilm formation are VpsT and VpsR and to know further about the status of expression of these genes in different *V. cholerae* strains, qRT-PCR will be applied to check the expression status of these genes in mutant cells, which may help to understand about the role of HapR. Further, *lonA* deleted cells showed low HAP production; here the role of VpsT and c-di-GMP will also be assessed. Further experiments with the constructed clones pPD1.6, pPD1.2, pPD768 expressing truncated PDE mutant proteins in different *V. cholerae* mutants, namely, Δ*dksA*Δ*lonA*, Δ*lonA* along with control strains will be examined for variation in HAP production, biofilm formation, virulence factor production etc. to assess further about the role of DksA in the regulation of virulence genes in *V. cholerae*.

Extramural / CSIR Funding

CSIR Emeritus Scheme (No. 21(1100)/20/EMR-II, CSIR, New Delhi.

Publications

1. Mehrotra, T., Konar, D., Pragasam, AK., Kumar, S., Jana, P., Babele, P., Paul, D., Purohit, A., Tanwar, S., Bakshi, S., Das, S., Verma, J., Talukdar, D., Narendrakumar, L., Kothidar, A., Karmakar, SP., Chaudhuri, S., Pal, S., Jain, K., Srikanth, CV., Sankar, MJ., Atmakuri, K., Agarwal, R., Gaind, R., Ballal, M., Kammili, N., Bhadra, RK., Ramamurthy, T., Nair, GB., Das, B. (2023) Antimicrobial resistance heterogeneity among multidrug-resistant Gram-negative pathogens: Phenotypic, genotypic, and proteomic analysis. *Proc Natl Acad Sci USA.* 120, e2305465120.
2. Saha, M., Pragasam, AK., Kumari, S., Verma, J., Das, B., Bhadra, RK. (2024) Genomic and functional insights into antibiotic resistance genes *floR* and *strA* linked with the SXT element of *Vibrio cholerae* non-O1/non-O139. *Microbiology (Reading)*. 170, 001424

Conferences Attended

1. Attended and Chaired a Session in the Indo-US International Conference and Workshop on Antimicrobial Resistance and Human Microbiome Under the aegis of Indo-US Vaccine Action Programme (VAP) Organized by Translational Health Sciences and Technology Institute (THSTI) and National Institute of Allergy and Infectious Diseases (NIAID) held during 15-18 November 2023 at THSTI Faridabad, India.
2. Attended CSIR-IICB Annual Research Conclave-2024 held on 25 January 2024 at Dr. JC Ray Auditorium, CSIR-IICB, Jadavpur Campus, Kolkata, India.
3. Attended and Chaired a Session in the 21th All India Congress of Genetics and Genomics and International Conference on Environmental Toxicogenomics: Ecosystem Health and Sustainability – Challenges and way Forward held during 05-07 February 2024 at Dr. Triguna Sen Auditorium, Jadavpur University, Kolkata, India.

Dr. Rupak K. Bhadra, ICMR Emeritus Scientist
Group Members: Dr. Priyanka Dhar, Research Associate
Collaborators: Dr. Bhabatosh Das, Associate Professor, Translational Health Science and Technology Institute (DBT), Faridabad, India.

Dr. Syamal Roy

Phytochemicals for mitigating the COVID-19 crisis: evidence from pre-clinical and clinical studies

Research Activites

Severe cases of COVID-19 often result in critical respiratory failure and multiorgan complications, correlating with elevated levels of inflammatory markers and cytokines in the bloodstream. Current therapeutic options primarily involve corticosteroids, antivirals like remdesivir, and monoclonal antibody-based immunomodulation such as tocilizumab. Yet, they pose limitations due to side effects and high costs, particularly for patients with comorbidities. Given the drawbacks of existing treatments, research has turned to phytochemicals, which have demonstrated anti-inflammatory, antiviral, and antioxidant properties in previous studies. This review article has catalogued 28 phytochemicals from various chemical groups that exhibit anti-COVID-19 activity through mechanisms such as inhibiting virus entry and replication and modulating intracellular signalling pathways to mitigate cytokine storms. These findings suggest a promising avenue for utilizing plant-derived compounds to address COVID-19 complications and highlight the need for further research to optimize formulations for better absorption and bioavailability.

Future Research Plans

E-protein of SARS-CoV2 as drug target

The E protein assumes a key role in the life cycle of the virion, especially in the processes of virus assembly and morphogenesis. This protein represents another structural element with potential implications as a target for drug development in the field of COVID-19 therapeutics. Remarkably, it has the ability to assemble into pentameric structures and function as an ion channel, earning it the name E channel or viroporin [Nieva et al (2012) Nat Rev Microbiol. 10(8), 563-74]. Further highlighting its importance is the observation of considerable similarity in the E proteins across BAT-CoV, SARS-CoV and SARS-CoV-2. It is interesting to note that while the SARS- CoV-2 and MERS-CoV E proteins show subtle differences, they share the ability to form ion channels—an attribute of significant importance in facilitating virus-host interactions. Of particular interest is the ionic conductivity aspect inherent to these proteins, a property that has potential advantages for the virus in its propagation. In addition, E protein ion channel activity is intricately linked to inflammatory cell activation, contributing to a complex pathogenic landscape. In addition to its role in ion channel activity, E protein affects intracellular protein transport and regulatory mechanisms. This multifaceted involvement represents another aspect of its potential application in the field of COVID-19 therapeutics.

Publications

Das, A., Khan, S., Roy, S and Das, S (2023) Phytochemicals for mitigating the COVID-19 crisis: evidences from pre-clinical and clinical studies. Exploration of Drug Science. 1, 336-376

Dr. Syamal Roy, ICMR Emeritus Scientist

Dr. Sourish Ghosh and his group members

Unravelling Molecular Mechanism of Non-lytic Viral Egress for RNA Viruses

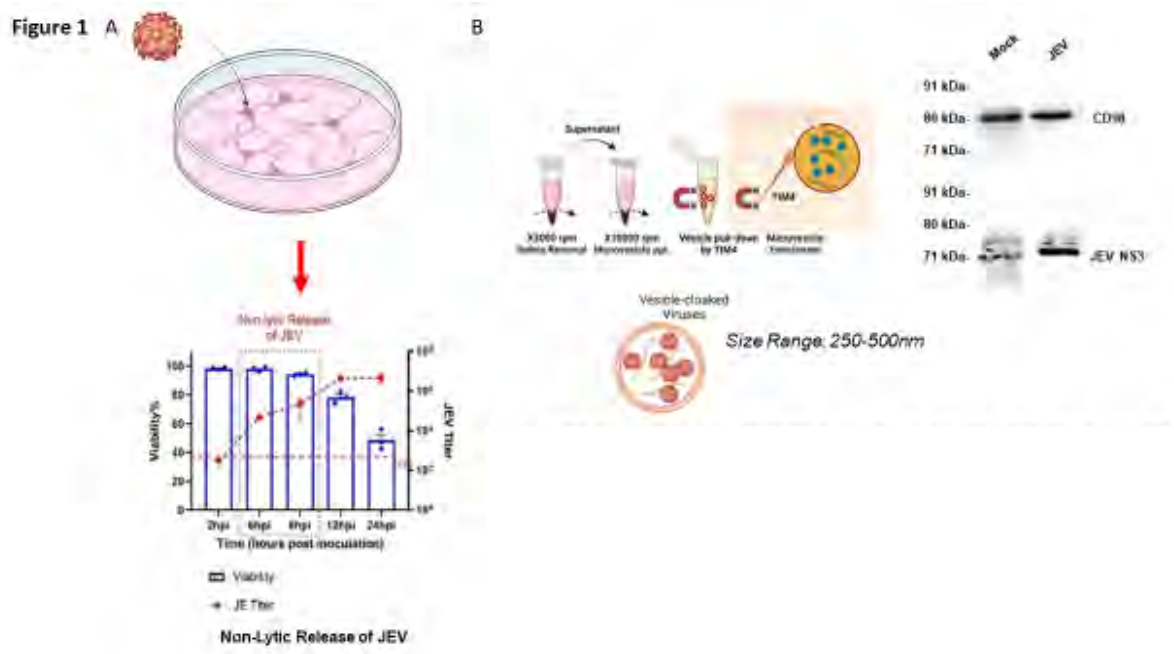
Research Activities

A. Role of non-coding RNAs sequestered along with Rotavirus inside Extracellular Vesicles.

Rotaviruses belonging to Reoviridae family, have double-stranded RNA as genome, are enteric viruses that infect gastro-intestinal (GI) tract, and transmit through fecal-oral route. It mainly causes infections in new-borns and children below 5. It has been observed that vesicular transmission of Rotavirus provides advantage in infectivity to the virus. In transmission virus particles remain stable inside vesicles protected from various enzymes and multiple virus particles being packaged together in a single vesicle help them to overcome innate immune response of a particular cell to establish infection (Ghosh et al., Cell, Host & Microbe, 2018). We also identified miRNAs are also sequestered inside these vesicles which may have role in subverting certain host responses to facilitate viral replication. We have sequenced and observed differential expression of 7 novel miRNAs that are upregulated in vesicles obtained from infected cells. Currently, we are analyzing the target pathways these miRNAs are targeting to facilitate the viral infection.

B. Extracellular Vesicle-mediated release and transmission of Japanese Encephalitis Virus.

Japanese Encephalitis Virus (JEV) is a neurotropic virus that causes severe encephalitis in children below 15 years, and has a case fatality rate ranging from 15-30%. It belongs to the Flavivirus family having a positive single stranded RNA as genome. JEV is endemic to India, and causes seasonal outbreaks during monsoon as mosquito is the vector for this virus. JEV has been researched in India for more than 3 decades, yet we made a seminal observation that JEV is egressing out of neurons inside Extracellular Vesicles. We have observed JEV to be egressing out without observable lysing of cells in cell culture supernatant. By western blotting we have confirmed presence of JEV non-structural protein and microvesicle marker CD98 in vesicles extracted from infected supernatant (Fig. 1). Nano-tracking analysis and Atomic Force Microscopy show these vesicles containing the virus has a size range between 250-600 nm. These vesicles have been further inoculated in naïve neuronal cells and 4-day old mouse pups to check infectivity. We observed replication of virus in both *in-vitro* and *in-vivo*, signifying infectivity of viruses carried inside vesicles.



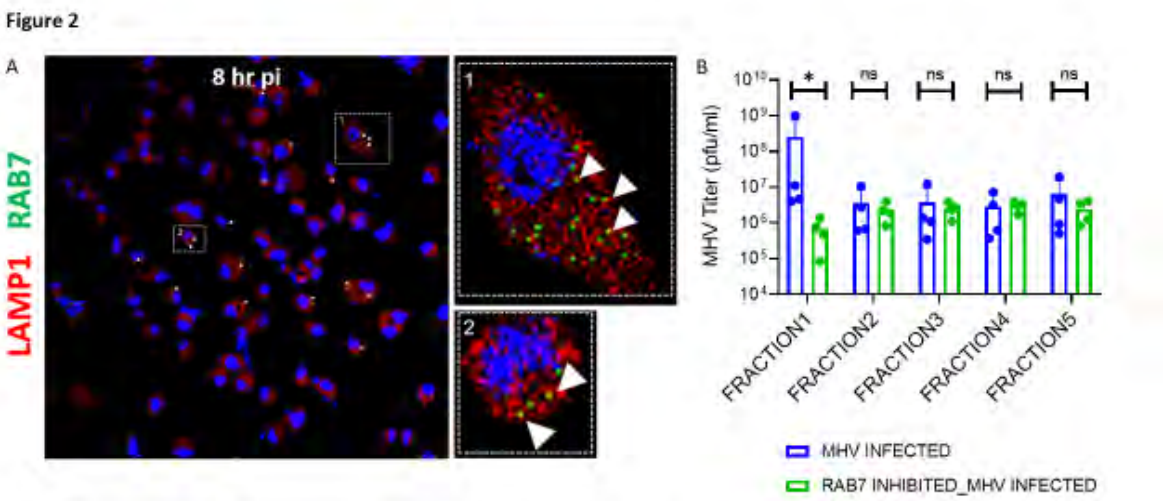
A. Time window of 6-8 hrs post inoculation showed release of viruses without significant cell death or decrease in cell viability % This signifies non-lytic release of JEV.
B. Vesicles released in supernatant in supernatant collected from the time window, were pulled down using TIM-4 bound magnetic beads. The vesicles isolated from mock and JEV supernatants showed presence of CD98 from both samples signifying presence of extracted microvesicle but only presence of JEV non-structural protein only collected from JEV infected cells.

C. Deciphering the transfer of -Coronaviruses after assemble from ERGIC compartments to Lysosomes.

Mouse Hepatitis Virus (MHV) along with SARS-Cov2 belong to the -Coronavirus. It has been observed in addition to the classical biosynthetic pathway, viruses are also egressing through lysosomal exocytosis (Ghosh et al., Cell, 2020). We observed that after assemble in ERGIC compartment the viruses during their non-lytic phase of egress are accumulating in lysosomes. They were not getting degraded in lysosomes as these lysosomes are de-acidified and inactive. And lysosomes have a natural property to move towards the plasma membrane, which is hijacked by these viruses for their egress. But still it is an enigma as to how these viruses after assembly are ending in lysosomes? Rab-7 is an important player in endosomal movement of vesicles. We observed an over-expression of Rab-7 as viruses enter the cells, and Rab-7 to co-localize with lysosome. With inhibition of Rab-7 expression, we specifically observed that viral load within lysosomes reduce (Fig. 2), indicating Rab-7 to be one of the key player in directing viruses towards lysosomes. We also observed the enhanced secretion of Lipid droplets in the early phase of infection, and there are several reports suggesting their movements towards lysosomes. We used Lipid droplet inhibitors and observed no change in replication of the virus intracellularly although viral egress was perturbed. Currently we are exploring this mechanism.

Future Research Plans

- Identifying miRNAs that sequestered along with Rotaviruses and pathways inhibited to facilitate the viral replication.
- Comparing effect of neuronal apoptosis and neuroinflammation when inoculated with JEV carried inside vesicle and free virus particle.
- Establishing the molecular mechanism of transfer of assembled viruses from ERGIC compartment to Lysosomes.
- In mammary gland, identify cells where Rotavirus and MHV replicates and compare transcriptomics of cells which replicate the virus and cells in the same tissue not replicating the virus.



A. Rab-7 colocalization with Lysosomes at 8 hrs. post inoculation with MHV-A59 in murine fibroblast cell line.
B. CID1067700, a pan-Rab-7 inhibitor, inhibits movement of assembled viruses to lysosomes, analyzed from various fractions from subcellular fractionation.

Extramural / CSIR Funding

- Role of small non-coding RNAs sorted inside Extracellular Vesicles for RNA Virus Persistence. SERB-Core Research Grant, 2024-2027, 34 Lakhs, (CRG/2023/004359)
- Tuning Lipid Droplets for Antiviral Interventions in Brain. DBT Call for Neuroscience, 2024-2027, 79.4 Lakhs, (BT/PR51484/MED/122/359/2024)
- Role of Mother-Neonate Dyad Interaction in resolving Pediatric Viral Infection. DBT-Wellcome Trust India Alliance Intermediate Fellowship, 2024-2029, 3.54 Cr, (IA/I/23/2/506972)
- Vesicular Transmission of Falvivirus & Its Role in Neurodegeneration, CSIR- FBR Project, 2024-2027, 69.4 Lakhs, FBR070305

Publications

Mondal, S., Ghosh S. (2023) Liposome-Mediated Anti-Viral Drug Delivery Across Blood-Brain Barrier: Can Lipid Droplet Target Be Game Changers? Cell Mol Neurobiol. 44(1):9.

Invited Lectures

1. Enteric Viruses' Unconventional Transmission Tale, National Brain Research Centre, Manesar, 6th October, 2023.
2. Unlocking RNA Virus Persistence Puzzle: Staying a Step Ahead of the Viruses, National Brain Research Centre, Manesar, 1st Organellar Biology & Membrane Trafficking Meeting, 8-10th October, 2023.
3. Navigating the Viral Maze: Unconventional Lysosomal Pathway in β-Coronavirus Release, Sinclairs, Kalimpong, BAW 2024: Frontiers in Disease Biology Conference, 27-30th March, 2024.

Member of Society

Member, American Society for Microbiology, 2017-present.

Awards

DBT-Wellcome Trust India Alliance Intermediate Fellowship, 2024-2029.

Dr. Sourish Ghosh, Senior Scientist
Group Members: Dr. Ankita Sarkar, DBT-RA; Mr. Sourav Mondal, UGC-JRF; Ms. Suparna Dhar, DBT-JRF; Ms. Bhaghyasree Mullick, UGC-JRF
Collaborators: Dr. Surupa Basu, Institute of Child Health, Kolkata; Dr. Manjari Kiran, University of Hyderabad, Hyderabad; Dr. Arindam Talukdar, Dr. Subhajit Biswas, Dr. Subhas Chandra Biswas, CSIR-IICB, Kolkata.

Dr. Subhajit Biswas and his group members

Study of the molecular details of virus infection and pathogenesis, particularly virus replication and viral protein translation (and trafficking) with the aim of developing novel strategies of diagnosis and intervention (antiviral candidates)

Research Activities

1. In-depth investigation of dengue virus-mediated pathogenesis in various cell lines towards identifying novel targets for counteracting DENV-mediated human diseases.
2. Virology and molecular analysis of dengue virus serotypes (laboratory strains vs. clinical isolates) in cell culture and characterization of NS1 protein in terms of production and detection by ELISA.
3. Our discovery that the human host is exposed to an RNA virus (Lepsey NLV 1) in Leptomonas seymouri (LS), another co-infecting protozoan parasite with Leishmania donovani (LD), i.e. the "LD-LS-Lepsey NLV1 triple pathogen" phenomenon, unveiled a new paradigm of research towards revisiting the mysteries of kala-azar/Indian leishmaniasis pathogenesis and management. We are currently investigating how the "triple pathogen" is interacting in macrophage culture in vitro in terms of cytokine profile and parasite survival.
4. Elucidating the globally observed "dengue and COVID-19" conundrum, for instance, how the serological cross-reactivity between DENV and SARS-CoV-2 is changing from Wuhan, Delta to Omicron era of COVID-19.

Future research plans

1. We will investigate the mode of egress of dengue virus in case of plaque-forming and non-plaque forming DENV strains in different cell types. The latter strains are representative of DENV clinical isolates. The role of extracellular vesicles in DENV egress from cells will be studied in detail.
2. We are currently pursuing questions such as how Lepsey NLV 1, a protozoan virus (present in Leptomonas seymouri, the co-infecting protozoan parasite with Leishmania donovani in Kala-azar patients) persists in the human system for so long, and in considerable numbers, making its recovery possible from even archived human serum samples.

3. Screening for antiviral candidates against coronavirus and DENV.

Extramural / CSIR Funding

Study of infection dynamics of Leishmania donovani in the presence of Lepsey NLV1 virus: Role of the virus in path-biogenesis of Kala-azar and its remediation. ICMR, 2024-27, 113.46 Lakhs, IIRP-0959-2023.

Publications

Sarker, S., Dutta, C., Mallick, A., Das, S., Das, Chowdhury, C., De, A., Gorai, S., Biswas S (2023).Pre-dominance of dengue non-cross-reacting SARS-CoV-2 spike antibodies during the Omicron era and their role in the ADE-mediated surge of Dengue virus serotype 3. *MedRxiv* 2023.09.08.23295136. https://www.medrxiv.org/content/10.1101/2023.09.08.23295136v1.full (under review in a Journal).

Patents

An easy-to-use diagnostic system for rapid dengue virus detection using fluorescence-based molecular probes. Subhajit Biswas, Surajit Ghosh, Soumi Sukla, Prasenjit Mondal, filing date 05/05/2021. Patent No. 22/09493/South Africa.

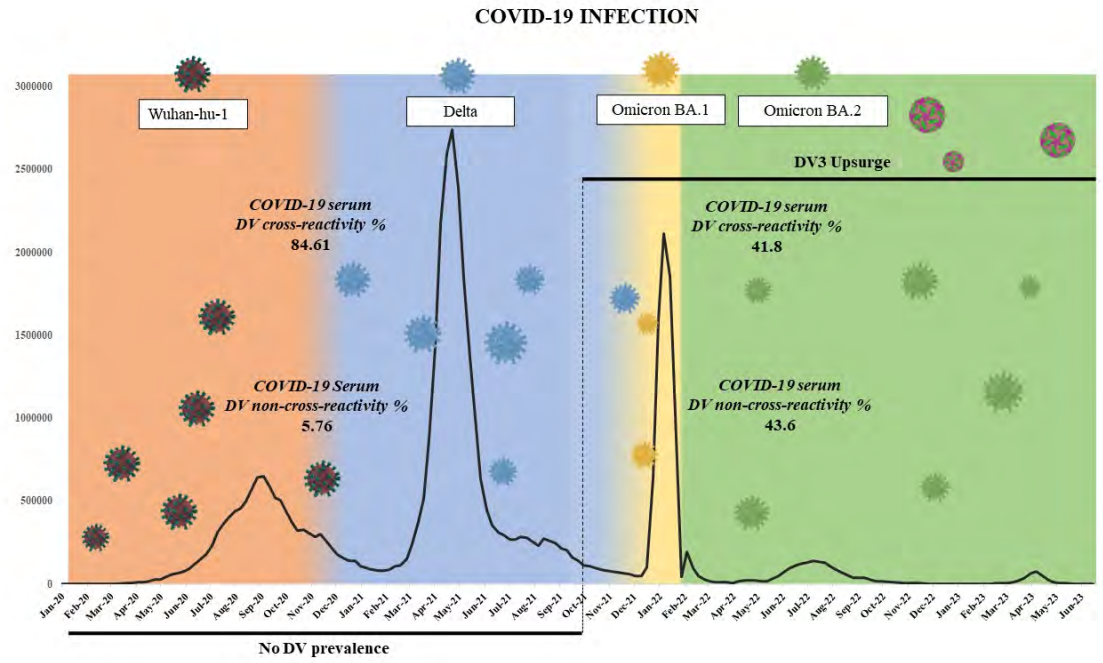


Figure 1: Month-wise pattern of COVID-19 infection waves (confirmed cases) in India and predominant variant(s) of SARS-CoV-2 from January, 2020 to June, 2023

From around October, 2020, the Delta variant wave predominated. Omicron BA.1 variant was discovered for the first time in India around November, 2021. All of 2022 and the first half of 2023 were dominated by Omicron BA.2 variant. The cross-reactivity percentage of COVID-19 serums with dengue virus (DV) was 84.61% (n=44/52) during 2020-21 which decreased to 41.8 % (n=23/55) during the Omicron waves (our studies). Also, there were negligible case reports of DV infection in Southeast Asia from January, 2020 to October, 2021. The DV3 strain became predominant in Southeast Asia from the latter half of 2021 and during 2022. The upsurge of DV3 coincided with the decrease in the prevalence of DV cross-reactive COVID-19 serum samples and the dominance of BA.2 variant. DV non-cross-reactive Omicron wave serum samples caused ADE for DV3 which might be the major cause of DV3 surge during the Omicron era.

Dr. Subhajit Biswas, Principal Scientist
Group Members: Abinash Mallick, CSIR-SRF; Chiroshri Dutta, CSIR-SRF; Supratim Sarkar, CSIR-SRF; Sayantan Das, UGC-JRF; Pritam Dey Sarkar, UGC-JRF; Dr. Priyanka Dhar, CSIR-RA

Dr. Sudipta Das and his group members

Fatty acids import mediated replication checkpoint in human malaria parasite *Plasmodium falciparum*

Research Activities

Plasmodium falciparum (*P. falciparum*) malaria, remains a severe public health burden globally. During cell cycle, *P. falciparum* shows autonomous and repeated rounds of asynchronous nuclear division. In *P. falciparum*, how the autonomous and asynchronous nuclear division is being achieved is a mystery. In order to commit for repeated rounds of autonomous DNA replication and nuclear division, *P. falciparum* needs to ensure optimum supply of nutrients. Fatty acids (FAs) are an important lipid for membrane biogenesis to sustain *P. falciparum* proliferation. Deprivation of nutrients prevents cell cycle initiation at the G1/S checkpoint in mammalian cells. It is unknown whether in *P. falciparum,* the deprived levels of lipids have any role to play in triggering autonomous and asynchronous cell cycle arrest. In proliferating *P. falciparum*, membrane biogenesis and nuclear division precedes cellularization. Hence inhibition of lipid biosynthesis due to altered levels of FAs, Diglycerides (DG), and Triglycerides (TG), might convey a negative signal at the onset of nuclear division results in cell cycle arrest until FAs, DG and TG reaches its normal level to resume lipid biosynthesis. Phospholipids (PL) are the major structural element of the *P. falciparum* membranes and phosphatidylcholine (PC) is the most abundant PL. In *P. falciparum*, there is NO *de novo* biosynthesis of FAs, hence for PL biosynthesis, FAs must be imported from human serum. In my laboratory, we have discovered that during membrane biogenesis and proliferation, *P. falciparum* imports FAs from human serum through a protein complex which is localized on the infected RBC surface. Abrogation of this complex leads to the deprived levels of FAs in *P. falciparum* which resulted in the cessation of DNA replication and parasite proliferation possibly via inhibition of parasite membrane biogenesis (Figure. 1). Inhibition of FAs import leads to reduced catabolism of TG in the parasites. Accumulation of TG is achieved due to the inhibition of TG catabolizing enzyme Tgl4 which is regulated by the phosphorylation/ dephosphorylation by Cylin/CDKs. Currently, in my lab we have shown that denaturation resistant parasite P2 protein on the infected RBC surface is essential for fatty acids import. Inhibition of P2 mediated fatty acids import leads to accumulation of TG and that might lead to the inhibition of PL biosynthesis. Inhibition of PL biosynthesis leads to abrogation of membrane biogenesis and cessation of parasite nuclear division and cell cycle progression. Currently, the checkpoints and the

entire cascades of events are being explored in my laboratory.

Future Research Plans

How import of FAs regulates parasite nuclear division during human infection and whether abrogation of PfP2 complex on the infected RBC surface using small molecules is a viable option to be considered as an anti-malaria drug target or as a vaccine candidate.

In our published work, we have shown that the inhibition of fatty acids import led to the enhanced triglyceride (TG) levels in the parasite. How, elevanted levels of TG is meaditing the regulation of replication via parasite memebrane biolgenesis is being explored.

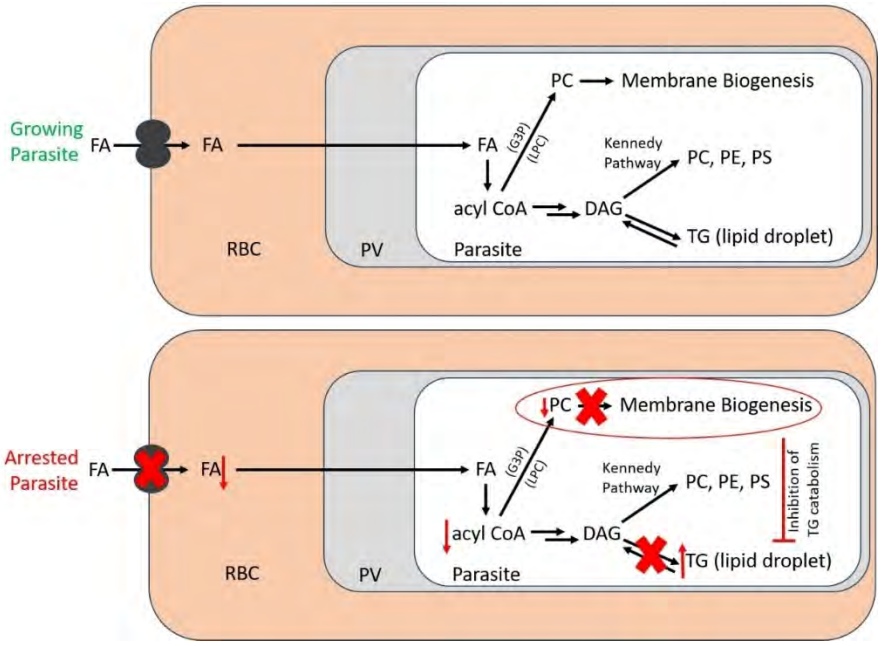
The entire protein complex having denaturartion resistant PfP2 tetramer which is responsible for fatty acids import has been identified. The mechanism of fatty acids import through this complex is being explored using cryo-electron microspcopy.

Extramural / CSIR Funding

- Exploring molecular details of unique cell division processes in apicomplexan parasites. Department of Biotechnology (DBT), 2018-2025, 150 Lakhs, BT/RLF/Re-entry/40/2016
- Membraneless nuclei demixing by surfactant proteins and phase separation during asymmetric nuclear division of intraerythrocytic closed mitosis of Plasmodium falciparum. Department of Biotechnology (DBT), 2023-2026, 84 Lakhs, BT/PR44703/MED/29/1587/2021

Publications

Das, S., Manna, A., Majumdar, O., Dhara, L. (2024) M-*O*-M mediated denaturation resistant P2 tetramer on the infected erythrocyte surface of malaria parasite imports serum fatty acids. iScience. 27,109760.



Dr. Sudipta Das, Ramalingaswami Fellow and Assistant Professor (AcSIR)
Group Members: Kaustuv Mukherjee, Postdoc; Paroma Mitra, Postdoc

Dr. Sujoy K. Das and his group members

Bacterial membrane targeted fusogenic nanoemulssion to accelerate the killing of *Staphylococcus aureus*

Research Activities

Bacterial infections caused by ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas. aeruginosa, Enterobacter* spp.*)* is one of the growing global concerns for health care sectors, causing wound infections, septicemia, pneumonia, bone and joint infections. As per the reports of WHO, *S. aureus* infections lead to 2 million illnesses and 23,000 deaths per year. Antibiotic associated adverse effects and emergence of bacterial resistant strains necessitates the development of an alternative yet effective approach. The nanotechnology based therapy has emerged as a potential therapeutic strategy to combat the bacterial infection. The innovative nanomaterials could enable interventions at the molecular length scale and are, therefore, an important cornerstone in building solutions. In spite of significant advances, it remains difficult to construct nanomaterials with precisely defined therapeutic effects, release of therapeutic molecule at targeting site and minimize any adverse effect to human health. The primary research focus of our group is to develop biomimetic and surface-functionalized nanomaterials for targeted drug delivery for infection control, tissue engineering application and medical device development.

Cationic metal nanoparticle conjugated fusogenic nanoemulsion (CFusoN) as a lipid solubilizing nanovesicle has been formulated for the effective treatment of *S. aureus* infection with a killing efficiency of 99.999% (Figure 1). The cationic nanoparticles conjugated nanoemulsion (*viz.* NECNP) (24.4 ± 2.9 mV) electrostatically bound with the negatively charged bacterial cell membrane (-10.2 ± 3.7 mV) causing alteration of the bacterial surface charge. The fluorometric and flow cytometry studies confirmed the bacterial membrane depolarization and altered cell membrane permeability leading to the cell death. The atomic force microscopic studies further demonstrated the damage of the cellular ultrastructure, while transmission electron microscopic image and membrane lipid solubilization analysis depicted the solubilization of bacterial membrane lipid bilayer along with the leakage of the intracellular contents. The cell membrane fatty acid analysis revealed that the methyl esters of palmitic acid, stearic acid and octadecadienoic acid isomers were solubilized after the treatment of *S. aureus* with CFusoN. The bactericidal killing efficiency of CFusoN is proposed to occur through the synergistic efficacy of the targeted attachment of CNP to the bacterial cells

along with the lipid solubilization property of NE. The CFusoN also effectively penetrated through the EPS layer and disrupted the mature biofilm of *S. aureus*. Consequently, CFusoN caused activation of the immune response through M1 macrophage polarization, leading to accelerated phagocytosis and finally complete biofilm disruption without any further recurrence of the infection. Interestingly, the biofilm-fibroblast co-culture model also demonstrated that CFusoN specifically disrupted the biofilm without compromising the fibroblast cells. Further, porcine skin wound infection model exhibited the enhanced wound cleansing potency of CFusoN in comparison to the commercially available wound cleansers. The obtained antibacterial activity, biocompatibility and skin wound disinfection efficacy of the NECNP demonstrated the formulation of a cell targeted CFusoN as a promising translatable strategy to combat the bacterial infection.

Future Research Plans

Novel drug delivery system using microneedle patch

Microneedle technology is emerged as a novel transdermal delivery system for sustained and precise delivery of active molecules into the specific skin layers in minimum invasive manner. The micron-sized (usually <1 mm) sharp needles pierce the stratum corneum and deliver drugs through microporous channels into deep skin layers without causing any pain. Therefore, drug administration using microneedle patches through skin is the potential alternative. We have fabricated tip dissolving microneedle patch loaded a combination of antimicrobial peptide and antibiotic to address the chronic skin infection. It is hypothesized that tip dissolving microneedle patch loaded with AMP and antibiotic could penetrate through the EPS of the biofilm and release the antimicrobial peptide and antibiotic within the biofilm, leading to the specific binding of the AMP to the bacterial membrane causing membrane depolarization. This led to the permeation of the antibiotic within the bacterial cells accelerating the killing of the biofilm resident and persister cells. This may lead to the effective elimination of the biofilms by combating the limitation of antibiotic resistance.

Cell-targeted photodynamic and phtothermal therapy

Photodynamic and phtothermal therapy emerges as a promising treatment strategy to reduce the potential risks of systemic toxicity, collateral healthy tissue damage and surgical trauma. We are designing formulation of light activated photosensitizer, which results in energy transfer cascades to yield cytotoxic reactive oxygen species, rendering apoptotic and necrotic cell death.

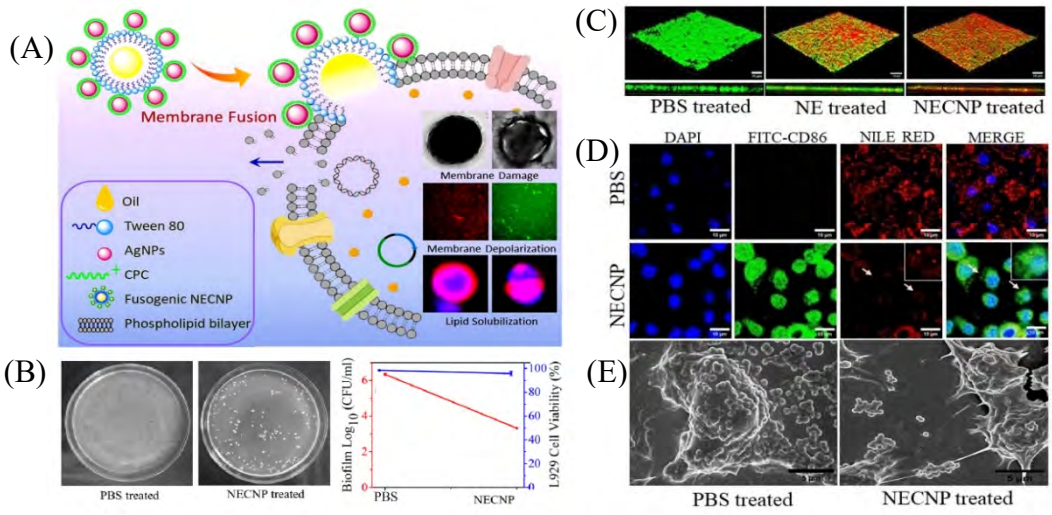


Figure 1: Schematic representation (A) of preparation of fusogenic NECNP. Antibacterial activity (B) of NECNP against *S. aureus* by plate count method. CLSM images (C) demonstrated excellent penetration and biofilm eradication properties of NECNP; Biofilm were stained with SYTO 9 (left panel), after the penetration of RhoB-NE (middle panel) and RhoB-NECNP (right panel). Immunofluorescence staining (D) and FESEM analysis (E) exhibiting bacterial phagocytosis after treatment of NECNP to macrophages. Scale bar, 10 and 5 µm respectively.

Extramural / CSIR Funding

1. Hemostat – A Lifesaving Bandage for Faster Bleeding Arrest, BIRAC, Govt. of India, 2023-2024, 46.65 lakh, (BT/AIR0711/PACE-17/19).
2. Development of antimicrobial peptide tagged nanoformulation for targeted combination therapy against *Pseudomonas aeruginosa*, DSTBT, Govt. of West Bengal, 2023-2026, 28.13 lakh, (2102(Sanc)/STBT-13015/3/2024-WBSCST)

Publications

1. Choudhary, P., Ramalingam, B., and Das, S.K., (2023) Rational design of antimicrobial peptide conjugated graphene-silver nanoparticle loaded chitosan wound dressing. *Int. J. Biol. Macromol.* 246, 125347.
2. Ramalingam, B., and Das S.K., (2023) Biomimetic strategy for fabrication of bifunctional graphene oxide-biomaterial aerogel as highly porous antifouling material for oil/water separation. *Chem. Eng. J.* 475, 145906.
3. Ramalingam, B., and Das S.K., (2023) Biofabricated graphene-magnetite nanobioaerogel with antibiofilm property: Response surface methodology based optimization for effective removal of heavy metal ions and killing of bacterial pathogens. *Chem. Eng. J.* 475, 145976.
4. Bose, S., Dahat, Y., Kumar, D., Haldar S., and Das, S. K., (2024) Membrane Targeted Multifunctional Cationic Nanoparticles Conjugated Fusogenic Nanoemulsion (CFusoN): Induced Membrane Depolarization and Lipid Solubilization to Accelerate the Killing of *Staphylococcus aureus. Mater. Horiz.* 11, 661-679. (Highlighted in Cover Page, February 2024 issue).

Cover Page Article

Materials Horizons, February 2024 Issue (Inside Front Cover)

Invited Lectures

Nanobiotics: Design of Functional Nanomaterial for Targeted Treatment of Bacterial Infection. 1st international conference on Drug Discovery and Development for Infectious Diseases: Cutting-Edge Research and Challenges, Eminent College of Pharmaceutical Technology, 3-4 March, 2023.

Member of Society

1. Life Member, Royal Society of Biology, London, United Kingdom,
2. Annual Member, American Chemical Society, Washington, DC 20036, USA, 2023-2024.
3. Life Member, National Academy of Biological Sciences, Chennai, Tamilnadu,

Dr. Sujoy K Das, Principal Scientist
Group Members: Ms. Somashree Bose, UGC SRF; Ms. Sivanghi Parhi, DBT SRF; Ms. Arpita Mukherjee, UGC SRF; Mr. Avishek Shaw, DBT JRF

Dr. Susanta Kar and his group members

Dissecting the role of host-dependent surviving factor(s) in determining survival, virulence and immunity in visceral leishmaniasis (VL)

Research Activities

In order to combat various infectious diseases, the utilization of host-directed therapies as an alternative to chemotherapy has gained a lot of attention in the recent past, since it bypasses the existing limitations of conventional therapies. The use of host epigenetic enzymes like histone lysine methyltransferases (KMTs) and lysine demethylases (KDMs) as potential drug targets has successfully been employed for controlling various inflammatory diseases like rheumatoid arthritis and acute leukemia. In our earlier study, we have already shown that the functional knockdown of KDM6B and ASH1L in the experimental model of visceral leishmaniasis has resulted in a significant reduction of organ parasite burden. Herein, we performed a high throughput virtual screening against KDM6B and ASH1L using > 53,000 compounds that were obtained from the Maybridge library and PubChem Database, followed by molecular docking to evaluate their docking score/Glide Gscore. Based on their docking scores, the selected inhibitors were later assessed for their *in vitro* anti-leishmanial efficacy. Out of all inhibitors designed against KDM6B and ASH1L, HTS09796, GSK-J4 and AS-99 particularly showed promising *in vitro* activity with IC_{50} <5 µM against both extracellular promastigote and intracellular amastigote forms of *L. donovani*. *In vitro* drug interaction studies of these inhibitors further demonstrated their synergistic interaction with amphotericin-B and miltefosine. However, GSK-J4 makes an exception by displaying an in different mode of interaction with miltefosine. Collectively, our *in silico* and *in vitro* studies acted as a platform to identify the applicability of these inhibitors targeted against KDM6B and ASH1L for anti-leishmanial therapy.

Progressive VL is known to be associated with macrophage metabolic alterations, leading to a switch from early glycolysis to late mitochondrial OXPHOS, however impact of this metabolic deviation on the phenotypic plasticity of macrophages (classical or alternatively activated) is poorly understood.

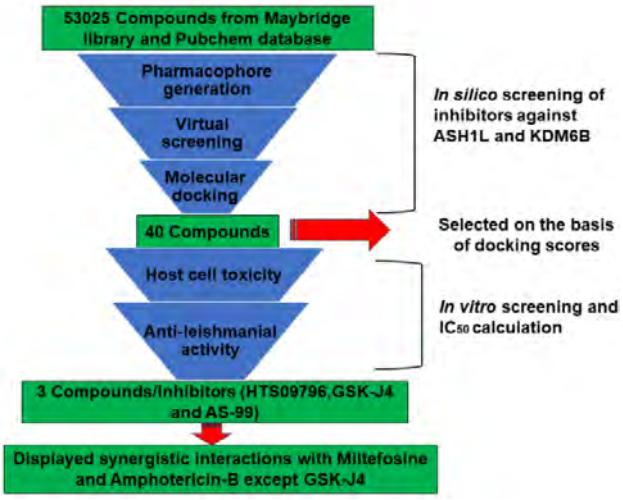


Figure 1: Work flow diagram of *in silico* and *in vitro* screening & identification of ASH1L & KDM6B inhibitors against experimental visceral leishmaniasis

Our preliminary study revealed that *L. donovani* induces a shift from glycolysis to mitochondrial OXPHOS in infected J774 macrophages. Enzyme kinetics studies further showed a significant upregulation of α-ketoglutarate dehydrogenase and isocitrate dehydrogenase at late hours of infection, indicating the presence of an intact TCA cycle in *L. donovani*-macrophages. Pre-treatment of infected macrophages with antimycin A (an inhibitor of oxphos) significantly reduced intracellular parasitemia (amastigote) at 48 hours post infection along with down regulation of parasite-protective alternative activation marker genes at mRNA level (Arginase 1 & Ym1). These observations indicate that *L. donovani* might exploit host metabolism machinery (particularly mitochondrial OXPHOS) for repolarizing host macrophages to an alternatively activated phenotype, as a part of their survival strategy.

Future Research Plans

- Identifying the parasite derived factors/cellular events associated mitochondrial biogenesis, TCA cycle intermediates and alternative activation/immunosuppression of *L. donovani*-infected macrophages
- Deciphering the mechanism of biogenesis and secretion of exosomes from host during visceral leishmaniasis and their role in immune evasion

Publications

Dutta, M., Qamar, T., Kushavah U., Siddiqi M.I., Kar, S., (2024) Exploring host epigenetic enzymes as targeted therapies for visceral leishmaniasis: *In silico* design and *in vitro* efficacy of KDM6B and ASH1L inhibitors. Molecular Diversity. (Online ahead of print).

Conferences Attended

Attended & chaired a session in the "21st All India Congress of Genetics and Genomics (AICGG) International Symposium on Environmental Toxicogenomics: Ecosystem Health and Sustainability - Challenges and Way Forward" at Jadavpur University, Kolkata dated 5th -7th February 2024.

Member of Society

1. Life member of Indian Society for Parasitology (Membership no.-777)
2. Life member of Indian Immunology Society (Membership no.- LM/IIS/191/12/11)
3. Life member of Society of Biological Chemists (India) (Membership no.-4350)
4. Member of Molecular Immunology Forum

Dr. Susanta Kar, Principal Scientist
Group Members: Mukul Dutta, CSIR SRF; Rittika Sarkar, UGC JRF; Prabha Prusti; CSIR JRF; Sandip Das, UGC JRF
Collaborators: Dr. Mrigank Srivastava, CSIR-CDRI, Lucknow; Dr. Ajit Chande, IISER, Bhopal

Dr. Umesh Prasad Singh and his group members

Discovery and development of therapeutics against infectious diseases and cancer

Research Activities

We are working on therapeutic development from natural sources/synthetic compounds, especially for infectious diseases (mainly antivirals for dengue and SARS-Cov2) and cancer.

We have shown through collaborative efforts with NII, New Delhi, that two gliptins (linagliptin and sitagliptin), which are anti-diabetic drugs, not only impede human DPP4 activity but also prevent ACE2-RBD interaction of SARS-Cov2 virus, which is crucial for virus growth (Mani *et al.,* 2023) Sitagliptin and linagliptin alone or in combination have the avidity to impede the development of pan-SARS-CoV-2 variants of concern, including original SARS-CoV-2, alpha, beta, delta, and kappa in a dose-dependent manner (Fig1). This opens up the path for these anti-diabetic drugs (gliptins) to be used as therapeutics for SARS-Cov2. This was a groundbreaking discovery with colossal future potential.

We have developed high throughput assays for testing and screening of synthetic as well as natural product compounds against various viral drug targets (dengue virus NS3/NS2B protease and SARS-Cov2 Mpro and PLpro enzymes). We have designed and tested numerous peptide-based molecules and many natural products/synthetic small molecules against these targets. The process has yielded many active inhibitors with IC50 of 1-5 uM against dengue and SARS-Cov2, which we are developing further.

We have discovered an inhibitor of dengue virus NS5-MTase with K_d of about 0.03 μM. This is one of the most active inhibitors so far for this less explored target of Dengue. The extract from which the compound is isolated can be used as prophylactic in endemic areas of Dengue fever for which no current treatment exists. Based on our above research, we have a CSIR-mission mode Phytopharma III project to develop the above extract as a therapeutic against dengue.

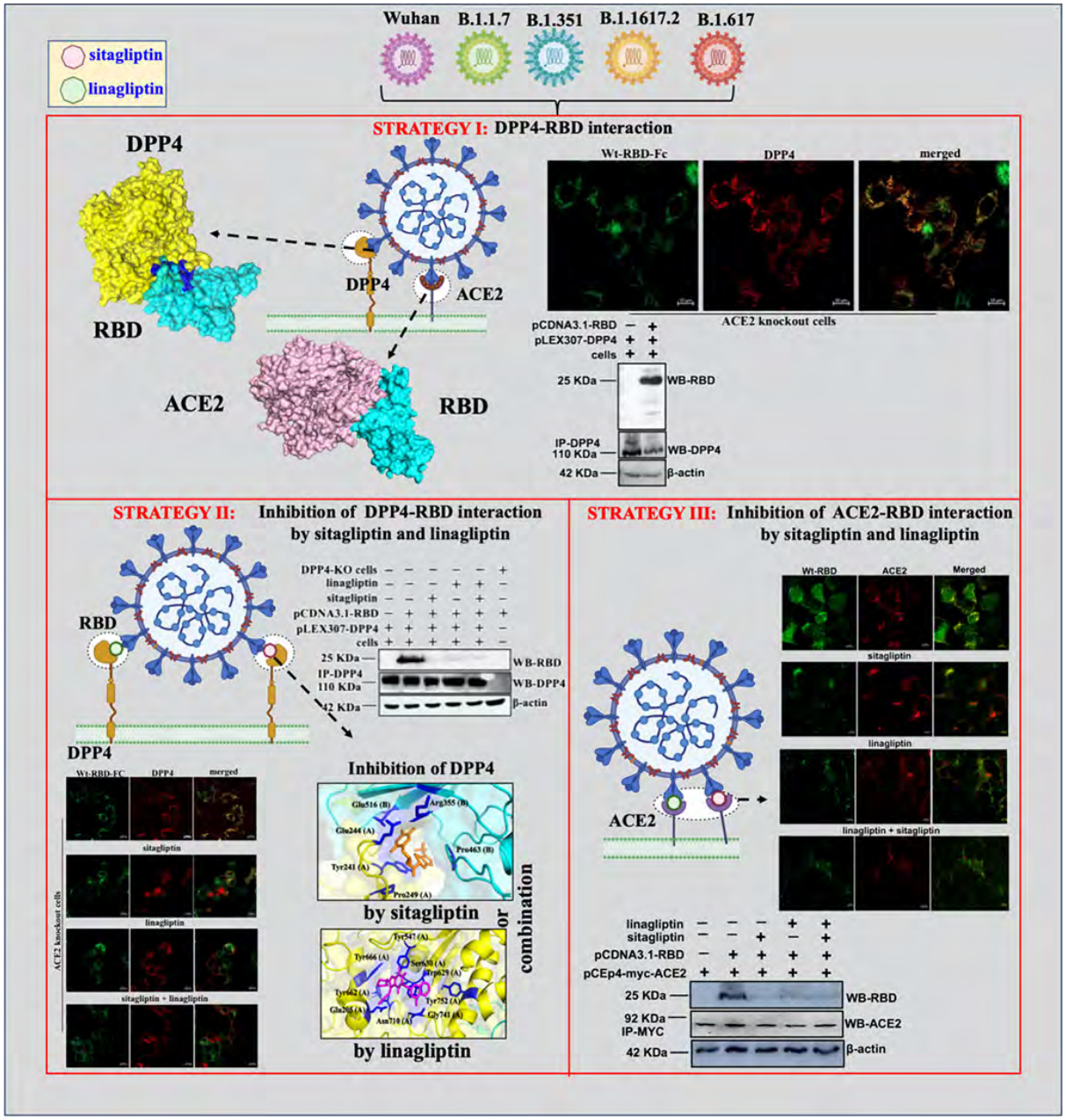


Figure 1: Inhibition of DPP4-RBD and ACE2-RBD interactions by DPP4 inhibitors sitagliptin and linagliptin.

We have discovered two limonoids, Swietenine (1) and Swietenolide (2), isolated from *S. macrophylla* seeds (Pal *et. al.* 2023). Both compounds show significant anti-CRC activity (in HCT-116 cell line) *in-vitro* having IC50 = 10.5µM (5.96 µg/ml) and 5.6µM (2.7 µg/ml), respectively, through inhibition of mouse double minute 2 (MDM2) homolog. It may be worth noting that the observed activity of comp-2 (IC_{50}=5.6µM) is comparable to that of the standard anti-cancer drug 5-FU (IC50= 5µM), which is rare in natural products. Compounds 1& 2 are 8.5 to 15.6 fold more active than crude CHCl3 extract. The Selectivity Index (S.I.) of isolated compounds 1 and 2 for cancer cells is about 7 and 13 fold, respectively, significantly better than the S.I. of extract (S.I. ~2) and hence may be helpful as agents against Human Colorectal Cancer. Efforts are being made to develop these molecules further as potential therapeutics against colon cancer.

Future Research Plans

We plan to develop the natural product-based phytopharmaceutical leads we obtained for dengue virus inhibition. We want to do pre-clinical development of this lead towards a clinical candidate. If successful, it can potentially be a first-in-class phytopharmaceutical-based natural product as a therapeutic agent against dengue.

We have also obtained several unnatural amino-acid-containing peptide leads with IC_{50} of about 1-2 µM against dengue virus NS3/NS2B protease. Efforts are being made to obtain optimized leads for their pre-clinical development.

Extramural / CSIR Funding

1. CSIR Phytopharmaceutical Mission (Phase III), CSIR, 2024-2026, 145.56 lakhs, (MMP075201)
2. Anti-viral mission CSIR: Discovery and Preclinical Development of Anti-virals for COVID-19 and other diseases, CSIR-anti-viral mission, 2021-2023, 6365.90 Lakhs (one of the Co-PIs).
3. Towards discovery and development of novel drugs and pharmaceuticals, CSIR–Deep ocean mission, 2024-2027, ~ 900 lakhs (one of Co-PIs).

Publications

1. Chaudhary, S., Rai, R.N., Jyothi, D., Singh, U.P. (2024) Solid-State Green Synthesis of Two (1:1) Organic Intermolecular compounds; their Physico-chemical, Thermal, Single Crystal Growth, and Atomic Packing Studies. *Materials Chemistry and Physics*. (accepted for publication)
2. Chatterjee, A., Roy, T., Jyothi, D., Mishra, V.K., Singh, U.P., Swarnakar, S. (2024) Melatonin Inhibits AGS Cell Proliferation by Binding to the ATP Binding Site of CDK2 Under Hyperglycemic Conditions. *Cell Biochem Biophys*. 07 March 2024.
3. Pal, P.C., Nag, S., Jyothi, D., Das, S., Saha, K.D. and Singh, U.P. * (2023) Swietenolide isolated from *Swietenia macrophylla* King in Hook seeds shows *in vitro* anti-colorectal cancer activity through inhibition of mouse double minute 2 (MDM2) homolog. *Nat. Prod. Res*. Jul 14:1-8.
4. Mani, S., Kaur, A., Jakhar, K., Kumari, G., Sonar, S., Kumar, A., Das, S., Kumar, S., Kumar, V., Kundu, R., Pandey, A.K., Singh, U.P., and Majumdar, T. (2023) Targeting DPP4-RBD interactions by sitagliptin and linagliptin delivers a potential host-directed therapy against pan-SARS-CoV-2 infections. *Int J Biol Macromol*. Aug 1; 245: 125444; Published online 2023 Jun 27.
5. Chaudhary, S., Rai, R.N., Jyothi, D., Singh, U.P. (2023) Solid state synthesis, thermal, spectral, optical, crystal structure and atomic packing studies of 2-(3-Hydroxyphenyl)-2,3-dihydroquinazolin-4(1H)-one. *Materials Lett.* 341; 134253.

Conferences Attended

1. 14th Neuto Update Kolkata meeting, CSIR-IICB, Kolkata, 25-26 th November, 2023.
2. The 8th International Conference on Molecular Signalling and 4th CeSin Symposium CSIR-IICB Kolkata, 16-18 March 2023.
3. 20th All India Congress of Genetics and Genomic, CSIR-IICB, Kolkata, 24-25 January 2023.

Member of Society

1. Life member, Chemical Research Society of India (CRSI) (LM-1200)
2. Life member, Indian Crystallographic Association (ICA) (LM-196)
3. Life member, Society of Biological Chemists, India (SBC) (LM-4558)

Dr. Umesh Prasad Singh, Senior Principal Scientist
Group Members: Mr. Purna Chandra Pal, NIPER SRF; Mr. Abhishek Lahiri, CSIR-SRF; Ms. Deeti Jyothi, CSIR-GATE-SRF; Ms. Sudesna Das, CSIR-SRF; Mr. Santu Paul, CSIR-JRF
Collaborators: Dr. Rajkishor Rai, CSIR-IIIM, Jammu; Dr. Tanmay Majumdar, NII, Delhi; Dr. R.N. Rai, Dept of Chemistry, Institute of Science, BHU, Varanasi; Dr. Kalichamy Alagarasu, ICMR-NIV, Pune; Dr. Manoj Kumar, CSIR-IMTECH, Chandigarh

Dr. Upasana Ray and her group members

Designing a virus like particle with spike protein-based peptide antigen purified from bacteria displayed in a high-density repetitive manner

Research Activities

Aim of the project was assembly of bacteriophage based self assembling vaccine matrix coated with viral peptide-based antigen purified from bacterial source and attached on the matrix using split inteine attachment system.

SARS-CoV-2 is an enveloped virus. The viral structural proteins, the envelope proteins are not rigidly arranged as compared to non-enveloped viruses. Rigidly arranged multivalent display is important for potent immune stimulation. We assembled a chimeric a VLP wherein the core of the particle was composed of the coat protein of *Acinetobacter* phage and peptide-based antigen from receptor binding domain (RBD) of SARS-CoV-2 spike protein has been used for display on the phage coat based VLP matrix using spy-tag/spy-catcher split inteine conjugation system that allows spontaneous, irreversible isopeptide bond formation.

Both the matrix as well as peptide have been purified from bacteria which is an easy platform for protein purification. We used the closed state of spike trimer for epitope mapping as this is the conformation of the spike that the immune system visualizes unlike the open state that appears when the virus tries to attach to receptor. One of our VLPs could elicit anti-spike antibodies in mice. The work demonstrates that peptide-based antigens displayed in high densities can induce neutralizing antibody production unlike free peptide. Careful choice of peptides can deliver better candidates. Also, considering small size, accommodating mutations is easier. Production in bacteria offers cheaper and robust purification option.

Key highlights are as follows:

- A peptide-based antigen from SARS-CoV-2 receptor binding domain (RBD) linked to the AP205 Virus like particle (VLP) could induce

neutralizing antibodies in mice.

- Both the peptide and VLP matrix can be purified from bacterial source, thus, making the platform relatively inexpensive and easy to handle.
- Small size of the peptide antigen allows easy modification to generate variant specific peptide antigens.
- The purified SARS-CoV-2 spike protein was found to be able to enter host cells. Thus purified spike protein has been used to establish a proof-of-concept neutralization assay model using 293FT cells expressing the ACE2 protein which is non-hazarduous in nature.

Epitope mapping of spike RBD region was performed using online tools. 3 peptides were selected. Antigens selected were from region of spike that does not get glycosylated, hence bacterial expression of protein could be used.

Self-assembly of phage coat protein AP205 and spy-tag spy-catcher conjugation-based attachment of antigens was used to attach the peptide antigens on the VLP matrix core (Figure 1). TEM and Cryo-EM (Figure 2) were performed to establish VLP formation and quality. VLP particles were found to be undistorted and intact

Out of the three peptide-based VLPs, one (APP2) could elicit neutralizing IgGs.

Mice sera were tested for total IgGs, IgG profile, antibody avidity as well as neutralizing antibodies. To determine the relative proportions of different subclasses in APP2 immunised sera, we used ELISA based tool (Figure 4,5). As seen in Figure 4, the relative abundancy of each subclass are: IgG2a>IgG1>IgG2b>IgG3. Also, the IgG2a was found to compose 40.2% of total IgG vs IgG1 sharing 32.4% of total IgG. IgG2b and IgG3 formed 21.7% and 5.7% of total IgG respectively (Figure 5). Hence, the induced IgG response manifested class switching to IgG2a and IgG1 indicating a strong potential in triggering significant immune effector functions. Both ELISA based as well as cell culture based neutralization assays were performed. We have designed a purified spike protein based neutralization assay system (Figure 6) using 293FT cells. Anti-APP2 sera could prevent the entry of spike protein in the cells as detected by western blot assay using the cell lysate for spike protein (Figure 7).

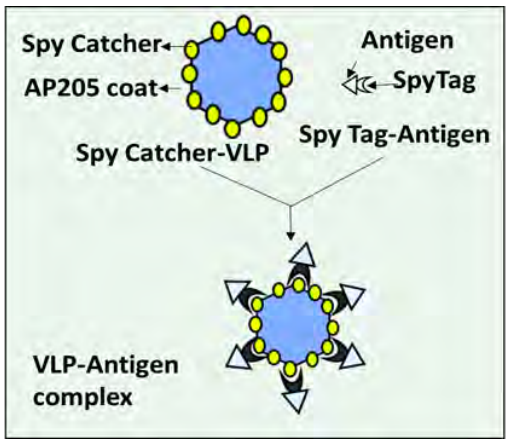


Figure 1: Schematic of VLP assembly

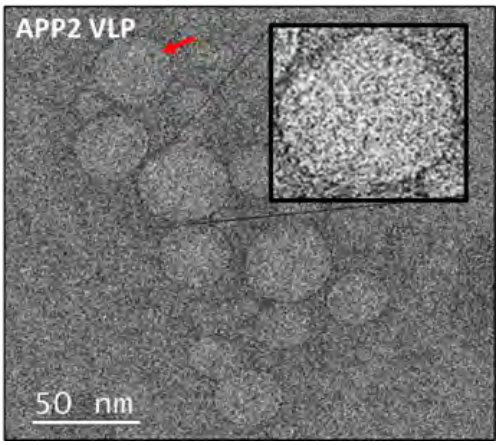


Figure 2: Cryo-EM image of APP2 VLPs

Mice based Immunization assay:

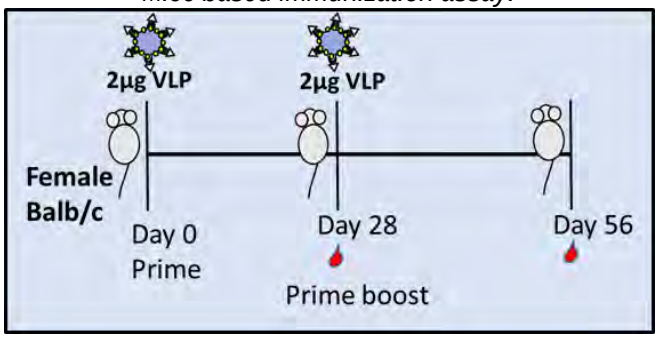
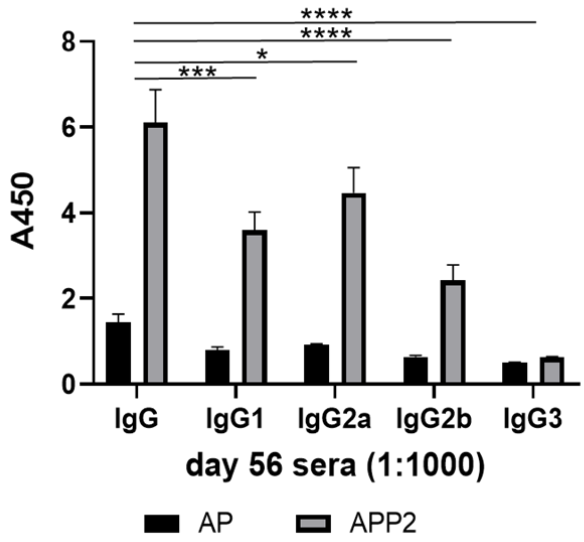


Figure 3: Schematic of Immunization schedule



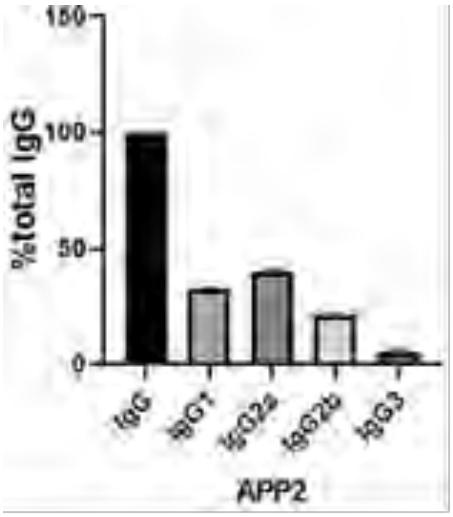
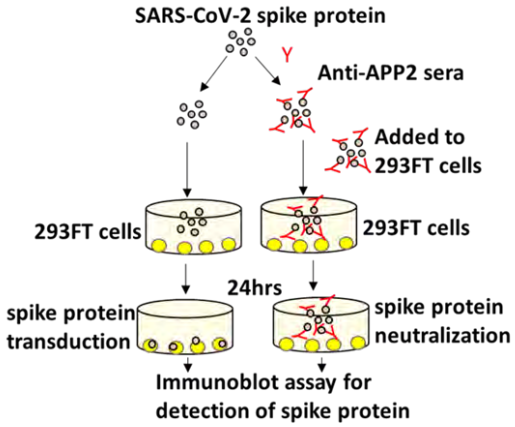


Figure 4 (left) and 5 (right): Antigen specific IgG subclass study to check for IgG1, IgG2a, IgG2b and IgG3 titres in the sera



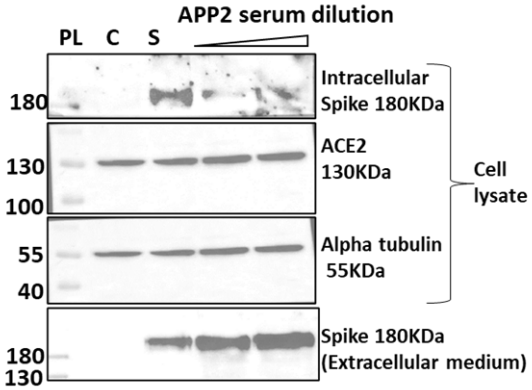


Figure 6. Design of neutralization assay system

Figure 7. Neutralization ass ay using anti- APP2 sera

Outcome of the work are as follows:

- Self assembled VLPs comprising of peptide purified from bacteria could generate neutralizing antibodies.
- Proof-of-concept non-infectious neutralization assay system
- Research paper (under 2nd revision)

In conclusion, the study suggests that peptide-based vaccine candidates can be effective when peptides are displayed in a multivalent, high-density manner on a higher order matrix. This approach enhances immune response compared to peptides in free form. The peptide antigen that elicited a strong IgG response was purified from bacteria, making it easy to handle. This vaccine design concept could be extended to other pathogens as well.

Future Research Plans

In future we plan to work with alternate assembly platforms and alternate split inteine systems.

Extramural / CSIR Funding

Part of the work was funded under CSIR project as follows:
Virus like particle-based vaccine against COVID-19, CSIR, 2020-2022, Rs 41 lakhs, MLP 144

Publications

Begum, F., Srivastava, A. K., Tripathi, P. P., Ray, U. (2023) A substrate for a cell free in vitro assay system to screen drugs targeting trypsin like protease-based cleavage of SARS-CoV-2 spike glycoprotein and viral entry. *J Med Virol* 95, e28796.

Patent

A recombinant construct for screening drugs against SARS-CoV-2 spike protein. Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava. Publication date: 4.5.2023, WO/2023/073733.

Book Chapters

Invited book chapter editor for a book by the Cameroon Academy of Young Scientists (CAYS). Chapters: 1) Indigenous knowledge without borders 2) Science diplomacy and international scientific cooperation

Invited Lectures

Viral Infections: Concepts and Safety Measures (A part of popular science lecture series). Invited by Indian National Young Academy of Science East Zone. Venue: Ramkrishnapur Balika Vidyalaya, Shibpur, Howrah, 8th December 2023.

Member of Society

1. Life member, Royal Society of Biology (RSB)
2. Member, Global Young Academy (GYA) (2022-2027)

Awards

1. Appointed as Ambassador of Royal Society of Biology (2023)
2. Featured under ‘Future Hopes’ in the book 'Vigyan Vidushi' - 75 Women Trailblazers of Indian Science, Vigyan Prasar (2023)

Dr. Upasana Ray, Principal Scientist
Group Members: Feroza Begum, CSIR-SRF; Sandeepan Das, CSIR-SRF; Md. Hasan Mallick, UGC-JRF; Subhadip Ghora, UGC-JRF
Collaborators: Prem Prakash Tripathi, Senior Scientist, CSIR-IICB, Kolkata

Molecular Genetics Division

This department has the mandates to identify mechanistic understanding of the importance of gene expression in regulation of mammalian cell physiology and its importance in disease pathogenesis. We are involved in mechanistic understanding of eukaryotic transcriptional regulatory mechanisms, long non-coding RNA-mediated regulation of gene expression and their implication in several cancer disease pathogenesis including various solid tumors as well as leukemia. Another area of research interest also involves around role of calcium signaling in pathogenesis of various plant diseases as well as salt resistance. Using a combination of basic and applied approaches, we will study the molecular basis of genetic disease and its probable therapy targeting diverse steps both in pre- and post-transcriptional events.

Dr. Ashok Kumar Giri

Targeting 'histone mark': Advanced approaches in epigenetic regulation of telomere dynamics in cancer

Research Activities

The integrity of telomeres is required for the maintenance of genomic stability and prevention of oncogenictransformation of cells. Recent evidence suggests the presence of epigenetic modifications as an important regulator of mammalian telomeres. Telomeric and subtelomericregions are rich in epigenetic marks that regulate telomere length through subtelomeric DNA methylation and telomerichistone modifications. Specific histone modifying enzymes (histone methyltrases and demethylases) play an integral role in forming telomeric histone codes necessary for maintaining the structural integrity for telomeres. Alterations of crucial histone moieties of histone modifiers regulate the subsequent changes inchromatinization of telomericDNA and may lead to cancerous outcomes. Herein, our review highlights the role of telomeric post-translational modifications of histones in relation to various diseases, especially cancer. The development of potential targeted epitherapeutic interventions in telomere deregulations is the key area of research that might provide new opportunities in the near future.

Association of ABCC4 G559T single nucleotide polymorphism with arsenic-induced precancerous hyperkeratosis.

Chronic arsenic toxicity, a global health issue, leads to multiple skin cancers. Only 15–20% of exposed individuals ever develop arsenic-specific skin lesions highlighting the role of genetic polymorphisms in inter-individual susceptibility. Multidrug resistance proteins (MRPs), encoded by ATP binding cassette transporter subfamily C (*ABCC*) genes are demonstrated to efflux arsenic metabolites. MRP4 encoded by *ABCC4* is a high-affinity efflux transporter of diglutathionylated monomethyl arsonous acid [MMA(GS)2] and dimethyl arsenic acid (DMAV). The association of ABCC4 polymorphisms with arsenicdisease susceptibility is unknown. The possible association of five previously characterized non-synonymous *ABCC4* SNPs with arsenic-induced premalignant hyperkeratosis was examined in the study. A total of 230 study participants were recruited from the highly arsenic-exposed district of Murshidabad in West Bengal, India (136 cases with arsenic-induced premalignant hyperkeratosis; 94 controls with no arsenic-specific skin lesions). Cases and controls were matched in exposure status and demographic variables apart from age. Exposure assessment was performed by total arsenic content analysis of water and urine, while genotyping was performed employing PCR-Sanger sequencing or PCR-RFLP. Our population was monomorphic for 4 of the 5 SNPs studied. Age-adjusted Odds ratio showed the presence of at least one T allele for *ABCC4* codon polymorphism confers protection against premalignant hyperkeratosis.

The probable reasons of arsenic susceptibility in a chronically exposed population of West Bengal.

Arsenic is potent human carcinogen which affects millions of people across the globe. Arsenic induced pre-cancerous and cancerous skin lesions are hall

marks of chronic arsenic toxicity. Even then, only 15%–20% of the population manifest arsenic-induced skin lesions but the rest do not, the reason for which in not very clear. Not only that, conjunctival irritations of the eyes, peripheral neuropathy and respiratory distress are the non-dermatological health effects which are often manifested in them in addition to the cancers of skin and other internal organs. In this work we have considered 233 arsenic exposed individuals with skin lesions and 205 arsenic exposed individuals without skin lesions from the highly arsenic affected Murshidabad district of West Bengal. We have compared arsenic exposure in the two groups through drinking water. Both the study groups have similar levels of arsenic exposure, drinking same arsenic laden water. Results show that higher amounts of arsenic were retained in the nails and hair of the skin lesion group compared to the no skin lesion group. Significant higher amounts of chromosomal aberration and micronucleus formation were found in the skin lesion group, than the no skin lesion group. Incidences of conjunctival irritations of the eyes, peripheral neuropathy and respiratory distress were much higher in the former group compared to the later. We, thus found that one group was more susceptible than the other, even with similar levels of arsenic exposure. We have tried to identify and discuss the probable reasons for this observation with reference to our previous works in the exposed population from West Bengal, India.

MicroRNA-129-5p-regulated microglial expression of the surface receptor CD200R1 controls neuroinflammation,

CD200R1 is an inhibitory surface receptor expressed in microglia and blood macrophages. Microglial CD200R1 is known to control neuroinflammation by keeping the microglia in resting state, and therefore, tight regulation of its expression is important. CCAAT/enhancer-binding protein β (CEBPβ) is the known regulator of CD200R1 transcription. In the present study, our specific intention was to find a possible posttranscriptional regulatory mechanism of CD200R1 expression. Here we investigated a novel regulatory mechanism of CD200R1 expression following exposure to an environmental stressor, arsenic, combining in silico analysis, in vitro, and in vivo experiments, as well as validation in human samples. The in silico analysis and in vitro studies with primary neonatal microglia and BV2 microglia revealed that arsenic demethylates the promoter of a microRNA, miR-129-5p, therebyincreasing its expression, which subsequently represses CD200R1 by binding to its 30-untranslated region and shuttling the CD200R1 mRNA to the cytoplasmic-processing body in mouse microglia. The role of miR-129-5p was further validated in BALB/c mouse by stereotaxically injecting anti-miR-129. We found that anti-miR-129 reversed the expression of CD200R1, as well as levels of inflammatory molecules IL-6 and TNF-α. Experiments with a CD200R1 siRNA-induced loss-of-function mouse model confirmed an miR-129-5p→CD200R1→IL-6/ TNF-α signaling axis. These main findings were replicated in a human cell line and validated in human samples. Taken together, our study revealed miR-129-5p as a novel posttranscriptional regulator of CD200R1 expression with potential implications in neuroinflammation and related complications.

Publication

1. Das, A., Giri, A.K., Bhattacharjee, P. (2024) Targeting 'histone mark': Advanced approaches in epigenetic regulation of telomere dynamics in cancer. *Biochim. Biophys. Acta Gene Regul. Mech.* 867, 195007
2. Giri AK, Banerjee N. (2024) The probable reasons of arsenic susceptibility in a chronically exposed population of West Bengal. *Mutat Res Genet Toxicol Environ Mutagen*. 894, 503725.
3. Sanyal, T., Ghosh, S., Giri, A. K., Leslie, E. M., Banerjee, M., Bhattacharjee, P. (2023) Association of *ABCC4* G559T single nucleotide polymorphism with arsenic-induced precancerous hyperkeratosis, *The Nucleus*.

Member of Society

- Environmental Mutagen Society of India
- Indian Science Congress Association
- All India Congress of Cytology and Genetics
- Indian Society of Human Genetics
- Society of Biological Chemists, India

Awards

- Elected as a Fellow of the Indian National Science Academy, New Delhi, with effect from 2013. Bahadur Shah Zafar Marg, New Delhi-110 002
- Elected as a Fellow of the National Academy of Sciences, India, from the year 2015. 5, Lajpat Rai Road, Mumfordganj, Prayagraj, Uttar Pradesh 211002

Dr. Ashok Kumar Giri, NASI-Senior Scientist
Collaborators: Pritha Bhattacharjee, PhD, University of Calcutta, Nilanjana Banerjee, PhD, Manovikas Kendra Rehabilitation and Research Institute for the Handicapped, Kolkata, Elaine M. Leslie, PhD University of Alberta Edmonton, Alberta, Canada, Debabrata Ghosh, PhD, CSIR-IITR

Dr. Debabrata Biswas and his group members

Understanding mechanisms of eukaryotic transcriptional regulation and leukemia development by MLL and MLL fusion partner proteins

Research Activities

Human MLL protein is a histone H3-K4 methyl transferase that is associated with transcriptional activation. Balanced chromosomal translocations between MLL and variety of MLL fusion partners (>80) give rise to both acute myeloid and lymphoid leukemia with two-year survival rate of <50%. Recently, attempts have been made towards understanding molecular mechanisms of action of MLL fusion partners and corresponding MLL fusion proteins in transcriptional regulation and leukemia development. These studies have suggested a unified mechanism of action of common MLL fusion partners in regulating transcription through their presence in a large multi-subunit Super Elongation Complex (SEC). However, mouse models of MLL fusion proteins suggest distinct mechanisms of action of individual MLL fusion proteins and corresponding leukemia development.

In support of this hypothesis, our earlier studies and few recent studies have shown that, in contrast to a large megadalton static complex, the MLL fusion partners form various sub-complexes with overlapping subunits for dynamic regulation of different steps of transcription. Further, few recent studies have also shown different requirement of MLL fusion partners (outside the context of SECs) for transcriptional regulation and leukemia development. Therefore, for better understanding of overall mechanisms of functional regulation and disease pathogenesis, more detailed analyses are required.

In our lab, we are currently exploring detailed mechanisms of action of few MLL fusion partners in transcriptional regulation that is both dependent and independent of SECs. Further, we would extend our studies towards exploring importance of these novel mechanistic understanding in MLL fusion-mediated leukemogenesis.

Aims and Objectives of our research are as follows:

- Detailed studies on role of human ZMYND8 protein in positive regulation of transcription
- Understanding of role of human TFIID complex in regulation of elongation control through promoter proximal pausing and its implication in temporal regulation of transcription during genotoxic stress

- Mechanistic understanding of role of human DBC1 protein in regulation of ELL functions within mammalian cells
- Temporal regulation of functions of SEC through post-translational modification of AFF1
- Mechanisms of regulation of transcription involving control of stability of P-TEFb complex components within mammalian cells

The following work has been achieved so far:

Degradation of CDK9 by ubiquitin E3 ligase STUB1 regulates P-TEFb level and its functions for global target gene expression within mammalian cells

Positive Transcription Elongation Factor b (P-TEFb) regulates expression of diverse sets of genes within mammalian cells that have implications in several human disease pathogeneses. However, mechanisms of functional regulation of P-TEFb complex through regulation of its stability are poorly known. In this study, we show an important role of C-terminus of Hsc70-Interacting Protein (CHIP aka STUB1) in regulation of overall level of CDK9 and thus P-TEFb complex within mammalian cells. STUB1 acts as a ubiquitin E3 ligase for proteasomal degradation of CDK9 involving N-terminal lysine 3 (K3) residue. Whereas, over-expression of STUB1 enhances, its knockdown reduces overall CDK9 degradation kinetics within mammalian cells. Interestingly, owing to the same region of binding within CDK9, CyclinT1 protects CDK9 from STUB1-mediated degradation. Factors that cooperatively bind with CyclinT1 to form functional complex also protects CDK9 from degradation by STUB1. Knockdown of STUB1 enhances CDK9 expression and thus P-TEFb complex formation that lead to global increase in RNA polymerase II CTD phosphorylation and transcriptional activation of diverse P-TEFb target genes. Thus, we describe an important functional role of STUB1 in regulation of transcription through modulation of overall level of P-TEFb complex formation within mammalian cells.

Future Research Plans

In future, majority of our research efforts would be directed towards addressing dynamic regulation of functional activity of different SEC factors during transcription-coupled DNA repair process. Especially we would like to focus more on regulation of SEC functional activity by various post-translational modification.

Extramural Funding (ongoing)

- *Mechanistic understanding of dynamic regulations of SEC functions during genotoxic stress-dependent global transcriptional inhibition and subsequent recovery for efficient DNA repair and cell survival.* Welcome Trust DBT India Alliance, 2023-28, 449.24 lakhs, (IA/S/22/1/506227).
- Mechanistic understanding of functional role of human TRIM28 and ELL in eukaryotic transcriptional regulation involving NELF complex. SERB, Department of Science & Technology (DST), 2023-26, 61.77 lakhs, (CRG/2022/000756).

Publications

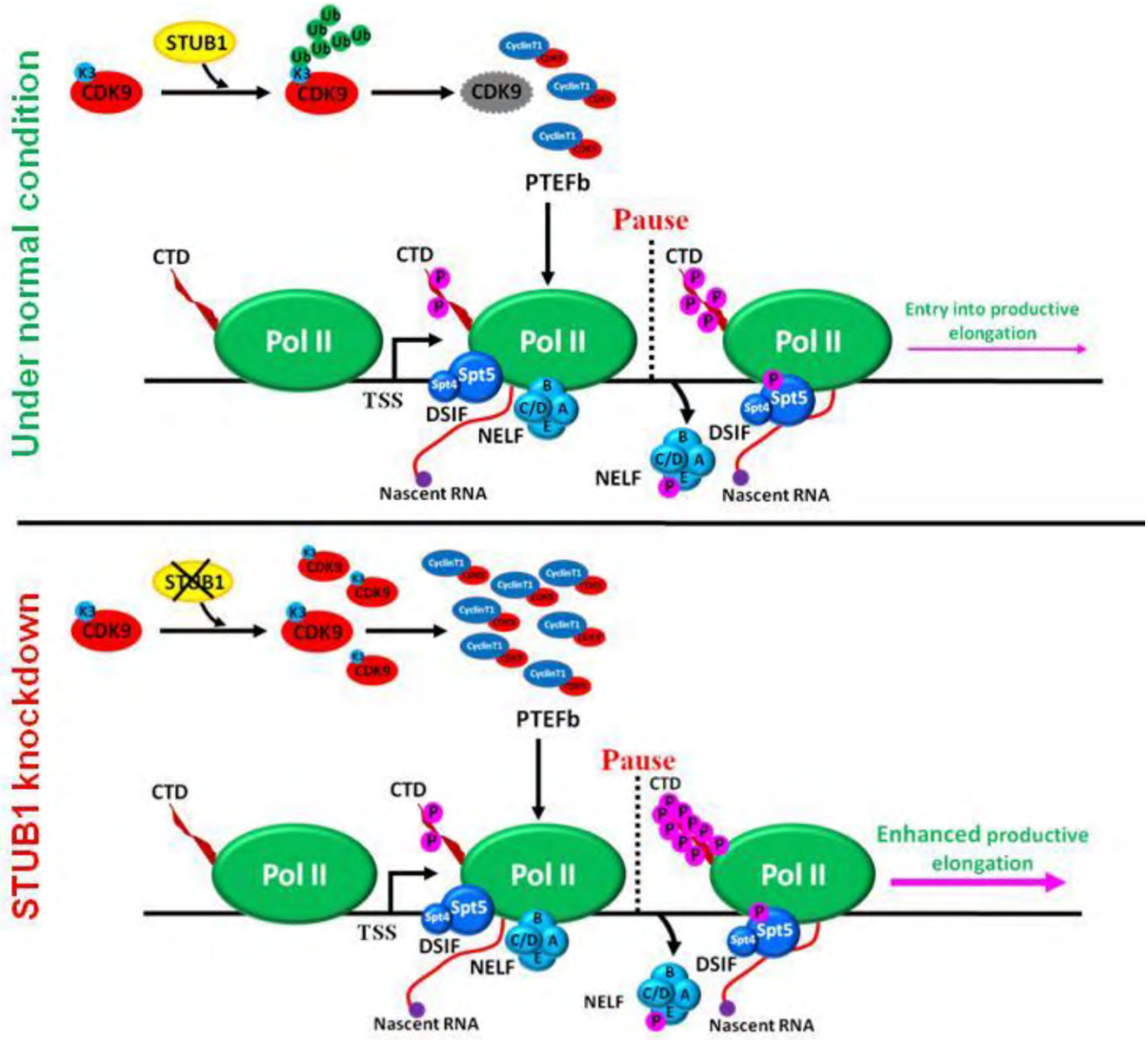
1. Nandy, A., Biswas, D. (2024) Basic techniques associated with studying transcription elongation both in vitro and in vivo within mammalian cells. *Methods* 221, 42-54
2. Basu, S., Nandy, A., Ghosh, A., Mall, DP., and Biswas, D. (2023) Degradation of CDK9 by Ubiquitin E3 Ligase STUB1 Regulates P-TEFb Level and Its Functions for Global Target Gene Expression within Mammalian Cells. *Mol Cell Biol*. 43, 451-471
3. Pal, S., Biswas, D. (2023) Promoter-proximal regulation of gene transcription: Key factors involved and emerging role of general transcription factors in assisting productive elongation. *Gene*. 878, 147571
2. Ghosh, A., Chakraborty, P., and Biswas, D. (2023) Fine tuning of the transcription juggernaut: A sweet and sour saga of acetylation and ubiquitination. *Biochim Biophys Acta Gene Regul Mech*. 866, 194944

Conferences attended

8th meeting of the Asian Forum for Chromosome and Chromatin Biology held at Jawaharlal Nehru Center for Advanced Scientific Research (JNCASR), Bangalore, from 4th-6th Nov, 2023.

Awards

Elected Fellow of the National Academy of Sciences, India (2024), awarded by NASI, 5, Lajpat Rai Road, Mumfordganj, Prayagraj, Uttar Pradesh 211002



Overall model of functional regulation of P-TEFb complex by STUB1 within mammalian cells

Overall model showing mechanisms of functional regulation of P-TEFb complex by STUB1 through regulation of level of CDK9 within mammalian cells. Under normal condition, STUB1-mediated ubiquitination of CDK9 at the key N-terminal lysine 3 (K3) residue maintains steady state level of CDK9 and thus P-TEFb complex for transcriptional activation of target genes. However, under reduced expression of STUB1, CDK9 level is increased that in turn also increases P-TEFb complex formation and its association with target protein complexes e.g. SEC. Enhanced formation of P-TEFb complex leads to global increase in Pol II CTD Ser2 and Ser5 phosphorylation resulting in enhanced productive elongation during the transcription cycle and thus causes increased expression of P-TEFb target genes.

Dr. Debabrata Biswas, Senior Principal Scientist
Group Members: Pamela Pal, JRF; Bakul Pal, JRF; Shrestha Mukhopadhyay, JRF; Sk. Anzar Hasnain, JRF; Prathama Talukdar, SRF; Arijit Nandy, SRF; Avik Ghosh, SRF; Poushali Chakraborty SRF; Ekjot Kaur Minhas, Project Assistant:
Collaborator(s): Dr. Benubrata Das, PhD, IACS, Kolkata; Dr. Kunal Rai, PhD, M. D. Anderson Cancer Center, Houston, Texas, USA

Dr. Smritisanjita Behera and her group members

Investigation of the early immune signal perception and regulation of plant immunity by sphingolipids during *Xanthomonas oryzae pv oryzae* (Xoo) infection in rice

Research Activities

Rice is the staple food of more than half of the world's population, and rice production in India is an important part of the national economy. Numerous pathogenic microorganisms cause rice diseases that lead to huge yield loss worldwide. For a reliable and affordable use of resistant cultivars, it is crucial to understand the molecular basis of plant host-pathogen interaction. Plants have two types of innate immunity. One is mediated by surface-localized pattern recognition receptors (PRRs). PPRs recognize pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs) and activate PRR-triggered immunity (PTI). The other one uses intracellular immune receptors that recognize virulence effectors secreted by pathogens and induce effector-triggered immunity (ETI) (Boller and Felix, 2009). PRRs recognize a wide range of ligands, including lipid, protein, nucleic acid, carbohydrate, etc. PAMPs such as bacterial flagellin, peptidoglycan, lipopolysaccharide, and fungal chitin are reported to be sensed by rice cells and trigger innate immunity. Due to the rapid evolution of the pathogens, resistant rice varieties also get infected after some years. Providing a robust and long-lasting resistance against Xoo is still a great challenge. In our lab, we have collected some susceptible rice varieties, some semi-resistant rice varieties, and two Indian isolates of Xoo. We are working to understand the basic immune pathway of rice against Xoo. We aim to find a solution to the existing challenge of providing broad-spectrum resistance against Xoo that would be a boon to our farmers.

We are currently addressing the following questions

- What are the important apoplastic players that help the survival of the resistant rice varieties during infection by Xoo?
- What are the dynamics of the Ca^{2+} signal during Xoo infection in rice? Do calcium signal and NADPH oxidase (OsRboh) together orchestrate the immunity against Xoo at the early stage of infection in rice?
- How microdomain dynamics play a role in pathogen perception in plants.

Some of the findings are as follows:

- Xoo OMVs elicit calcium signals in both the root

and leaf of *Arabidopsis thaliana*.

- Xoo OMVs internalize into the plasma membrane of the host plant (rice).
- E. coli OMVs cannot internalize into the plasma membrane of rice as efficiently as pathogen Xoo.
- Both Xoo and E. coli OMVs induce elevation of lipid order of the rice root plasma membrane.
- Lipid order increase in CR dhan in response to Xoo and E. coli OMV treatment are significantly different.

Future research plan

In the future, we would like to identify the content of Xoo OMV and understand the role of Xoo OMV in evoking an immune response in rice. This finding will be helpful in developing a strategy for a transgene-free approach to provide resistance against pathogenic bacteria.

Extramural funding

"Investigation of the regulation of plant immunity by sphingolipids in rice", Start-up research Grant, SERB, Department of Science and Technology (DST), 2022-24, 27.7 Lakh, (SRG/2022/00229)

Publications

1. Mittal, D., Gautam, J. K., Varma, M., Laie, A., Mishra, S., Behera, M., Vadassery, J. (2023). External jasmonic acid isoleucine mediates amplification of plant elicitor peptide receptor (PEPR) and jasmonate-based immune signalling. *Plant Cell Environ*. Accepted

Conferences attended

- Presented a poster in the Regional Young Investigators' Meeting held at, Presidency University, New Town, Kolkata, held on 6-8th December 2023
- Delivered an invited lecture in the National Symposium on "Plant Biology in the Post-Genomic Era: Strategies for Crops and Mankind," Organized by the Department of Biotechnology & Department of Microbiology, Sister Nivedita University, Kolkata. held on 8th and 9th February 2024.

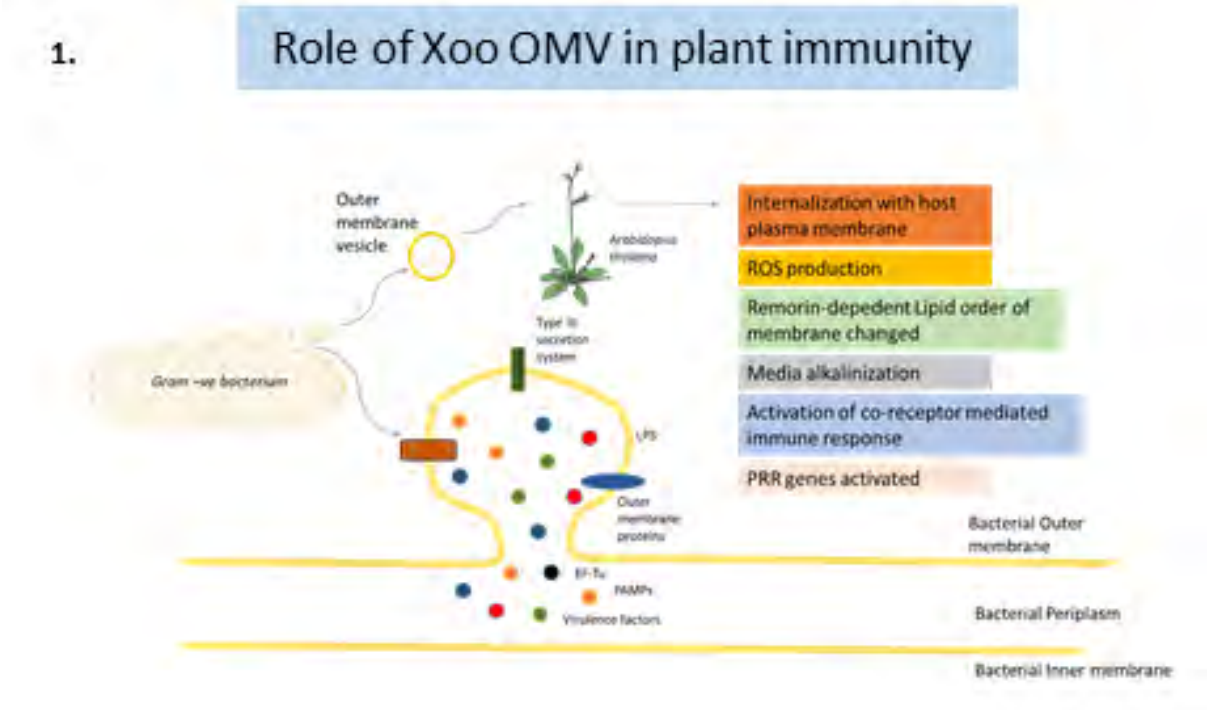


Figure 1: Overview of the reported role of *Xanthomonas oryzae pv oryzae* OMV

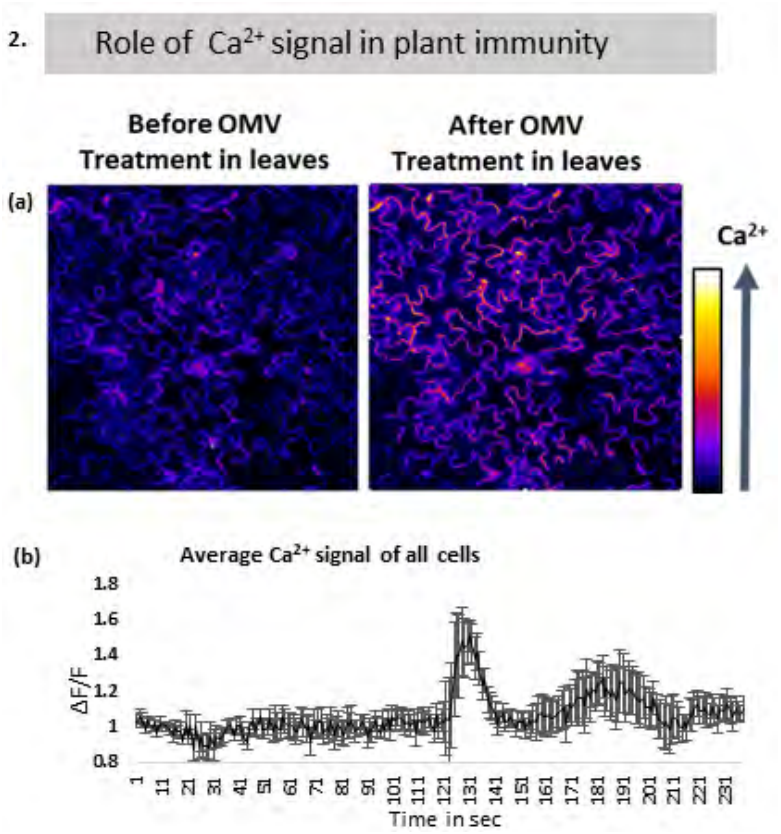


Figure 2: OMV-induced Ca^{2+} signals in Arabidopsis leaves expressing the genetically encoded Ca^{2+} indicator RGECO1 (a) The change in Ca^{2+} concentration plotted over time (b)

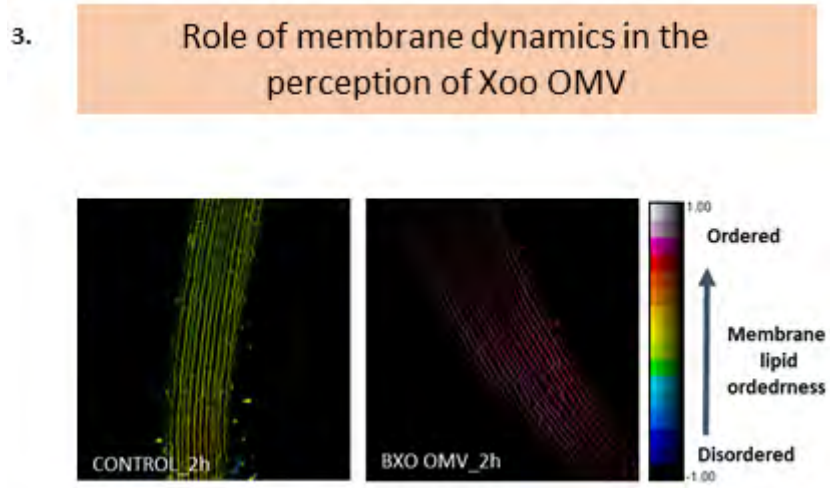


Figure 3: *Xanthomonas oryzae pv oryzae* OMV induced change in membrane lipid order

Dr. Smrutisanjita Behera, Scientist
Group Members: Ishani Mondal, UGC-JRF; Sandeep Barman, UGC-JRF; Hrimeeka Das, UGC-JRF; Ritu Chaterjee, project JRF
Collaborators: Dr. Sucheta Tripthy, Senior Principal Sciensist, CSIR-IICB, Kolkata, Jyothilakshmi Vadassery, Scientist V, National Institute of Plant Genome Research (NIPGR)

Organic and Medicinal Chemistry Division

The Organic and Medicinal Chemistry (OMC) Division at CSIR-Indian Institute of Chemical Biology comprises dedicated scientists with diverse expertise spanning synthetic organic chemistry, catalysis, chemical biology, medicinal chemistry, natural product chemistry, and supramolecular chemistry. The division's strength lies in its heterogeneity, bringing together scientists from various fields under one roof, enabling IICB to tackle scientific problems from multiple perspectives. These scientists play a crucial role in initiating numerous research activities aimed at addressing pressing biological, environmental, and chemical issues facing the nation. Actively involved in developing green chemical processes and technologies, the division contributes to enhancing self-sustainability in Indian pharmaceutical, agricultural, and chemical industries. Additionally, through symbiotic collaboration between chemists and biologists, the division addresses biomedical challenges, contributing to the vision of a healthier India.

Dr. Arindam Talukdar and his group members

Target Based Design, Synthesis, Development and Validation of Novel Small Molecules Modulators against Auto-Immune Disorders, Cancer, Metabolic and Neglected Tropical Diseases

Research Activities

Development of Antiviral agents against COVID-19: As a part of Antiviral Mission of CSIR, our lab has set up a drug discovery platform on antivirals and created a Pan-CSIR screening facility at CSIR-IICB. Moreover, several drug candidates are being developed as entry-inhibitors of SARS-CoV-2.

Design and development of novel small molecules ameliorating Non alcoholic Steatohepatitis (NASH): Nonalcoholic fatty liver disease (NAFLD) is the most chronic liver disease in which >5% steatosis has occurred in the absence of significant alcohol consumption, monogenic hereditary disorders, and steatogenic medications. Also, it is strongly associated with type 2 diabetes and obesity. NAFLD is subdivided into two classes based on histological outcome. There are no current therapeutics to prevent NASH. Our lab is mainly focusing on novel small molecules as a therapeutic intervention for NASH in a rational way starting with Quinazolinediones and Quinazolinones cores. We have filled two patents and one publication in ACS Journal of Medicianl Chemistry on the molecules from these cores.

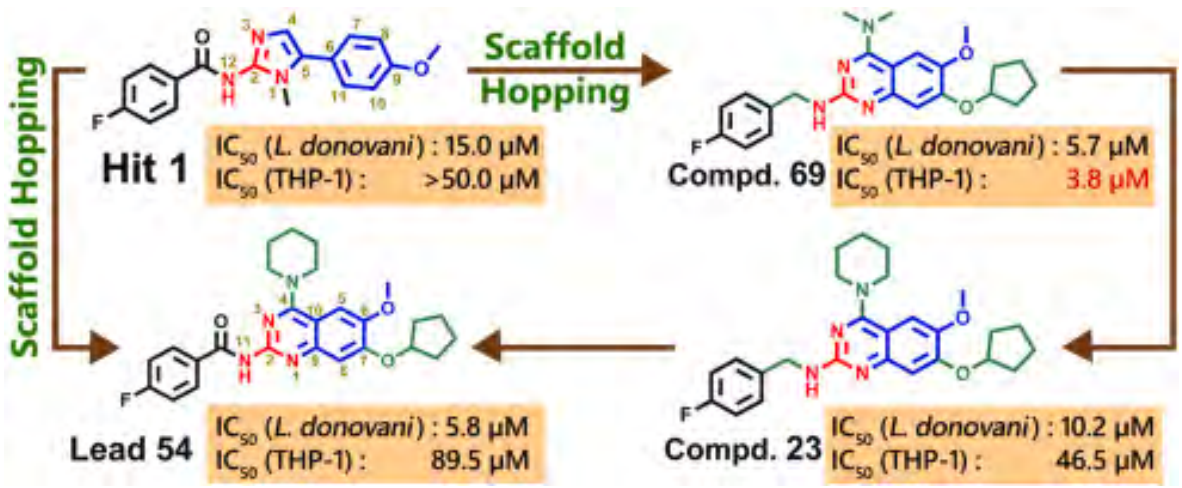
Development of new drugs for Leishmaniasis: Leishmaniasis is a disease caused by parasites of the Leishmania type which is spread by the bite of certain types of sandflies. Most prominently it can be observed on underdeveloped areas specially in Africa, Brazil, Nepal, and Bangladesh. In India Bihar, Jharkhand, UP, West-Bengal are the prevalent area for this disease. So our lab is focused on curing this traumatic disease by designing the small molecules in a rationalized way. I've set up a bilateral collaboration between IICB, Monash University, and

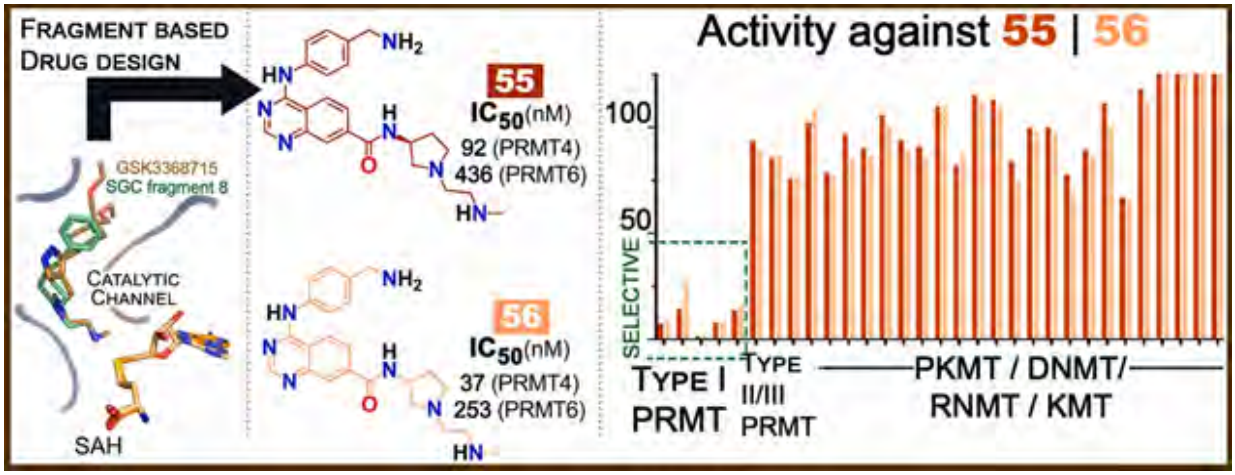
the University of Melbourne, Australia to develop new drugs for Leishmaniasis. A grant was approved under the Australia-India Strategic Research Fund (AISRF) (Indo-Australian Biotechnology Fund stream to the Department of Biotechnology, Government of India. It culminated in a publication in European Journal of Medicinal Chemistry.

Development of small molecules to modify epigenetic enzymes: The main focus is to perform structure-based design and synthesis of small-molecule regulators of epigenetics modifying enzymes such as histone methyltransferases (HMT) as tools to unravel the complex biology of epigenetics and contribute towards epigenetic-based drugs for the treatment of a number of diseases such as cancer, autoimmunity, diabetes, or neurological disorders. From an international collaboration with Structural Genomics Consortiun, Canada, several potent candidates have been developed.

Future Research Plans

Targeting mechanosensitive membrane channels to activate T-cells: Piezo1, a mechanosensitive ion channel, conducts membrane tension to flow of Ca+ ions into the cells. Hardly one or two agonists are available, which can open the Piezo1 channel of T cells, even without external force, in turn activating the cells. We developed Yaddle1, an agonist with comparable activity and better solubility, with prospects as vaccine – adjuvant.





Extramural / CSIR Funding

1. Design and Development of Selective inhibitors of protein arginine methyltransferase 1 involved in epigenetic modifications Start Year: February 2020. End Year: August 2023. Core Research Grant-CRG/2019/000853. DST-SERB. Rs 4172428. (PI)
2. Antiviral Mission CSIR: Discovery & Pre-clinical Development of Antivirals for COVID-19 & other diseases. CSIR Mission Mode project. Rs 2,47,00,000. (Nodal)
3. Non-alcoholic Fatty Liver Disease (NAFLD): Novel Pathogenetic mechanism and therapeutic development. CSIR, 2020-25, 490 lakh, MLP-138 (Co-PI)

Publications

1. Das, N., Roy, J., Patra, B., Saunders, E., Sarkar, D., Goon, S., Sinha, B.P., Roy, S., Roy, S., Sarif, J., Bandopadhyay, P., Barik, S, Mukherjee, S., McNamara, N., Varghese, S., Simpson, K., Baell, J., McConville, M., Ganguly, D.*, Talukdar, A*. (2024). Hit-to-lead optimization of 2-aminoquinazolines as anti-microbial agents against Leishmania donovani. European Journal of Medicinal Chemistry. 269, 116256.
2. Sarkar, D., Chowdhury, S., Goon, S., Sen, A., Dastidar, U.G., Mondal, M.A., Chakrabarti, P.*, Talukdar, A *. (2023). Discovery and Development of Quinazolinones and Quinazolinediones for Ameliorating Nonalcoholic Fatty Liver Disease (NAFLD) by Modulating COP1-ATGL Axis. Journal of Medicinal Chemistry. 66, 24, 16728.
3. Talukdar, A. *, Sarkar, D. (2023). Catalyzing the Future of Medicinal Chemistry Research in India. Journal of Medicinal Chemistry (Editorial). 66, 16, 10868. https://doi.org/10.1021/acs.jmedchem.3c01304
4. Bhattacharya, D., Shi Ming, L. A., Paul, B., Ghosh, D.U., Santhakumar, V., Sarkar, D., Chau, I., Li, F., Ghosh, T., Vedadi, M., Talukdar, A *. (2023). Development of selective class I protein arginine methyltransferase inhibitors through fragment-based drug design approach. European Journal of Medicinal Chemistry. 260, 115713.

Patents

1. Indole based small molecule antivirals against SARS-COV-2. Arindam Talukdar, Israful Hoque, Binita Patra, Nirmal Das, Krishan Gopal Thakur, Rajesh Ringe, Nittu Singh, Akshay Joshi, Ravneet Singh Chawla. Application No. 202411023758, Filing date 26/03/2024, 0216NF2023
2. Agonism-antagonism In Endosomal TLRs By Modulating Chemical Features In 8-oxopurine: Process For Preparation And Application Thereof. Arindam Talukdar, Dipyaman Ganguly, Dipika Sarkar, Shrestha Pattanayak, Uddipta Ghosh Dastidar, Purbita Bandopadhyay, Bishnu Prasad Sinha, Shreya Roy, Jafar Sarif, Ranit D. Rozario, Trisha Ghosh, Rimica Das. Application No. 202411016656 Filing date 07/03/2024, 0030NF2024
3. Purine based small molecule modulators for PPARγ in ameliorating non-alcoholic fatty liver disease: Preparation and application thereof. Arindam Talukdar, Partha Chakrabarti, Sunny Goon, Dipayan sarkar, Sujay Krishna Maity, Avinil Dassharma, Debomita Bhattacharya, Soupayan Pal, Himadri Sekhar Sarkar. Filing date: 05/12/2023, 0217NF2023.
4. Small molecules for Adoptive T-cell therapy (ACT) through activation of the mTOR signalling pathway, preparation and use thereof. Arindam Talukdar, Shilpak Chatterjee, Sunny Goon, Dipika Sarkar, Puspendu Ghosh, Uddipta Ghosh Dastidar, Trisha Ghosh. Application No. 202311034981, Filing date: 18/05/2023, 0075NF2023
5. PROTACS for Ask1 Protein Degradation: Preparation and Use Thereof. Arindam Talukdar, Himadri Sekhar Sarkar, Partha Chakrabarti, Israful Hoque, Abhishek Sen, Uddipta Ghosh Dastidar, Anindita Dey. Application No: 202311034982. Filing date 18/05/2023, 0076NF2023.

Invited Lectures

1. A Chemical Switch for Agonism-Antagonism Transformation in Toll-like Receptor 7: Lead Optimization Towards Potent Dual TLR7/9 Antagonist Against Psoriasis. Frontier in Organic Chemistry Symposium-V. Biocon Bristol Myers Squibb Research & Development Center (BBRC), Bangalore, 12 September 2023.
2. Fragment-based Drug Discovery of Potent and Selective Type I Protein Arginine Methyltransferase (PRMT) Inhibitors. 8th Asian forum for Chromosome and Chromatin Biology, JNCASR, Bangalore. 4th-6th November 2023
3. Activity Guided Rational Design, Synthesis and Lead Optimization of Purine Based Dual Toll-Like Receptor 7 and 9 Antagonists Against

Psoriasis. Annual Convention of Chemists ACC-2023, IIT Delhi. 20-21st December 2023.

4. Academic drug discovery as a way for affordable drugs. National Science Day: Accelerating drug discovery and development in India using indigenous technologies through collaborations between academia, industry, and government institutions. Sun Pharma Gurgaon, 28 Feb 2024.

Conferences Attended

1. Frontier in Organic Chemistry Symposium-V. Biocon Bristol Myers Squibb Research & Development Center (BBRC), Bangalore, 12 September 2023
2. 8th Asian forum for Chromosome and Chromatin Biology, JNCASR, Bangalore. 4th-6th November 2023
3. Annual Convention of Chemists ACC-2023, IIT Delhi. 20-21st December 2023.
4. National Science Day: Accelerating drug discovery and development in India using indigenous technologies through collaborations between academia, industry, and government institutions. Sun Pharma Gurgaon, 28 Feb 2024

Member of Society

Life member, Chemical Biology Society of India.

Dr. Arindam Talukdar, Senior Principal Scientist

Group Members: Dipayan Sarkar, SRF; Debomita Bhattacharya, SRF; Dipika Sarkar, SRF; Binita Patra, SRF; Israful Hoque, SRF; Anindita Dey, JRF; Soupayan Pal, GATE JRF; Rimica Das, JRF; Uddipta Ghosh Dastidar, Project Associate II; Sunny Goon, Project Associate II; Trisha Ghosh, Project Associate II; Nirmal Das, Project Associate I; Himadri Sekhar Sarkar, Postdoctoral Research Associate

Collaborators: Dr. Dipyaman Ganguly, Principal Scientist, Cancer Biology & Inflammatory Disorder, CSIR IICB; Dr. Partha Chakrabarti, Principal Scientist, Cell Biology & Physiology, CSIR IICB; Dr. Shilpak Chatterjee, Senior Scientist, Cancer Biology & Inflammatory Disorder, CSIR IICB; Prof. Jonathan Baell, Monash University, Australia; Prof. Malcolm McConville, University of Melbourne, Australia; Prof. Masoud Vedadi, Structural Genomics Consortium, Canada

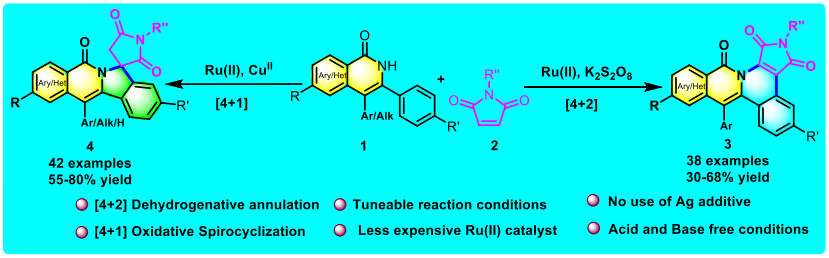
Dr. Biswadip Banerji and his group members

Design, Synthesis of 'New Molecular Entities' by Novel Methodologies Exploiting Late-stage C-H Activation Strategy and Their Efficacy Studies

Research Activities

Ru(II) Catalyzed Oxidative Dehydrogenative Annulation and Spirocyclization of Isoquinolones with N-Substituted Maleimides

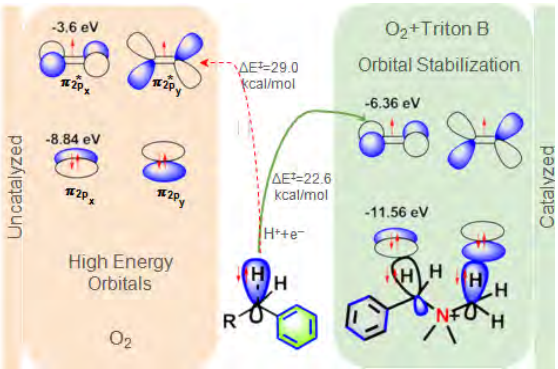
Ruthenium(II) catalyzed additive-free oxidative, dehydrogenative annulation of different malemides on 3,4-disubstituted isoquinolone to afford fused and spiro-cyclized isoquinolo-isoquinolone and isoindolo-isoquinolone derivatives is reported here. By simply changing solvent and oxidizing agents, under two different conditions, it produced two different poly-*N*-heterocyclized products. Isoquinolone-NH was strategically used as the internal directing group in the ortho C−H activation using Ru(II) catalyst. Mechanistically dehydrogenative, oxidative C−C followed by C−N cross-coupling and aza-Michael reaction pathway led to the corresponding fused and spiro-products, respectively. A diversified library of eighty-one (81) such two valuable products were synthesized by employing this methodology. Drug-like this diverse library of molecules is planned to be screened against different cancer cell lines in the future.



Ref: Advanced Synthesis & Catalysis, 2024, doi.org/10.1002/adsc.202300963.

Metal-Free Activation of Molecular Oxygen by Quaternary Ammonium-Based Ionic Liquid: A Detail Mechanistic Study

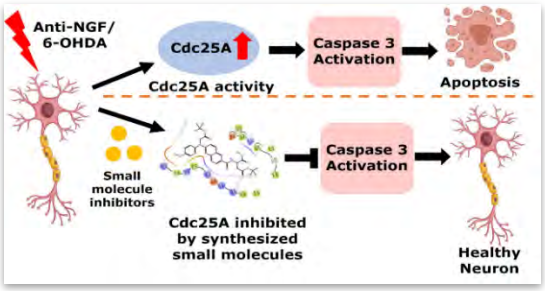
Oxidation is a very common chemical and biological process and often requires transition metals as catalysts. However, a recent trend in redox chemistry is the use of the metal-free processes to oxidize common reagents. Herein we have developed a detailed mechanistic study of metal-free oxygen (O_2) activation protocol on benzylamine/alcohols using simple quaternary alkylammonium-based ionic liquids to produce products such as amide, aldehyde, imine, and in some cases, even aromatized products. The reaction mechanism, involved the conversion of molecular oxygen into a hydroperoxyl radical via a proton-coupled electron transfer process. Furthermore, first-principles calculations using density functional theory (DFT) revealed that reaction coordinates and transition state spin densities have a unique spin conversion of triplet oxygen leading to formation of singlet products via a minimum energy crossing point. Next, domain-based local pair natural orbital coupled cluster, (DLPNO–CCSD(T)), and complete active space self-consistent field, CASSCF(20,14) methods complemented the above findings. Partial density of states analysis showed stabilization of π* orbital of oxygen in the presence of ionic liquid (Triton B), making it susceptible to hydrogen abstraction in a mild, metal-free condition. The current results described the origin of O_2 activation within the context of molecular orbital (MO) theory and opened up a new avenue for the use of ionic liquids as inexpensive, multifunctional and high-performance alternative to metal-based catalysts for O_2 activation.



Ref: Journal of the American Chemical Society. 2024, 146 (10), 6912-6925.

Small-Molecule Cdc25A Inhibitors Protect Neuronal Cells from Death Evoked by NGF Deprivation and 6-Hydroxydopamine

Alzheimer's disease (AD) and Parkinson's disease (PD) are the most common neurodegenerative diseases that are presently incurable. There have been reports of aberrant activation of cell cycle pathways in neurodegenerative diseases. In the present study, we have synthesized a small library of molecules targeting Cdc25A and tested their neuroprotective potential in cellular models of neurodegeneration. Several of these small-molecule inhibitors significantly prevented neuronal cell death induced by nerve growth factor (NGF) deprivation and 6-hydroxydopamine (6-OHDA) treatment. Lack of NGF signaling leads to neuron death during development and has been associated with AD pathogenesis. The NGF receptor TrkA has been reported to be downregulated at the early stages of AD, and its reduction is linked to cognitive failure. 6-OHDA, a PD mimic, is a highly oxidizable dopamine analog that can be taken up by the dopamine transporters in catecholaminergic neurons and can induce cell death by reactive oxygen species (ROS) generation. Some of our newly synthesized molecules inhibit Cdc25A phosphatase activity, block loss of mitochondrial activity, and inhibit caspase-3 activation caused by NGF deprivation and 6-OHDA. Thus, Cdc25A inhibition could be a therapeutic possibility for neurodegenerative diseases, and these Cdc25A inhibitors could be effective treatments for AD and PD in the future.

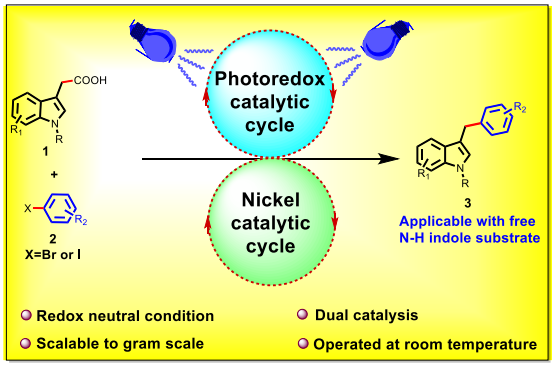


Ref: ACS Chem. Neuroscience, 2023, 14, 7, 1226–1237

Merging Photoredox with Nickel Catalysis for Decarboxylative Arylation of Indole-3-Acetic Acids with Aryl Halides

Late-stage functionalization of indoles can be a valuable strategy for modifying different existing indolyl-drugs and natural products to get their new analogues. This study reports the photoredox-metal catalyzed decarboxylative arylation strategy of

indole-3-acetic acids with aryl halides. Here, photoredox-catalysis was synergistically merged with nickel-catalysis to synthesize biologically important 3-benzyl indoles with good functional group tolerance.



Ref: ChemPhotoChem. 2024, e202300338

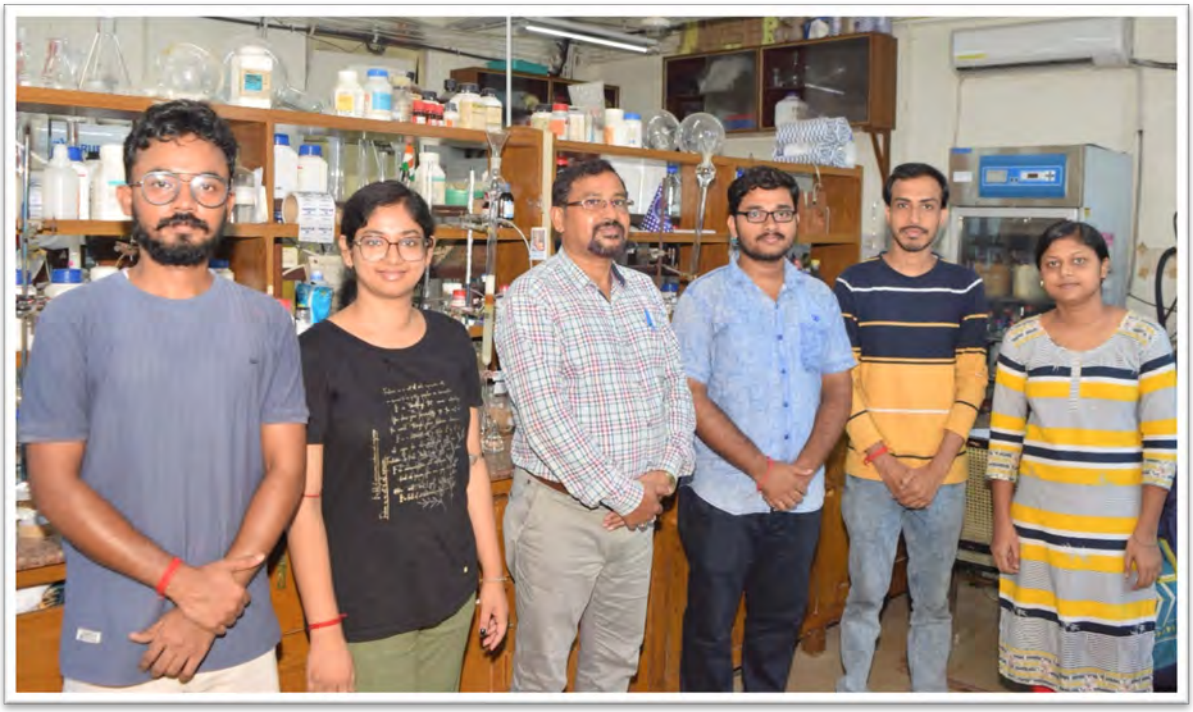
Future Research Plans

The future research endeavors from my group will be mainly focused on the following areas like photo-redox chemistry, CO2 fixation to generate high-value chemicals, metal-catalyzed late stage C-H activation protocol to synthesize NCEs, Biomarkers/sensors, therapeutic intervention to diseases by SAR-based new inhibitors synthesis & their evaluations etc.

Publications

1. Adhikary, S and Banerji, B. (2012) Iodine Mediated One-Pot Synthesis of Polyarylated-Oxazoles from Internal Alkynes. ChemistrySelect. e202300076.
2. Pramanik, S. K., Sanphui, P., Das, A. K., Banerji, B and Biswas, S. C. (2023) Small-Molecule Cdc25A Inhibitors Protect Neuronal Cells from Death Evoked by NGF Deprivation and 6-Hydroxydopamine; ACS. Chem. Neuroscience. 14, 7, 1226–1237.
3. Vijay, B. P., Manna, A., Srinath, R., Adhikary, S and Banerji, B. (2023) Pd-Catalyzed Regioselective Domino C−C Bond Formation to Access N-Fused Benzimidazo-Indolo-Isoquinoline Heterocycles,; Eur. Jour. Org. Chem., 26, 28, e202300256.
4. Seal, K. and Banerji, B (2024) Ru(II) Catalyzed Oxidative Dehydrogenative Annulation and Spirocyclization of Isoquinolones with N-Substituted Maleimides; *Adv. Syn. Catal*, doi.org/10.1002/adsc.202300963.
5. Guin, A., Bera, S., Pathi, V. B. and Banerji, B (2024) Merging Photoredox with Nickel Catalysis for Decarboxylative Arylation of Indole-3-Acetic Acids with Aryl Halides; *ChemPhotoChem*. e202300338.
6. Khamaru, K., Pal, U., Shee, S., Lo, R., Seal, K. Ghosh, P., Maiti N. C. and Banerji., B (2024) Metal-free Activation of Molecular Oxygen by Quaternary Ammonium-based Ionic Liquid: A Detail Mechanistic Study.; *J. Am Chem. Soc*. 146 (10), 6912-6925.

Dr. Biswadip Banerji, Chief-Scientist
Group Members: Abhyuday Guin, SRF; Krishnendu Khamaru, SRF; Vijay Pathi Babu, SRF; Debabrata Sarkar, SRF; Subhankar Shee, SRF; Arindam Manna, SRF; Kaushik Seal, SRF; Asikul Sk, SRF; Arpan Adhikary, SRF



Dr. Chinmay Chowdhury and his group members

Synthesis of Novel Heterocycles of Biological Interests

Research Activities

The quinoline nucleus is considered as a privileged structural motif, constituting the core structure of a large number of natural products, pharmaceuticals, and agrochemicals in addition to its considerable use in the development of OLEDs, catalysts, and ligands for asymmetric synthesis. Consequently, synthesis of quinolines has always been an active area of research since the publication of *Skraup synthesis* in 1880. Among the various derivatives, 4-substituted quinolines, which have received immense interest soon after the discovery of quinine, are used as template for the development of various types of drugs. Surprisingly, 4-vinyl-quinolines are less explored despite their presence in pharmacologically active substances (e.g., $PI3K_{\alpha}$ inhibitors) and dyes (e.g., ethyl red) as compared to 2-vinylquinolines which proved to be important in various bioactive agents including drugs (e.g., *Montelucast*).

On the other hand, 2*H*-Chromenes also claim attention because of their presence as core structure in a large number of natural products, bioactive agents and others compounds having applications in material sciences. Due to their significant importance, extensive studies have been made for the constructions of 2*H*-chromenes.

In addition, among various nitrogen heterocycles α-carbolines are considered as privileged structural motifs in medicinal chemistry. Thus *mescengricin* acts as a neuronal cell protecting agent, *grossularines* exhibit anticancer activity, and *implitamide* is used to treat atherosclerosis; other members are reported to inhibit CDK-1, CDK-5 and GSK-3 kinases. In addition, α-carboline based thiophene derivatives find applications in organic semiconductors, thin-film transistors and phosphorescent light emitting devices.

The aforesaid fact underlines the necessity of convenient and practical methods for the general synthesis of 4-substituted quinolines and chromenes, and α-carbolines.

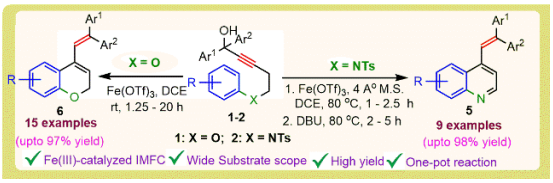
Aims and Objectives:

1. Development of a straightforward and general synthesis of 4-(2,2-Diarylvinyl)- quinolines and 4-(2,2-diarylvinyl)-2*H*-chromenes through iron(III)-catalyzed reactions.
2. Synthesis of 2- and 4-substituted α-carbolines via [3+3]-annulations of tosyliminoindolines with α, β-unsaturated aldehydes under palladium catalysis.
3. Synthesis of 14-aryloxy analogs of andrographolide derivatives to check their

efficacy against SARs-COV-2.

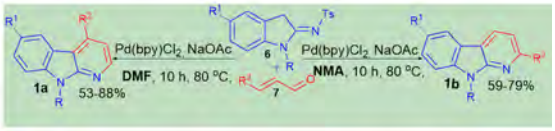
Work Progress:

We have acheived an efficient method for the general synthesis of 4-(2,2-diarylvinyl)quinolines 5 through iron(III)-catalyzed carboannulations of homopropargyl amines 1 (Scheme 1). Replacing the substrates 1 by ether derivatives 2 and employing the same catalyst led to the formations of 4-vinyl substituted 2*H*-chromenes 6 at room temperature and produced water as the only by-product thus tracing a green path. A plausible reaction mechanism has been proposed to explain the product formations. Moreover, the high yields (up to 98%) achieved using simple substrates, environmentally benign low-cost catalyst, and less hazardous reaction conditions makes the methodology inherently attractive.



Scheme 1: Iron(III)-catalyzed synthesis of 4-(2,2-Diarylvinyl)quinolines 5 and 4-(2,2-diarylvinyl)-2H-chromenes 6

In addition, we have described a palladium catalyzed cyclocondensation reaction of tosyliminoindolines 6 and α, β-unsaturated aldehyde 7 resulting in the synthesis of α-carbolines 1a and 1b having substituents at C4 and C2, respectively (Scheme 2). The nature of the solvent determines the regioselectivity of the reaction, directing the alkenylation to either C3 or NTs group attached to C2-position of 6. Mechanistically, this cascade reaction proceeds through either *carba*-Michael (in DMF) or *aza*-Michael (in NMA) pathway followed by intramolecular cyclization of the intermediate. A preliminary photo-physical study on selected products has also been achieved; few α-carbolines displayed significant absorbance and emission properties.



Scheme 2. Palladium catalyzed synthesis of 4- and 2-substituted α-carbolines (1a and 1b)

Future Research Plans

1. Development of convenient method for the synthesis of benzofuro[3,2-b]pyrroles and benzofuro[3,2-b]indoles via palladium-catalyzed 5-exo-dig cyclizations of acetylenic substrates followed by DDQ mediated dehydrogenative Diels-Alder reactions.
2. Palladium-catalyzed straightforward method for indolo[3,2-b]indoles and pyrrolo[3,2-b]indoles.
3. Synthesis of 14-aryloxy analogs of andrographolide derivatives to check their efficacy against SARs-COV-2.

Extramural / CSIR Funding

1. Discovery and preclinical development of anti-virals for covid-19 and other diseases (CSIR, HCP-41).
2. Pan-CSIR cancer research program: Making cancer care affordable empowering women health focussing on breast and gynaecological cancer of Indian relevance (CSIR, HCP-40).

Publications

1. Dey, S. and Chowdhury, C. (2023) Metal-catalyzed straightforward and practical method for the synthesis of 4-(2,2-diarylvinyl)quinolines and 4-(2,2-diarylvinyl)-2*H*-chromenes using Fe(III)-catalyzed intramolecular annulations of homopropargyl alcohols. *J. Org. Chem. 2023, 88, 7539−7550*.
2. Chatterjee, S.; Khatun, R.; Ali, M.; Chowdhury, C. A solvent controlled regioselective synthesis of 2- and 4-substituted α-carbolines under palladium catalysis. under revision of *Chemical Communications*, 2024, xxx

Dr. Chinmay Chowdhury, Chief Scientist
Group Members: Sarat Chatterjee, SRF; Raghunath Das, JRF; Aparajita Mandal, JRF; Debasmita Mondal, PA
Collaborators: Dr. Krishan Gopal, CSIR-IMTECH, Chandigarh; Dr. Biswajit Mukherjee, Jadavpur University, Kolkata; Dr. Subhajit Biswas, IICB, Kolkata.

Dr. Deepak Kumar and his group members

Phytochemical investigation of *Pterocarpus santalinus* heartwood

Research Activities

- Isolation and characterization of compounds from *P. santalinus* heartwood
- Development of methods for extraction, isolation and purification

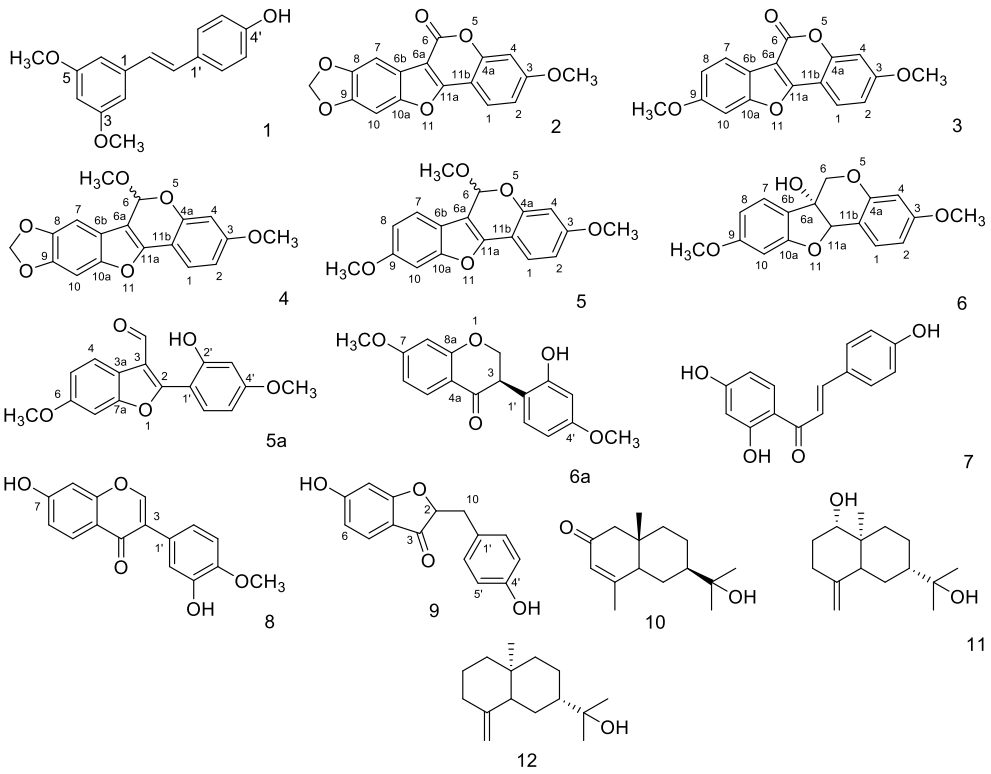
Pterocarpus santalinus L., belonging to the Fabaceae family, is commonly referred to as red sanders, red sandalwood, and rakt-chandan. Its native habitat is confined to the forest range situated in the Andhra Pradesh region of Southern India. Notably, the plant is distinguished by its elegant deep red heartwood, which is extensively exploited commercially for the production of furniture, musical instruments, and handicrafts besides its remarkable medicinal properties. The phytochemical investigation of heartwood led to the isolation of one undescribed pterocarpene and eleven known compounds along with two artifacts. Of these, six compounds are being reported for the first time from *P. santalinus* heartwood, and two as natural products.

Future Research Plans

In future, majority of our research efforts would be directed towards the development of novel extraction methodologies prompting utilization of *P. santalinus*.

Extramural / CSIR Funding

1. Phytopharmaceutical development of Sesquiterpene coumarin enriched fraction of Ferula assa-foetida gum against Parkinson's disease. Council of Scientific and Industrial Research (CSIR), 2024-2027, 174 Lakh.
2. Development of Extract of *Piper betle* leaves for treatment of Breast and ovarian Cancers. Council of Scientific and Industrial Research (CSIR), 2021-2026, 50 Lakh.
3. Identification of potential leads from Indian traditional medicinal plants against NAFLD. Council of Scientific and Industrial Research (CSIR), 2020-2025, 50 Lakh.
4. Evaluation of anti-cancerous potential, in silico pharmacological analysis and molecular mechanism of Kanchanar guggulu in ovarian cancer μ Tumor spheroids and in in vivo models. Central Council for Research in Ayurvedic Sciences (CCRAS), 2023-2025, ~ 44 Lakh.
5. Identification and characterization of phytochemical properties of Mistletoe. Swasthyaniketan Integrated Healthcare and Research Foundation, Bengaluru, 2022-2024, 21.24 Lakh.



Publications

1. Darshani, P., Sarma, S. S., Gajbhiye, R. L., Srivastava, A. K., Kumar, D.* (2024) Isolation, characterization, in-vitro and in-silico assessment of undescribed bioactive constituents from *Pterocarpus santalinus* L. heartwood. *ACS Omega*. Accepted manuscript.
2. Darshani, P., Sarma, S.S., Tripathy, P., Kumar, D.* (2024) Ultrasonication-assisted optimization of pterostilbene extraction from *Pterocarpus santalinus* heartwood using response surface methodology. *Ind Crops Prod*. 118409. https://doi.org/10.1016/j.indcrop.2024.118409.
3. Banerjee, C., Barman, R., Darshani, P., Pillai, M., Ahuja, S., Mondal, R., Pragadheesh, V. S., Chakraborty, J.*, Kumar, D*. (2024) α-Viniferin, a dietary phytochemical, inhibits Monoamine oxidase and alleviates Parkinson's disease associated behavioral deficits in a mice model. *Neurochem Int*. 174, 105698. https://doi.org/10.1016/j.neuint.2024.105698.
4. Mandal, T., Shukla, D., Pattanayak, S., Barman, R., Ashraf, R., Kumar, S., Kumar, D., Srivastava, A. K.* (2024) Ellagic acid Induces DNA damage and apoptosis in cancer stem like cells via mitochondrial dysfunction mediated ROS-generation and overcomes cisplatin induced stemness. *ACS Omega*. Accepted Manuscript.
5. Bose, S., Dahat, Y., Kumar, D., Haldar, S., Das, S. K.* (2023) A membrane targeted multifunctional cationic nanoparticle conjugated fusogenic nanoemulsion (CFusoN): induced membrane depolarization and lipid solubilization to accelerate the killing of Staphylococcus aureus. *Mater Horiz*. 11, 661-679. doi: 10.1039/d3mh01102j.

Conferences Attended

32nd CRSI National Symposium in Chemistry (CRSI-NSC-32), Birla Institute of Technology and Science, Pilani (BITS Pilani), Pilani Campus. 1-4 February 2024.

Dr. Deepak Kumar, Senior Scientist

Group Members: Yogita Dahat, CSIR-SRF; Chayan Banerjee, UGC-SRF; Raju Barman, CSIR-Project-JRF; Shreya Sen Sarma, CSIR-Project Associate; Puja Tripathy, CSIR-JRF; Biswajit Singh, Project Assistant

Collaborators: Dr. Joy Chakraborty, Sr Scientist, CSIR-Indian Institute of Chemical Biology, Kolkata; Dr. Amit K Srivastava, Sr Scientist, CSIR-Indian Institute of Chemical Biology, Kolkata

Dr. Indrajit Das and his group members

Supporting Electrolyte-Free Electrochemical Oxidative C–H Sulfonylation and Thiocyanation of Fused Pyrimidin-4-ones in an All-Green Electrolytic System

Research Activities

An electrooxidative C–H functionalization is a widely accepted route to obtain sulfur-containing arenes and heteroarenes. However, this process often involves using non-recyclable supporting electrolytes, (co)solvents like hexafluoroisopropanol, additives like acid, or catalysts. Using additional reagents can increase costs and waste, reducing atom efficiency. Moreover, unlike other nitrogen-containing heterocycles, there have only been sporadic reports of electrochemical C–H functionalization in fused pyrimidin-4-ones, and an electrolyte-free process has yet to be developed. We demonstrate that such anodic coupling reactions can be performed in an all-green electrolytic system without using such additional electrolytes or HFIP, maintaining a high atom economy. This C–H functionalization strategy utilizes inexpensive sodium sulfinates and ammonium thiocyanate as sulfonylating and thiocyanating agents in an undivided cell at a constant current, using a mixture of CH_3CN/H_2O as solvent at room temperature. Thus, fused pyrimidin-4-ones can be selectively converted into C3-sulfonylated and -thiocyanated derivatives in moderate to good yields.

The electrochemical oxidative C–H functionalization method is a sustainable and environmentally friendly approach for creating C–S bonds in arenes and heteroarenes. It is a promising alternative to traditional methods using transition-metal catalysts and oxidants. This method has made significant progress in recent years because the products containing sulfones, thiocyanates, or thioethers are crucial building blocks in many pharmaceuticals and agrochemicals. However, excessive amounts of non-recyclable supporting electrolytes are often required to decrease the resistance and lower the potential in the system, which can complicate the

purification process and decrease atom efficiency. This also increases waste and adds to expenses, failing to comply with green chemistry's crucial guidelines. Finding the proper electrolyte is also challenging, and solvents or co-solvents like 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), additives like acids, or catalysts such as tetrabutylammonium iodide (TBAI) are used to enhance the reaction performance. An electrolyte- and additive-free process is rare, particularly during the C–H sulfonylation of arenes and heteroarenes. However, using substrates as electrolytes and coupling agents is more cost-effective, sustainable, and atom-economical, eliminating the need for additional reagents that could interfere with the reaction and decrease overall efficacy. For instance, sodium sulfinates, frequently used as a sulfonylating agent under electrochemical oxidative conditions, can play a dual role in the presence of a solvent or co-solvent water. Therefore, developing a practical approach for creating C–S bonds in an all-green electrolytic system is essential (Figure 1).

To summarize, an electrochemical C–H functionalization method for adding sulfonyl and thiocyanate groups to fused pyrimidin-4-ones has been developed using inexpensive sodium sulfinates and ammonium thiocyanate, respectively, in a CH3CN/H2O solvent mixture. This protocol stands out from other anodic oxidation methods because it doesn't need supporting electrolytes, additives, catalysts, or (co)solvents such as HFIP. Additionally, this method is more sustainable, eco-friendly, and atom-economic, and it can be conducted at room temperature under open air. Notably, no reported electrochemical methods exist for the C–H functionalization of fused pyrimidin-4-ones without supporting electrolytes, including C–S bond formation methods. This straightforward electrochemical approach is a less expensive and non-toxic option for functionalizing fused pyrimidin-4-ones and only releases hydrogen gas. It has also been successfully applied to large-scale synthesis, and converting the resulting products into various sulfur-containing products offers excellent potential for academic and industrial applications.

Future Research Plans

Electrochemical oxidative and reductive functionalization of the arenes and heteroarenes.

Extramural / CSIR Funding

Innovative Processes and Technologies for Crop Protection Chemicals" [Agromission-2]; Duration: Apr 2023 to Mar 2026; HCP 0049; Cost in Lakhs: 199.888; Project status: Ongoing; Role: Project leader and co-ordinator from CSIR-IICB

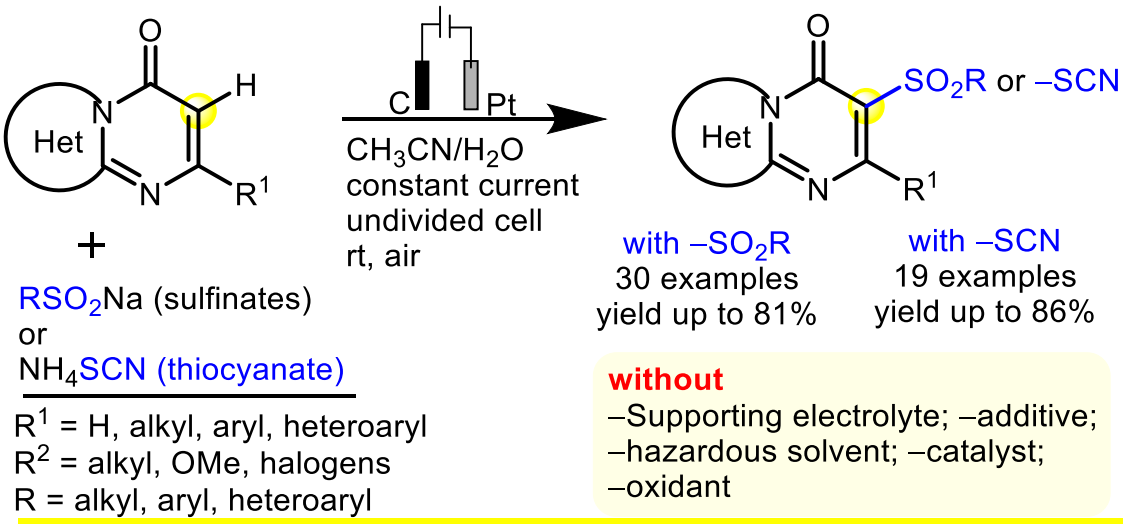


Figure 1. Supporting electrolyte-free electrochemical oxidative C–H sulfonylation and thiocyanation in fused pyrimidin-4-ones.

Publications

1. Biswas, S., Ghosh, S., and Das, I. (2024) Supporting Electrolyte-Free Electrochemical Oxidative C−H Sulfonylation and Thiocyanation of Fused Pyrimidin-4-Ones in an All-Green Electrolytic System. *Chem. Eu. J.* 30, e202303118.
2. Saha, J., Banerjee, S., Malo, S., Das, A. K., and Das, I. (2024) A Torquoselective Thermal 6π-Electrocyclization Approach to 1,4-Cyclohexadienes via Solvent-Aided Proton Transfer: Experimental and Theoretical Studies. *Chem. Eu. J.* 30, e202304009.
3. Maity, R., Bankura, A., and Das, I. (2023) Electrochemical cascade sequences for the remote C7–H bond thiocyanation of quinoxalin-2(1*H*)-ones with ammonium thiocyanate. *Green Chem*. 25, 7774.
4. Saha, J., Banerjee, S., Malo, S., Das, A. K., and Das, I. (2023) Thermally-Activated Geometrical Regioselective *E* → *Z* Isomerization-Enabled Cascade Sequences of Conjugated Dienals: Experimental and DFT Studies. *Chem. Eur. J*. 29, e202302335.

Patents

An Improved Process for Synthesis of Mandipropamid. Indrajit Das, Jayanta Saha, Sumit Biswas, Subhadeep Ghosh, filing date 26/04/2024, Indian Patent application number 202411033733

Conferences Attended

32nd CRSI National Symposium in Chemistry (CRSI-NSC-32), Birla Institute of Technology and Science, Pilani (BITS Pilani), 1-4 February 2024

Dr. Indrajit Das, Principal Scientist

Group Members: Jayanta Saha, SRF; Abhijit Bankura, SRF; Siddhartha Malo, SRF; Sumit Biswas, SRF; Subhadeep Ghosh, JRF; Sampurna Roy, PA-1 (HCP41); Alomgir Shah Kabir, PA-1 (HCP49)

Collaborators: Prof. Abhijit Kumar Das, Senior Professor, Department of School of Mathematical & Computational Sciences, Indian Association for the Cultivation of Science, Kolkata; Prof. Debashree Ghosh, Department of School of Chemical Sciences, Indian Association for the Cultivation of Science, Kolkata

Dr. Indu Bhusan Deb and his group members

Development of Catalytic and Electrochemical Approaches for Late-Stage Functionalization and Synthesis of Potential Bioactive Molecules

Research Activities

We are actively involved in doing research in the field of the catalysis research area (electrochemical synthesis/C-H bond activation/functionalization) to develop affordable, efficient, and innovative as well as industry-friendly synthetic processes for the synthesis of functionalized molecular structures including dibenoxazine, dibenzodiazepines, acridine, succinimide employing transition metal(free)-catalysis employing the concept of electrochemical synthesis and transition metal-catalyzed (Pd, Fe, Co, Ni, Ru, Rh & Ir) C–H/C–X bond activation and metal-free C–H/C–X bond functionalizations. Employing catalysis, and electrochemical synthesis we have developed the methodologies to synthesize functionalized spirocycles and heterocycles. We have published publications Organic Letters 2023, 25, 8199-8204, Chemical Communications. 2023 , 59, 13899-13902, Chemical Communications, 2023, 59, 7751-7754 and and one Indian Patents. We have developed the process for the synthesis of an agrochemical mandipropamid.

Our objectives are: 1) Development of electro-catalyzed, Metal-free, and transition metal-catalyzed cost-effective, affordable and industry-friendly C(sp3)-H activation/functionalization process for the late-stage functionalization of pharmacophores such as benzoxazines, anthrone, and quinoline tetrahydroisoquinoline 2) Development of a process for the synthesis of the generic version of FDA approved drugs and Agrochemicals. Employing this chemistry we have developed various methhods for the synthesis of functionalized molecules as follows.

a) Electrochemical C(sp3)-C(sp3) Cross-Dehydrogenative Coupling: Enabling Access to 9-Substituted Fluorescent Tetrahydroisoquinolines: The manuscript is ready for publication and for patent.

b) Oxazolinyl-Assisted Synthesis of Indene-tethered amino-alcohol via Rh(III)-Catalyzed [3+2] Cascade Ring-Closing/Ring-Opening Strategy via C-H bond activation: An unprecedented atom-economic redox neutral regioselective Rh(III)-catalyzed cascade (3+2) annulation of 2-Phenyloxazoline with α, β-unsaturated nitro olefins has been accomplished furnishing a novel set of nitro-functionalized indene tethered amino alcohols through a ring-closing/ring-opening strategy via the formation of two new C-C bonds and the cleavage of C-O bond under silver free mild reaction condition with broad substrate scope. Also, we showcased detailed mechanistic

studies to rationalize the formation of high–value 6, 5-fused carbo-cyclic moieties. This methodology is extremely functional from the standpoint of step economy and atom economy for the synthesis of a diverse array of nitro-substituted indenylamine derivatives. This work is published in Organic Letters 2023, 25, 8199-8204 (Figure 1).

c) A Condition-Tuned Selective Unorthodox Redox Approach to Indole-3-Carboxylic Acids and Anthranilic Acids via Carbon Atom Translocation: We have demonstrated the use of suitable reagents towards the synthesis of diverse, indole-3-carboxylic acid derivatives with high functional group tolerance, thereby generating a broad substrate scope with excellent yields. This protocol is applicable for the synthesis of C2-deuterated indole 3-carboxylic acids. The making of desired ICA and AA derivatives is most important as these have been used as a key intermediate to synthesize several biologically active molecules including tropisetron. We have extended our methodology as a cost-effective and industry friendly generic process for the synthesis of tropisetron (Navoban), a commercially available drug as serotonin 5-HT4 and 5-HT6 antagonists. Which has been published in Chemical Communications. 2023 , 59, 13899-13902 and filed for patent world PATENT PCT/IN2022/050940, 20/10/2022. By slightly tuning the reaction conditions, a divergent synthesis of the library of anthranilic acids has also been established (Figure 2).

d) Synthesis of Indene-fused Spiro-Dibenz(ox)azepines via Rh(III)-Catalyzed Cascade Regioselective C−H Activation/Annulation: We have successfully developed a silver-free Rh(III)-catalyzed redox-neutral regioselective [3+2]-spiroannulation of dibenz(ox)azepines and α,β-unsaturated conjugated ynones via one-pot cascade C-H activation/annulation strategy giving access to structurally important multi-substituted dibenz(ox)azepine containing α-aroyl spiro-indenamine derivatives in good to excellent yields. The manuscript is published in Chemical Communication, 2023, 59, 7751-7754. This work has been selected by RSC for cover page (Figure 3).

e) A process for the synthesis of 2-(4-chlorophenyl)-2-hydroxy-N-(3-methoxy-4-(prop-2-yn-1-yloxy)phenethyl)acetamide, a key intermediate of Mandipropamid: The mission's (HCP-49) main objective is to develop a cost-effective generic process for off-patent or soon-to-be-patent agrochemicals that are important to Indian farmers under the mission of Make in India and the Atmanirvar mission. The targeted agrochemical Mandipropamid as fungicide was originally developed and marketed by Syngenta. We have developed a cost-effective and industry friendly process for the synthesis of Mandipropamid by using commercially available cheap starting materials and reagents. The developed process has been filed for the patent by our group " Patent Number: IN 202311081168 date 29 Nov 2023" (Figure 4).

We are actively involved in API mission (HCP-50) to develop a cost-effective process for the synthesis of tenofovir. We are also involved in developing the process for the synthesis of palbociclib in PAN -CSIR Cancer mission (HCP-40).

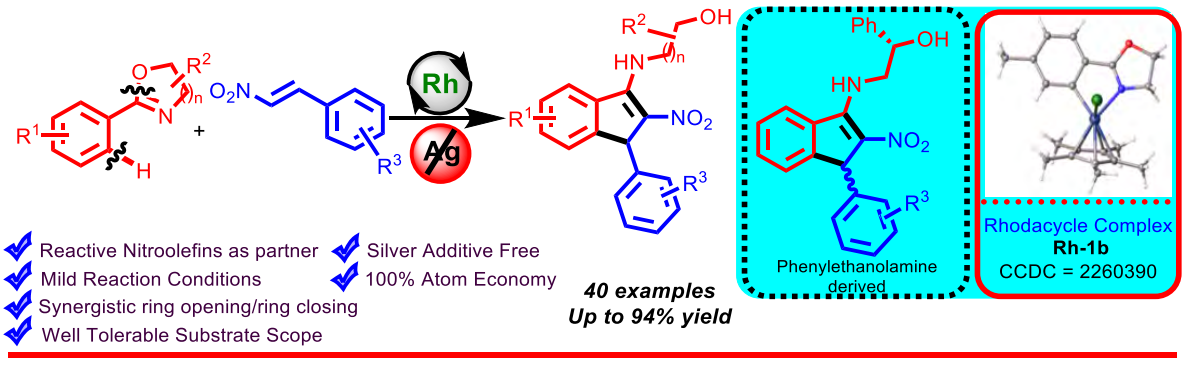


Figure 1: Rh(III)-Catalyzed C-H Bond Activation Reaction For The Synthesis Of Indene-Tethered Amino-Alcohol

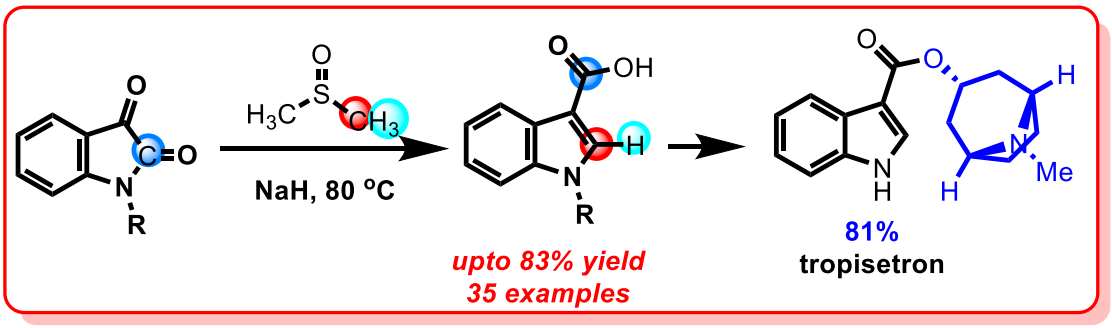


Figure 2: A Condition-Tuned Selective Unorthodox Redox Approach to Indole-3-Carboxylic Acids and

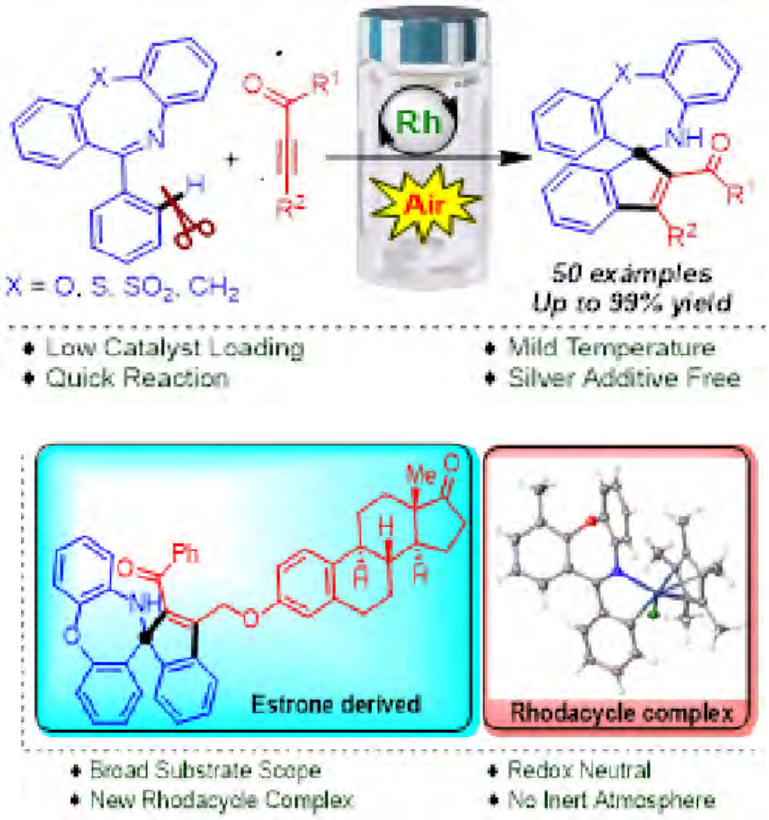


Figure 3: Synthesis of Indene-fused Spiro-Dibenz(ox)azepines via Rh(III)-Catalyzed Cascade.

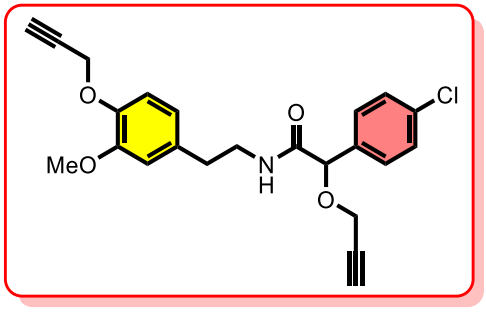


Figure 4: Mandipropamid, an agrochemical.

Future Research Plans

1. Our group will be engaged in the development of the process for the synthesis of the broad spectrum of pharmaceutically relevant (chiral and achiral) molecules employing Electrocatalysis, photocatalysis and Metal (free)-catalysis. Bioactivity study of newly synthesized molecules will be pursued.
2. In the area of translational research, our group will be engaged in developing an affordable process for the synthesis of key intermediates and key starting material for the synthesis of API agrochemicals.

Publications

1. Mondal, I., Roy, S., Naskar, K., Karmakar, S., Chowdhury, M., and Deb, I. (2023) [3+2] Cascade
2. Ring-Closing/Ring-Opening Strategy: Access to N-Indene-tethered Amino-alcohols. *Org. Lett. 25,* 8199–8204.
3. Bhowmik, A., Naskar, K., Roy, S., Karmakar, S., Sarkar, W., Mondal, I., Sana, A., and Deb, I. (2023) A Condition-tuned Unorthodox Approach to Indole-3-carboxylic Acids and Anthranilic Acids via Carbon Atom Translocation. *Chem. Commun*. *59,* 13899-13902.
4. Naskar, K., Karmakar, S., Mondal, I., Sarkar, W., Roy, S., and Deb, I. (2023) Synthesis of Indene-fused Spiro-Dibenz(ox)azepines via Rh(III)- Catalyzed Cascade Regioselective C−H Activation/Annulation. Chem. Commun. 59, *7751-7754*.
5. Mondal, I., Naskar, K., Roy, S., Deb, I. A process for the synthesis of 2-(4-chlorophenyl)-2-hydroxy-N-(3-methoxy-4-(prop-2-yn-1-yloxy)phenethyl)acetamide, a key intermediate of Mandipropamid: Patent Number: IN 202311081168 date 29 Nov 2023

Extramural / CSIR Funding

SERB, DST, 12/2020-12/2023, CRG/2020/004792: INR 41.7 Lakh: Title: Cooperative Metal-Catalyzed Carboboration/Carbosilylation of Alkynes/ Alkenes via C-H Activation. Objective: Development of a catalytic system for alkene and alkyne functionalization.

Member of Society

1. Life member of Chemical Biology Society, Kolkata
2. Life member of the Chemical Research Society of India (CRSI), Bangalore

Dr. Indu Bhusan Deb, Senior Principal Scientist
Group Members: Shantonu Roy, CSIR-SRF; Imtiaj Mondal, UGC-SRF; Koushik Naskar, UGC-SRF; Sudip Karmakar, CSIR-SRF; Moumita Chowdhury, UGC-JRF; Dr. Moumta Saha, NPDF; Dr. Mandira Nandi, RA-Project; Dr. Anisha Purkait, RA-Project

Dr. Manish Debnath and his group members

Development of Aptamer-based Assay for the Detection of Protein receptors on Extracellular Vesicles

Research Activities

The accurate identification of non-structural protein-4 (NSP4) expressed on the surface of Rotaviral extracellular vesicles is important for virus detection and to investigate viral transmission. In this context, we are primarily involved in developing RNA aptamers (i.e. synthetic antibodies) that could identify and target the NSP4 protein epitope on viral extracellular vesicles. These RNA aptamers were synthesized using SELEX, in which a large library of RNA was screened against NSP4, and the selected RNA molecules were amplified and enriched in a multi-step process. These aptamers were developed for targeting purified NSP4 protein using the SELEX method. For this, large (10^16) RNA libraries of chemically modified RNA molecules were screened against immobilized NSP4 (Figure 1). The bound RNA structures were amplified and enriched as a starting material for subsequent cycles. After 4 cycles of SELEX, a negative selection step was added to the process, where the bovine serum albumin was used as negative selection control. All RNA molecules were fluoro-modified at a 2'-ribose position, in addition to the base modifications, to protect them from degradation. A recently established *in vitro* transcription system was exploited, enabling the incorporation of chemical entities like benzyl, sialic acid, and amino acid moieties into nucleotide bases, dramatically increasing their binding affinity towards their target. Preliminary studies in our laboratory suggested that the chemical modification increased the affinity of the aptamers by ~50 - 100-fold. After 10 to 15 rounds of SELEX, the bound aptamers are recovered and characterized.

This research aims to develop a detection strategy for identifying protein markers present on the surface of extracellular vesicles. The strategy involves leveraging aptamer technology, advancing beyond traditional antibody-based methods. While aptamers have been utilized for cancer cell vesicles, their application for viral samples remains unexplored. The proposed dual-labeled probe-based detection system promises enhanced sensitivity by minimizing

false positives compared to single fluorophore-labeled antibody systems. Additionally, hybridization chain reaction (HCR) and AI-based technologies will be employed, which offer a cost-effective, enzyme-free alternative to PCR with similar or higher detection efficiency. This research marks a breakthrough in diagnostic methodology, offering an innovative approach to detecting protein markers on extracellular vesicles, thereby bringing innovation in diagnostic tools in the healthcare landscape.

The key objectives of this project are as follows: 1) To design and develop aptamers against NSP4 protein marker; 2) To investigate the affinity and selectivity of these aptamers for their respective target over other proteins; 3) To design and develop an assay system for the easy detection of NSP4 protein marker from extracellular vesicle samples.

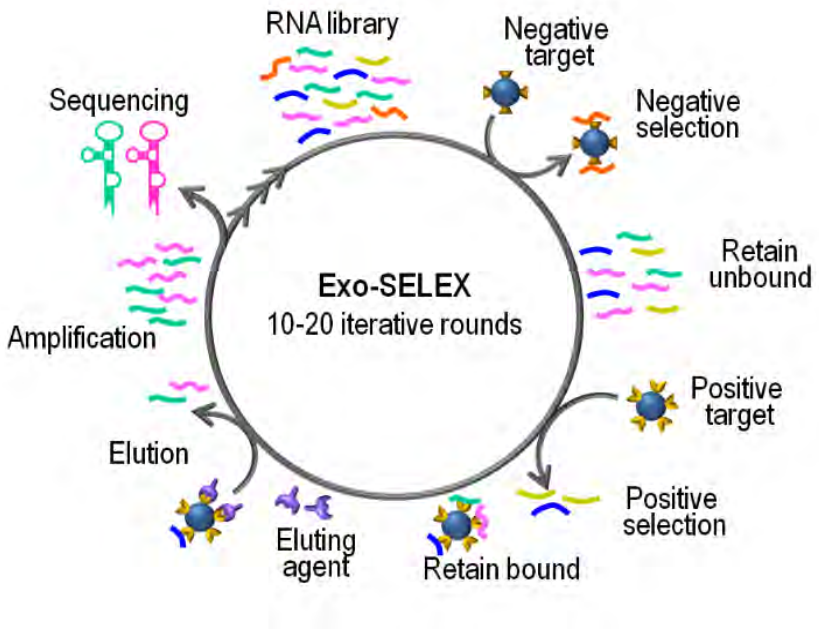
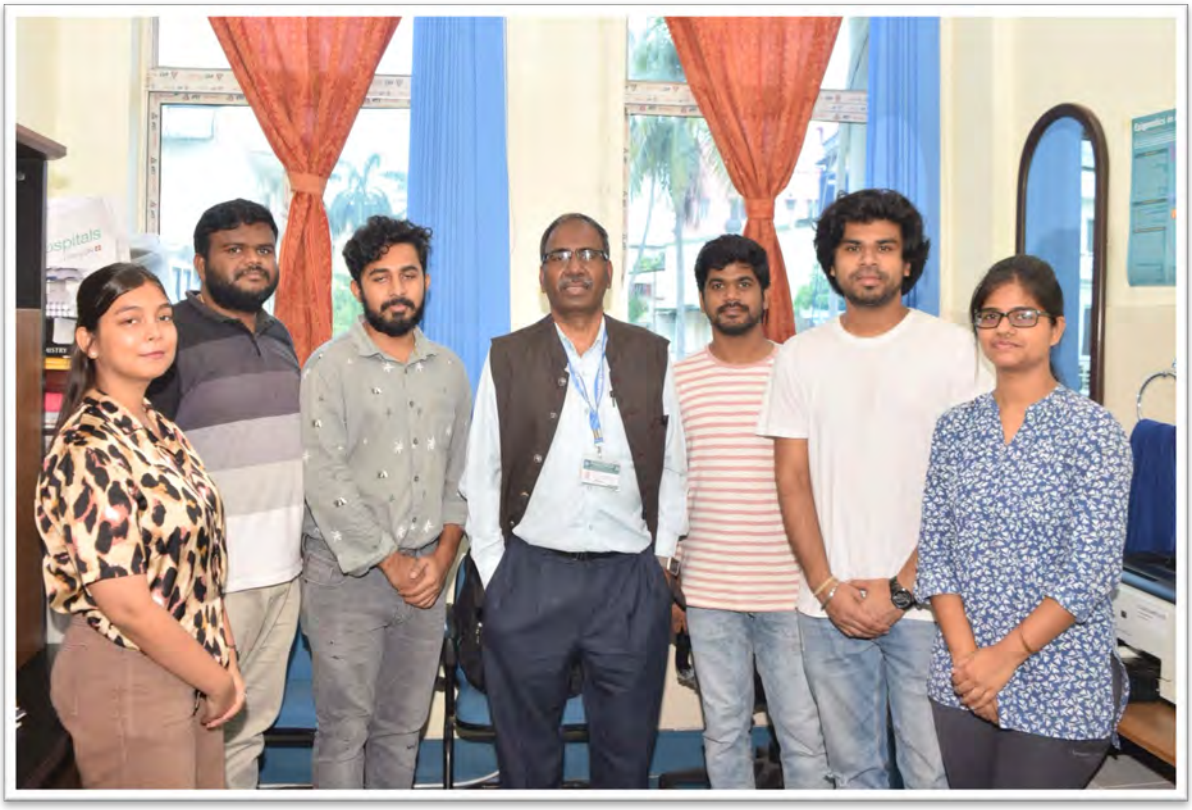


Figure 1. Representation of the SELEX method to produce aptamers from RNA library.

Dr. Manish Debnath, Scientist
Group Members: Pranotosh Das, UGC-JRF; Souvik Sen, ICMR-JRF; Avimanyu Das, UGC-JRF
Collaborators: Dr. Biswadip Banerji, CSIR IICB; Dr. Sourish Ghosh, CSIR IICB.



Dr. Parasuraman Jaisankar and his group members

Development of lead molecules of natural and synthetic origins with specific targets against metabolic and infectious diseases

Research Activities

Our primary focus revolves around crafting lead molecules endowed with anti-cancer, anti-leishmanial, anti-bacterial, anti-ulcer, and anti-viral properties. Additionally, our endeavors extend to crafting fluorescent probes for potential utilization in live cell imaging. Through our research, we've unearthed the potent anti-ulcer characteristics of various synthesized compounds, achieved by inhibiting MMP-9. Furthermore, we harness enzymes sourced from edible origins as catalysts in organic reactions, yielding specific epigenetic enzyme inhibitors, and synthesizing precursors to pharmaceutically active compounds. Our exploration also delves into asymmetric organic transformations, employing chiral ligands/catalysts to produce bioactive scaffolds. Additionally, our group delves into the introduction of stable atropisomerism, enhancing the optical richness of compounds and fostering target selectivity within a promiscuous scaffold.

Aims and Objectives

- To craft lead molecules of natural origin targeting specific diseases.
- To investigate medicinal plants, emphasizing the isolation and characterization of bioactive molecules.
- To pioneer axial chiral systems and employ both organo and biocatalysts for asymmetric synthesis.
- To innovate fluorescent probes with applications tailored for live cell imaging.

Work Achieved

Development of Synthetic Inhibitors for Metabolic Diseases

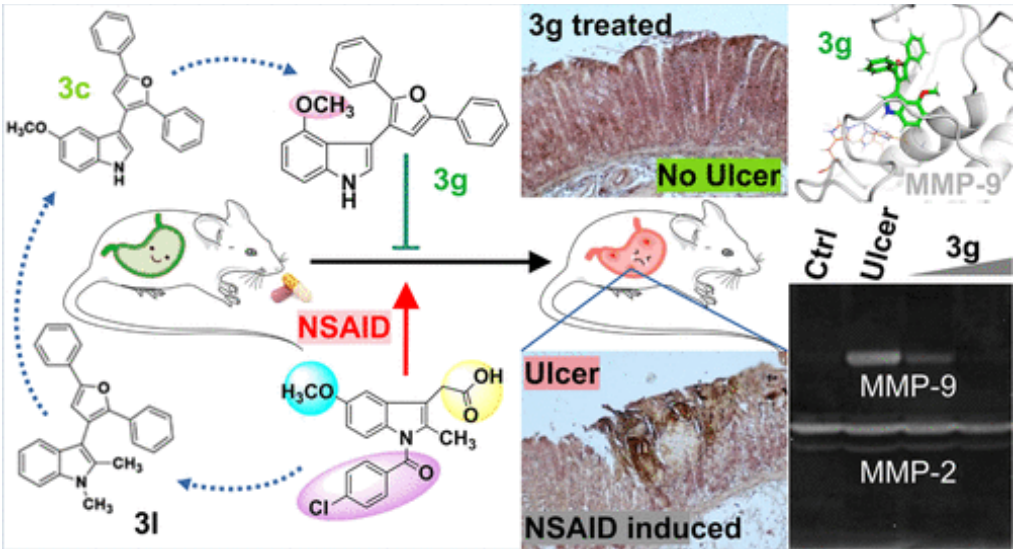
The most extensively used medication for anti-inflammation, rheumatic illnesses, osteoarthritis, and pain relief across the world is mainly the nonsteroidal anti-inflammatory drugs (NSAIDs). They are taken by about 30 million people on a regular basis, although they have several drawbacks including gastric inflammation and about 107,000 individuals are hospitalized each year as a result of NSAID-related gastropathy. Extensive research has shown that in addition to acid secretion, several factors such as mitochondrial oxidative stress,

reactive oxygen species (ROS), gastric mucosal blood flow, level of antioxidant, perturbation of extracellular matrix (ECM) remodeling, and cell apoptosis all play significant roles in the pathogenesis of ulceration in the gastrointestinal (GI) tract. ECM remodeling is attributed to the activities of various matrix metalloproteinases (MMPs). Among different MMPs, the MMP-9 or gelatinase B activity, in particular, is frequently engaged in the breakdown of basement membrane collagens during tissue remodeling. In a variety of human illnesses, the upregulation of both pro and active MMP-9 contributes to disease pathogenesis. The increase in MMP-9 activity relates to inflammation in the GI tract, where the integrity of the gastric ECM is compromised as a result of illness or injury, such as a gastric ulcer caused by Helicobacter pylori infection, NSAIDs, alcohol, and stress.

NSAIDs like indomethacin, ibuprofen, naproxen, etc., can harm the gastroduodenal mucosa through a variety of molecular events including suppression of gastric prostaglandin synthesis, damage in gastric epithelium, decrease in gastric mucosal blood flow, and impairment of mucus bicarbonate secretion. In this study, we identified a unique pharmacological strategy including chemical alteration of indomethacin to convert it from ulcerogenic to antiulcer lead optimization. This approach has identified 3-indolyl furanoid (3g or 3c) derivatives from parent indomethacin, which inhibits MMP-9 and is thus responsible for curing gastric ulcers. Furthermore, we have investigated the biochemical function of 3-indolyl furanoids (3g or 3c) for MMP-9 inhibition by a series of assays (chemical and structural), demonstrating that the molecule finally binds specifically into the MMP-9 catalytic domain, resulting in its inhibition during gastroprotection.

Newly Synthesized 3-Indolyl Furanoid Inhibits Matrix Metalloproteinase-9 Activity and Prevents Nonsteroidal Anti-inflammatory Drug-Induced Gastric Ulceration

Indomethacin, a known nonsteroidal anti-inflammatory drug (NSAID) induces gastric inflammation, causing degradation of the extracellular matrix by specific matrix metalloproteinases (MMPs). We investigated the antiulcer efficacy of 3-indolyl furanoids (3g and 3c, i.e., methoxy substitution at 4- and 5-positions of the indole ring, respectively), derived from indomethacin. Interestingly, 3g protected against indomethacin-induced gastropathy in vivo by inhibiting MMP-9. Our work established a chemical modification strategy for the development of safer NSAIDs. Moreover, in vitro and in silico studies confirmed that 3g inhibited MMP-9 activity with an IC_{50} value of 50 µM by binding to the catalytic cleft of MMP-9, leading to ulcer prevention. Pharmacokinetics was presented as the mean concentration–time profile in the rat plasma, and the extraction efficiency was greater than 70%, showing a C_{max} of 104.48 µg/mL after 6.0 h (t_{max}) treatment with half-life and area under the curve being 7.0 h and 1273.8 h µg/mL, respectively, indicating the higher antiulcer potency of 3g.



Synthesis of 3-Indolyl Furanoids as Inhibitors of Indomethacin-Induced Gastric Injury

In the present study, we synthesized a series of 3-furanyl indoles via selective one-pot synthesis by

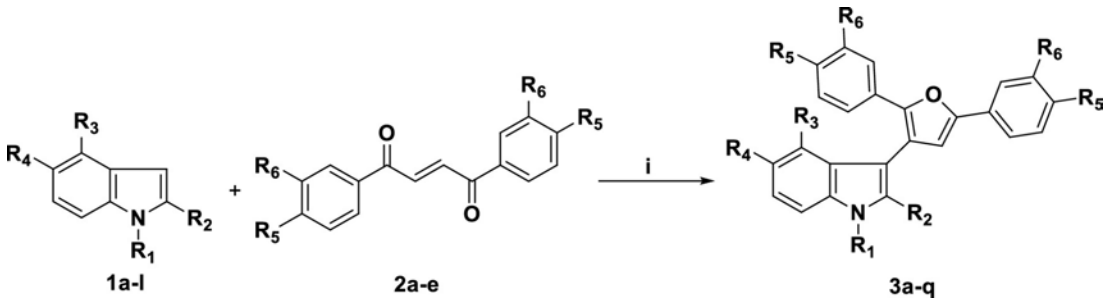
Friedel–Crafts alkylation followed by Paal–Knorr cyclization. The synthetic route for the targeted 3-indolyl furanoid derivatives (3a–q) is shown in Scheme 1. The procedure involves the introduction of a 1,4-dicarbonyl moiety on the indole framework via Friedel–Crafts alkylation with (*E*)-1,4-diaryl-2-buten-1,4-diones (2), which could be transformed into furan rings via Paal–Knorr cyclization by using *p*-TsOH as a catalyst to yield desired compounds 3a–q (Scheme 1).

Antiulcer Efficacy of 3-Indolyl Furanoids under Oral Administration

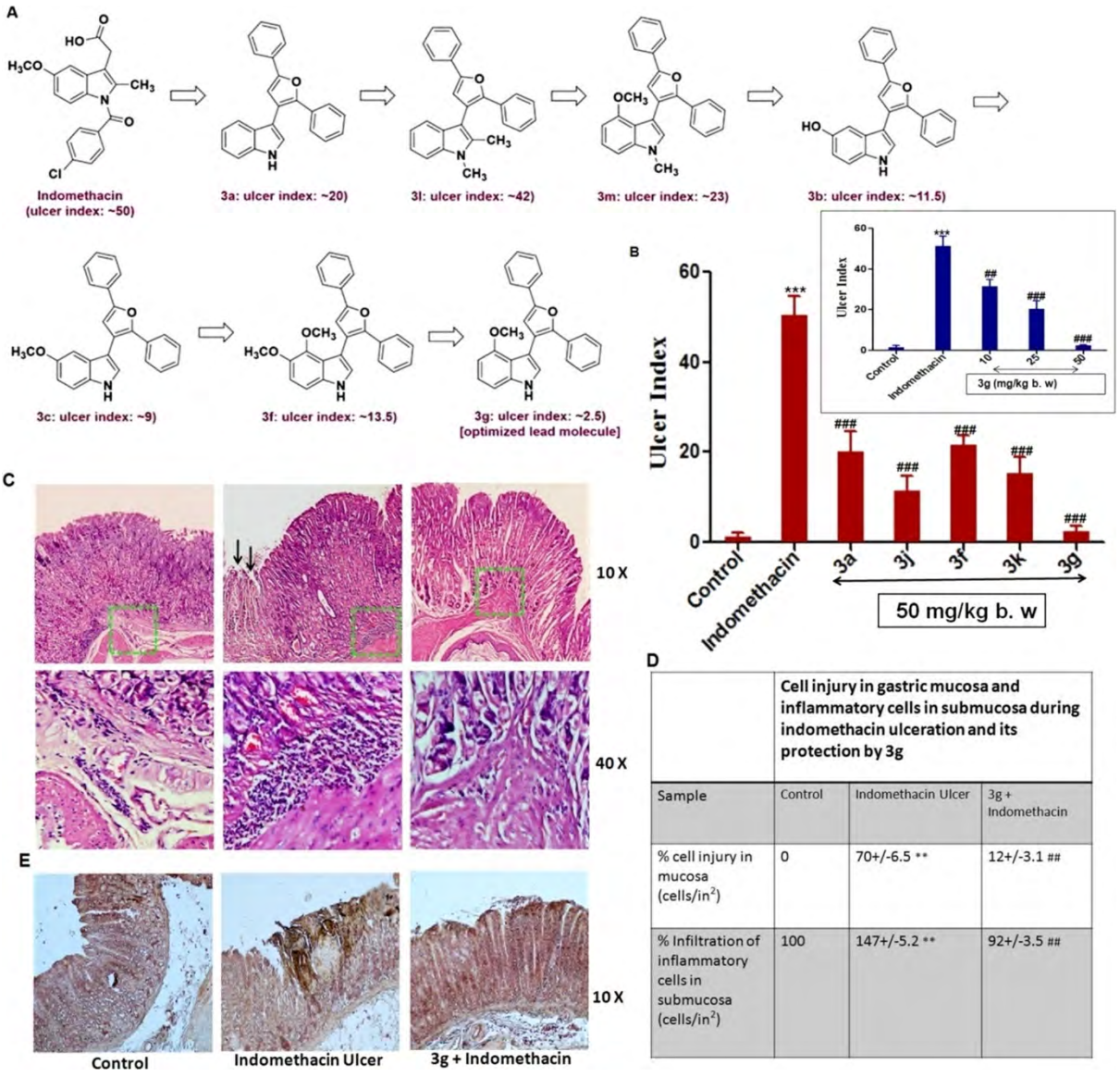
The antiulcer efficacy of 3-(2,5-diphenylfuran-3-yl)-1*H*-indole (3a) showed 62% efficacy when administered orally. However, despite the presence of common indole scaffold 3a, the potency of each compound is influenced by the nature of the substituent group present in it. Initially, we investigated the effects of substitution around the indole skeleton to get better activity than 3a against ulcers. To facilitate effective protein–ligand binding at the metalloenzyme zinc coordination site, screening of 3-(2,5-diphenylfuran-3-yl)-1*H*-indol-5-ol (3b) bearing a hydroxy group at indole C5 expectedly showed enhanced ulceration inhibition (78%). Further modulating 3b and inducing hydrophobicity for 3c by incorporation of OCH_3 at C5 of the indole ring indeed resulted in 83% inhibition in the ulcer index under oral administration. However, a moderate effect was observed for the C4/C5 OCH_3-bisubstituted 3-indolyl furanoid (3f), which could be because of restriction in ligand flexibility in the target protein active site (Figure 1).

3g and 3c Downregulate MMP-9 by Binding with the Catalytic Pocket of the Protease during Protection against Indomethacin-Induced Gastric Ulcers in Mice

Among all new 3-indolyl furanoids, 3g exhibited significantly higher ulcer inhibitory activity (ulcer index for 3g = 2.5 ± 0.86) in vivo as well as inhibition of MMP-9 expression and activity (Figure 2). 3g may have some regulatory effect on the transcription factor involved in MMP-9 expression, which needs further study. In contrast, the mechanism of inhibition was better resolved for the 3g/MMP-9 or 3c/MMP-9 complex (ulcer index for 3c = 9 ± 2.4) when analyzed by the in silico study. It was pertinent to mention that *m*- and *p*-substituents on the phenyl rings of the furanyl group with methyl, chlorine, or bromine (3n–q) exhibited lower antiulcer activity against MMP-9. From these results, it was revealed that the methoxy group either at the 4- or 5-position of the indole ring of new structurally proposed 3-furanyl indoles exhibited the most potent antiulcer property through inhibition of MMP-9 activities both in vitro and in vivo. Notably, when the substituents around indole were 4,5-dimethoxy (3f), the antiulcer activity was remarkably low (74% inhibitory effect). In particular, 3g exhibited the most promising optimized molecule for the treatment of gastric ulcers and other inflammatory diseases via inhibition of MMP-9 (Figures 2). Thus, 3g was chosen as the lead molecule for further study. A dramatic reduction in MMP-9 activity (pro and active) occurred with 500 µM 3g when incubated for 3 h with purified human MMP-9 as judged by gelatine zymography. The half-maximal inhibitory concentration (IC_{50}) for binding with MMP-9 was found to be ~50 µM, indicating moderate-to-tight binding which was nicely corroborated with in silico binding data for 3g with MMP-9.



Scheme 1: Reagents and Conditions: (i) *p*-TsOH (0.5 equiv), CH_2Cl_2, 1–6 h, and reflux



	Cell injury in gastric mucosa and inflammatory cells in submucosa during indomethacin ulceration and its protection by 3g		
Sample	Control	Indomethacin Ulcer	3g + Indomethacin
% cell injury in mucosa (cells/in^2)	0	70+/-6.5 **	12+/-3.1 ##
% Infiltration of inflammatory cells in submucosa (cells/in^2)	100	147+/-5.2 **	92+/-3.5 ##

Figure 1: 3g prevents indomethacin-induced gastric injury. (A) General scheme for the synthesis of 3-indolyl furanoids and their ulcerogenic potential was expressed as the ulcer index (UI) using a mice model for indomethacin-induced gastric ulcer. (B) Graphical representation of UI for different 3-indolyl furanoids (50 mg/kg body weight). Compound 3g showed the best ulcerogenic activity. The inset shows the 3g dose versus the ulcer index. (C) Haematoxylin–eosin staining of tissue sections of the gastric epithelium and submucosa in control, ulcerated, and 3g + indomethacin-treated tissues revealed disruption and exfoliation of the gastric epithelial layer during ulceration (black arrowheads), whereas gastric tissues in 3g-treated mice (50 mg/kg b.w.) showed minimal injury and an intact epithelial layer. Unless otherwise stated, the remaining tests used a 50 mg/kg b.w. 3g dosage. (D) Adobe Photoshop was used to divide microscopic pictures of each group into 1 in^2 boxes. In three separate studies on each group, the cells of each box from the mucosal and submucosal regions were counted. Results are reported as mean ± standard error (SE). *** = $p < 0.001$ versus control, ### = $p < 0.001$ versus indomethacin, $n = 5$ in each group, and experiments were done in triplicates. (E) TUNEL assay showed suppression of the apoptosis of the gastric mucosa of ulcerated mice by compound 3g. The images were observed in an Olympus microscope. Images at 10× and 40× magnification were captured using Camedia software (E- 20P 5.0 Megapixel).

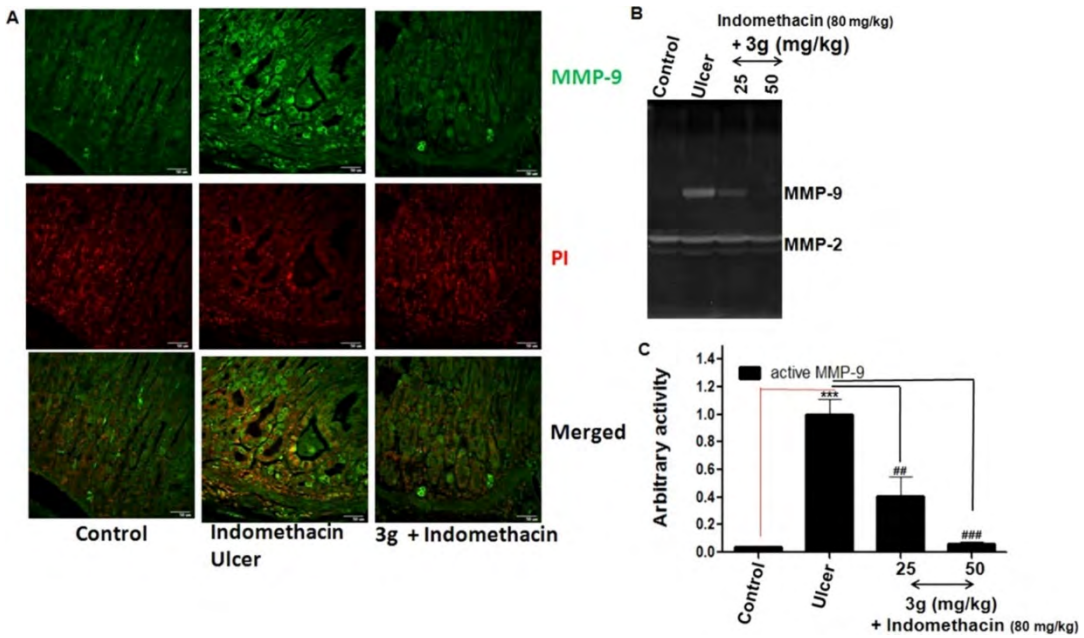


Figure 2: 3g downregulates in vivo MMP-9 expression and activity in NSAID-induced gastric ulcer in mice. (A) MMP-9 was immunostained with anti-MMP-9 antibody and FITC (green) conjugated secondary antibody and nuclei were stained with PI (red). Reduction of MMP-9 expression during gastroprotection by 3g in indomethacin-induced gastric ulcer. (B) Gelatin zymography for the assessment of MMP-9 activity in gastric tissue extracts of mice from NSAID ulcerated and 3g-treated groups. (C) Histographic representation of the arbitrary activity of active MMP-9 versus different samples. Results are reported as mean ± SEM. *** = $p < 0.001$ versus control, ### = $p < 0.001$ versus indomethacin, $n = 5$ in each group, and experiments were done in triplicates.

Toxicity Studies through Repeat Daily Dosing of 3g and Pharmacokinetic Profiling of 3g in Rats

To investigate the potential use of MMP-9 activation inhibitors as therapeutic agents, 3g was evaluated in the mouse indomethacin-induced gastric ulcer model, a widely used animal model of human gastro-inflammatory disease, including ulceration. The goal of this study was to see how effective prolonged oral 3g therapy was and to see whether there were any side effects. Animals were scored based on a clinical observation scale of lethargy, abdominal distension, fur loss, and hunching. At the tested dosages of 3g (150 or 300 mg/kg body weight/day for 25 days), we detected no mortality or clinical symptoms of toxicity during the treatment period. Female mice weighed 4 g less than male mice on average, which is in agreement with the normal sex-specific weight differential. The treatment and control groups did not vary in terms of body weight (Figure 3).

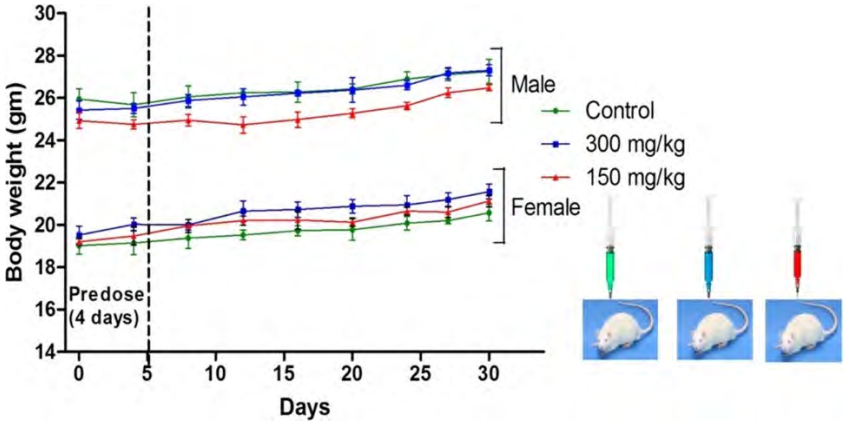


Figure 3: Toxicity studies of 3g in BALB/c mice. Male and female BALB/c mice ($n = 10$) received indicated doses of 3g by oral gavage. Body weights were determined 4 days before the start of the treatment and then throughout the period of treatment until day 30. Data points represent mean body weight.

Pharmacokinetic experiments in Sprague-Dawley rats were carried out to determine the time course of action and disposal of 3g in vivo. Figure 4 depicts the average concentration–time profile in plasma samples for 3g. In the range studied, the curve was linear, and the extraction efficiency was better than 70%. It displays a progressive increase in drug concentration to a maximum value (C_{max} = 104.48 µg/mL) at around 6.0 h (t_{max}) after treatment, followed by a polyexponential drop with a rather lengthy terminal phase, with half-life and area under the curve of 7.0 and 1273.8 h, respectively.

Future Research Plans

- Development of high-affinity BET Bromodomain Ligands as anticancer agents and SynTEFs for activation of FXN and other genetic diseases.
- Development of Synthetic and Natural Product-based inhibitors against histone methyltransferases (G9a/GLP).
- Target-oriented development of small molecules against COVID-19, *Leishmania Donovani*, and *Chagas diseases*.
- Elucidating the mechanism of small molecular fluorescence probes for Lipid droplets (LD) and exploring their qualitative and quantitative estimation of LDs in various disease models for a wide range of biomedical applications.
- The ongoing effort includes the development of stable atropisomers for biological applications.
- Synthesis of new lead compounds of natural product origin and their analogues with various biological activities, focusing especially on anticancer, antimicrobial, anti-leishmanial, and anti-inflammatory compounds.
- Extraction, isolation, purification of compounds, and evaluation of their biological activities from medicinal plants are also ongoing.

Publications

1. Goel, N., Garg, A., Nagendra, C., Reddy, A. M., Biswas, R., Natarajan, R., and Jaisankar, P.* (2024) *In-vitro* and *in-silico* Cholinesterase inhibitory activity of bioactive molecules isolated from the leaves of *Andrographis nallamalayana J.L. Ellis* and roots of *Andrographis beddomei C.B. Clarke*, *J. Mol. Structure*, 1301, 137406.
2. Rudra, D. K., Chatterjee, S., Pal, U., Mandal, M., Ray Chaudhuri, S., Bhunia, M., Maiti, N.C., Besra, S.E., Jaisankar, P.,* and Swarnakar*, S. (2023) A newly synthesized 3-indolyl furanoid inhibits matrix metalloproteinase-9 activity and prevents nonsteroidal anti-inflammatory drugs-induced gastric ulceration, *J. Med. Chem.,* 66, 13, 8917-8928. [Published as Cover Page Article]

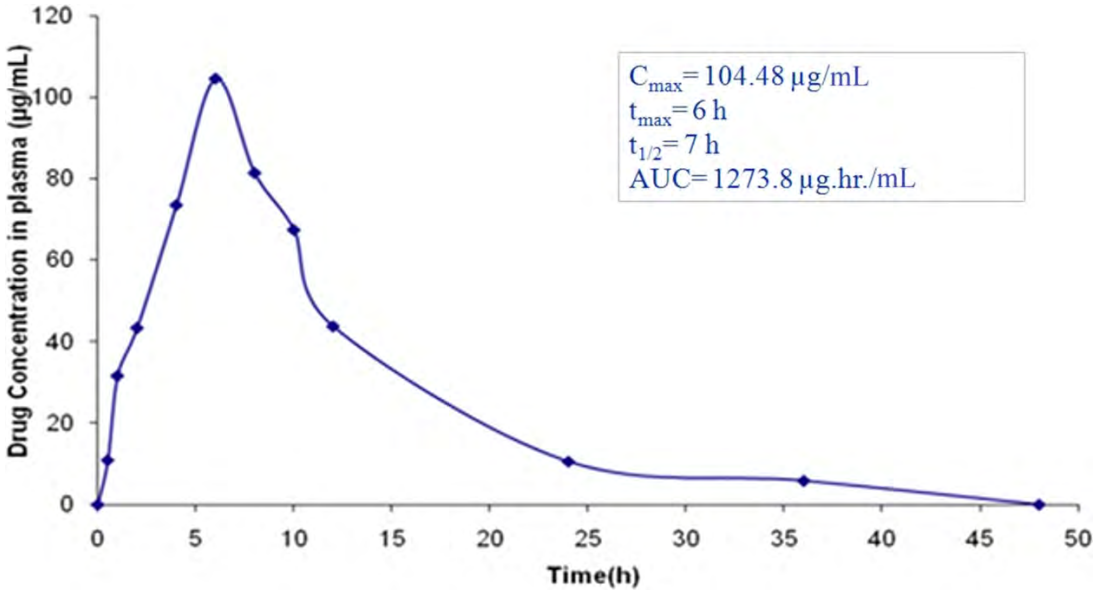


Figure 4: Pharmacokinetic profiling of 3g. BALB/c mice received a single dose of 250 mg/kg body weight 3g by oral gavage. Plasma 3g levels were determined by high-performance liquid chromatography (HPLC). Values represent mean plasma levels ± SEM.

Patents

1. Jaisankar, P., Garg, A., Gupta, S., Ravichandiran, V., and Bandyopadhyay, A. 3,3'-Biindole based florescence dye probe and application thereof, Indian Patent, 2023, Application Number 202311039884.
2. Garg, A., Jaisankar, P., Gupta, S., Ravichandiran, V., and Bandyopadhyay, A. rRNA Selective Fluorescent Bio-Probe for Tracking Viscoelastic Nature of Intracellular Nucleolus, Indian Patent, 2023, Application Number 202311085302.
3. Garg, A., Jaisankar, P., Gupta, S., Ravichandiran, V., and Bandyopadhyay, A., Indole Based Fluorescent Bio-Probe for the Super-Resolution Wash-Free Live Cell Imaging of Endoplasmic Reticulum, Indian Patent, 2023, Application Number 202311085301.

Awards / Honours

1. Elected as Vice-President of Chemical Biology Society (CBS), India, Bhubaneshwar, 2023
2. Elected as President, Royal Society of Chemistry (RSC), Eastern India Section, Kolkata, 2023
3. Elected as Global Outreach Contributing Member of American Society for Microbiology, USA, 2024

Conferences/Events Organized

1. Skill Development programs of CSIR-IICB, 2023- 2024 organized by CSIR-IICB, Kolkata, India.
2. Organized the International Conference entitled" International Conference on Metabolic Diseases (ICMD) 2023 at CSIR-IICB, Kolkata as Organizing Secretary on 19th August 2023.
3. Research Conclave of CSIR-IICB as organizing Chairman, 25th January, 2024

Invited Talks

1. Role of quality assurance in GLP Facility: NIPER-Kolkata: Workshop on Good Laboratory Practice (GLP). February 9, 2024
2. 3-Indolyl furanoid inhibits matrix metalloproteinase-9 activity and prevents nonsteroidal anti-inflammatory drug-induced gastric ulceration: University of Hyderabad: 9th International Conference on Molecular Signalling (ICMS-2024). February 1-3, 2024.
3. Bioactive Novel Molecules of Synthetic and Natural Product Origins in Drug Discovery for Cancer and Neglected Infectious Diseases, Guwahati: Zoology Dept., Guwahati University. September 1, 2023.

Conferences Attended

1. DST-Sponsored Faculty Development Training on Research for Societal Good through Social Responsibility, Amrita Vishwa Vidyapeetham, Coimbatore, November 20-24, 2023.
2. 9th International Conference on Molecular Signalling (ICMS-2024), University of Hyderabad, Hyderabad, February 1-3, 2024.

Dr. Parasuraman Jaisankar, Chief Scientist
Group Member: Vivek K. Gupta, ICMR-SRF; Nipun Abhinav, SRF, NIPER; Narendar Goel, SRF, NIPER; Aakriti Garg, SRF, NIPER; Shrabanti Kumar, DST-Women Scientist; Sudip Dey, DST Inspire SRF; Mohammed Rafi, Project Fellow; Sunnapu Prasad, Project Fellow; Bedabrata Ray, DST Inspire JRF
Collaborators: Dr. Arun Bandyopadhyay, CSIR-IICB; Dr. Mabali Rajan, CSIR-IICB; Dr. Ramalingam Natarajan, CSIR-IICB; Dr. H. K. Majumdar, CSIR-IICB; Dr. Snehasikta Swarnakar, CSIR-IICB; Dr. V. Ravichandiran, NIPER-Kolkata' Dr. Sreya Gupta, NIPER-Kolkata

Dr. Ranjan Jana and his group members

Development of Sustainable Cross-Coupling Reactions for API Synthesis

Research Activities

The development of privileged medicinal scaffolds is the key step in the drug discovery programs. We have initiated a cutting-edge C-H activation technology for the synthesis of heterocycles and other medicinally relevant molecules. Furthemore, this technology is particularly important for the late-stage diversification of functional molecules. C-H activation in organic synthesis (CHAOS) not only accelerate the synthesis but also allow us to achieve molecules which was unimaginable before. Furthermore, multiple C-H activation in a cascade manner will enable us to achieve molecular diversity as well as complexity from simple, readily available, inexpensive starting materials. This approach will generate a library of multifunctional molecules for Alzheimer's Disease, breast cancer etc. Furthermore, cost effective processes for the off-patent drug and agrochemicals will be developed. Recently, we have initiated a research program for the utilization of biomass-derived chemicals, CO_2, HCOOH, SO_2, etc., as feedstock chemicals for waste to wealth conversion (Fig. 1).

Future Research Plans

We are developing sustainable cross-coupling reactions using earth abundant, inexpensive transition metals such as iron, cobalt, nickel etc. replacing palladium catalyst. We are also developing the nature-mimetic visible light photoredox catalysed metal-free chemical transformations at room temperature. We like to apply this cutting-edge technology for the synthesis and late-stage modification of amino acids to generate non-proteinogenic amino acids for chemical biology and medicinal chemistry applications. Alkene difunctionalization, biomass velorization and CO_2, SO_2 utilization for sustainable development and waste to wealth generation (Fig 2). We aim to 1) Late-stage diversification via site-selective C-H activations for the synthesis of unnatural amino acids; 2) Visible light mediated decarboxylative cross-coupling reactions using inexpensive carboxylic acids as cross-coupling partner; 3) Carbene and nitrene chemistry for metal-free C-C and C-N cross-coupling reactions; 4) Alkene difunctionalization and CO_2, SO_2 utilization for

sustainable development; 5) Application of the synthetic methodology for the synthesis of APIs.

Extramural / CSIR Funding

1. Development of Visible-Light Photoredox and Transition Metal Dual Catalytic Alkene Difunctionalization Reactions. SERB, Department of Science & Technology (DST), 2021-24, 25.3 Lakhs, CRG/2021/006717.
2. Making Cancer Care Affordable" Empowering Women's Health: Focusing on Breast and Gynaecological Cancers of Indian Relevance. CSIR, 2020-25, 1000 lakhs, HCP-40.
3. Innovative Process and Technologies for Crop Protection Chemicals (Agromission II). CSIR, 2023-2026, 199.888 lakhs, HCP-49.
4. Active Pharmaceutical Ingredients for Affordable Health Care. CSIR, 2023-2025, 110 lakhs, HCP-50.

Publications

1. Begam, H. M.; Das, P.; Das, S.; Mondal, S.; Jana, R* (2023) HFIP-assisted, cobalt-catalyzed three-component electrophilic C-H amination/cyclization/directing group removal cascade to naphtho[1,2-d]imidazoles, ChemCommun, *59,* 5595-5598.
2. Nandi, S.; Das, P.; Das, S.; Mondal, S.; Jana, R* (2023) Visible-light-mediated β-acylative divergent alkene difunctionalization with Katritzky salt/CO_2, *Green Chem., 25,* 3633-3643.
3. Manna, K.; Jana, R* (2023), Palladium-Catalyzed Cross-Electrophile Coupling between Aryl Diazonium Salt and Aryl Iodide/Diaryliodonium Salt in H_2O–EtOH, *Org. Lett*. 25, 341–346.
4. Manna, K.; Begam, H. M.; Jana, R* (2023) Transition-Metal-free Dehydrogenative Cyclization via α-(Csp^3)−H Activation of Ether and Thioether, Synthesis, 55, 1543-1552.

Invited Lectures

1. Molecular Diversity through Casacde C-H Activation, International Conference on Organometallics and Catalysis (ICOC), Goa, 30th Nov-2nd Dec. 2023.
2. Molecular Diversity through Casacde C-H Activation, Emerging Trends in Chemical Sciences University of Calcutta, 9th Feb, 2024.
3. Molecular Diversity through Casacde C-H Activation, IITKGP, Emerging Trends in Chemical Sciences, 7-9th March, 2024.
4. Molecular Diversity through Casacde C-H Activation, IACS, International Conference on Catalysis, 11-13th March, 2024.

Conferences Attended

32nd CRSI National Symposium in Chemistry, BITS, Pilani, 01-04 February, 2024.

Dr. Ranjan Jana, Senior Principal Scientist

Group Members: Subhodeep Das, CSIR-SRF; Shuvam Mondal, CSIR-SRF; Kangkan Pradhan, CSIR-SRF; SK Abdur Rahaman, DST INSPIRE, JRF; Supriyo Das, UGC-JRF; Soumyajit Pal, DST INSPIRE-JRF; Sourav Mandal, UGC-JRF; Amit Banerjee, HCP-49- Project Associate I

Dr. R. Natarajan and his group members

Development of synthetic supramolecular receptors and crystal engineering of functional molecules

Research Activities

The field of supramolecular chemistry has seen significant advancements in the design and synthesis of novel organic and metal-organic cage molecules. These structures act as synthetic receptors with high specificity for the recognition, sensing, and transport of vital physiological analytes. Crystal engineering techniques have been pivotal in modifying the properties of functional molecules and drugs, enhancing their performance and efficacy. Porous cocrystals, engineered through these methods, show great promise for the storage and recognition of environmentally and biologically important molecular species. Our research is focused on the design, synthesis, and application of novel supramolecular structures, particularly organic and metal-organic cages. These studies are at the forefront of supramolecular chemistry, crystal engineering, and the development of functional materials for various applications, including sensing, recognition, transport, and catalysis.

Organic cages: We reported the synthesis of cofacial organic cage molecules containing aggregation-induced emissive (AIE) luminogens (AIEgens) through four-fold Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) “click” reactions. The shorter AIEgen, tetraphenylethylene (TPE), afforded two orientational isomers (TPE-CC-1A and TPE-CC-1B). The longer AIEgen, tetrabiphenylethylene (TBPE), afforded a single isomer (TBPE-CC-2). The click reaction employed is irreversible, yet it yielded remarkable four-fold click products in 40 %. The phenyl rings around the ethylene core generate propeller-shaped chirality owing to their orientation, which influences the chirality of the resulting cages. The shorter cages are a mixture of PP/MM isomers, while the longer ones are a mixture of PM/MP isomers, as evidenced by their x-ray structures. The newly synthesized cage molecules are emissive even in dilute solutions (THF) and exhibit enhanced AIE upon the addition of water. The aggregated cage molecules in aqueous solution exhibit turn-off emission sensing of nitroaromatic explosives, with selectivity to picric acid in the 25-38 nanomolar detection range.

Water-soluble organic cages are attractive targets for their molecular recognition and sensing features of biologically relevant molecules. Here, we have successfully designed and synthesized a pair of water-soluble cationic cages employing click reaction as the fundamental step followed by the *N*-

methylation of the triazole rings. The rigid and shape-persistent 3D hydrophobic cavity, positively charged surface, H-bonding triazolium rings, and excellent water solubility empower both cages to exhibit a superior affinity and selectivity for binding with adenosine-5'-triphosphate (ATP) compared to cyclophanes and other macrocyclic receptors. Both cage molecules (PCC·Cl and BCC·Cl) can bind a highly emissive dye HPTS (8-hydroxypyrene-1,3,6-trisulfonic acid trisodium salt) to form non-fluorescent complexes (Figure 1). The addition of ATP resulted in the stronger cage⊂ATP complexes with the retention of HPTS emission upon its displacement. The resultant indicator-displacement assay system can efficiently sense and quantify ATP in nanomolar detection limits in buffer solutions and human serum matrix. Spectroscopic and theoretical studies revealed the synergistic effect of π···π stacking interaction between the aromatic moiety of the cationic cages and the adenine moiety of ATP, as well as the electrostatic and hydrogen bonding interaction between the phosphate anion of ATP and triazole protons of cages, played the pivotal roles in the sensing process.

Cocrystal Engineering: There is a strong and urgent need for efficient materials that can capture radioactive iodine atoms from nuclear waste. We present a novel strategy to develop porous materials for iodine capture by employing halogen bonding, mechanochemistry and crystal engineering. 3D halogen-bonded organic frameworks (XOFs) with guest-accessible permanent pores are exciting targets in crystal engineering for developing functional materials, and we report the first example of such a structure. The new-found XOF, namely TIEPE-DABCO, exhibits enhanced emission in the solid state and turn-off emission sensing of acid vapors and explosives like picric acid in nanomolar quantity. TIEPE-DABCO captures iodine from the gas phase (3.23 g g^{-1} at 75 °C and 1.40 g g^{-1} at rt), organic solvents (2.1 g g^{-1}), and aqueous solutions (1.8 g g^{-1} in the pH range of 3-8); the latter with fast kinetics. The captured iodine can be retained for more than seven days without any leaching, but readily released using methanol, when required. TIEPE-DABCO can be recycled for iodine capture several times without any loss of storage capacity. The results presented in this work demonstrate the potential of mechanochemical cocrystal engineering with halogen bonding as an approach to develop porous materials for iodine capture and sensing.

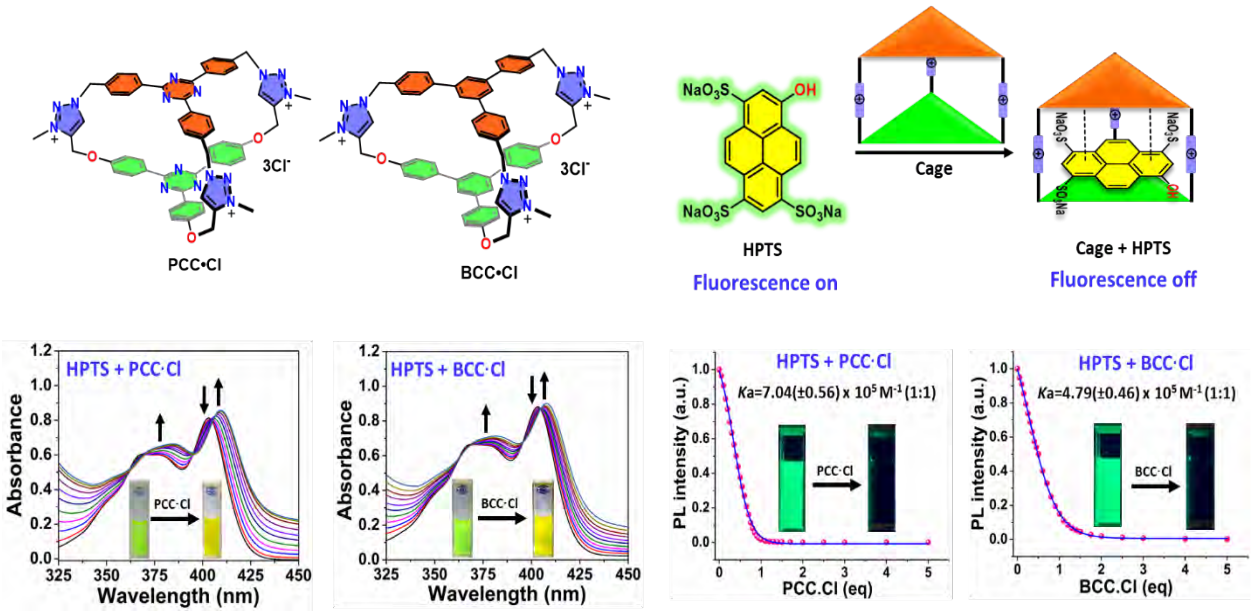


Figure 1: Molecular structures of PCC·Cl and BCC·Cl and ATP sensing through indicator displacement

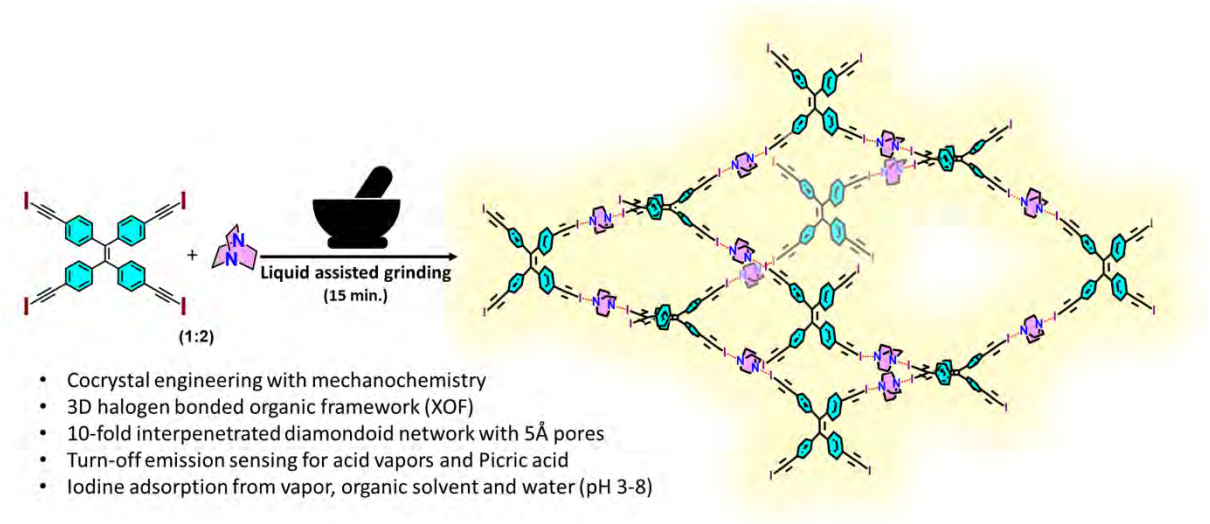


Figure 2: Halogen bonded porous and multifunctional cocrystal through mechanochemistry

Future Research Plans

Our future research activities include i) development of novel organic and metal-organic cages and acyclic receptors towards recognition and sensing of biologically and physiologically relevant molecules and ions, and delivery of drugs, ii) cocrystal engineering of active pharmaceutical ingredients.

Publications

1. Maji, S., Samanta, J., and Natarajan, R. (2024). Water-Soluble Triazolium Covalent Cages for ATP Sensing. *Chem. Eur. J.* 30, e202303596.
2. Maji, S., Samanta, J., Samanta, K., and Natarajan, R. (2023). Emissive Click Cages. *Chem. Eur. J.* 29, e202301985.
3. Maji, S., and Natarajan, R. (2023). A Halogen-Bonded Organic Framework (XOF) Emissive Cocrystal for Acid Vapor and Explosive Sensing, and Iodine Capture. *Small* 19, 2302902.

Dr. R. Natarajan, Senior Principal Scientist
Group Members: Raju Biswas, SRF; Sandipan Ghorai, SRF; Suman Maji, SRF; Bhaswati Paul, SRF; Suvajit Pal, PA

Dr. Rashmi Gaur and her group members

Activity guided isolation of bioactive phytomolecules from Indian Medicinal Plants for drug discovery

Research Activities

Natural products are a source of new lead molecules in drug discovery research. Various drugs currently used as therapeutic agents are derived from natural sources. Earlier, natural products due to their complexity gained less attention from pharmaceutical companies. At present advancements in technology, helped to overcome the challenges which resulted in increased scientific interest in drug discovery from natural sources. An integrated interdisciplinary approach using advanced technologies is necessary for successful natural product drug development. The main goal of my lab will be to use modern approaches in bioactivity-guided extraction, isolation, development of natural product analogs, and bioassays with a high-throughput capacity to establish druggability and patentability of novel natural product analogs.

Pharmacognostic profiling of bioactive phytomolecules from unexplored and medicinally important plants viz. *Myena spinosa* of North East India. The plant has shown significant activity against SARS-Co-2, PLPro.

Pharmacognostic profiling of bioactive phytomolecules from onion (*Allium cepa*) peel. The plant has shown significant activity against SARS-Co-2, PLPro

- Activity guided extraction, Isolation and characterization of bioactive phytomolecules from medicinal plants.
- Chemical transformation of isolated phytomolecules for enhancing the potential biological activities and their SAR studies.

Future Research Plans

Extraction, isolation, synthetic modification and identification of isolated phytomoleculers using different spectroscopic techniques from Indian medicinal plants. Herbal formulation viz. pharmaceutical and nutraceutical of bioactive fractions of the plant.

Extramural / CSIR Funding

Chemopreventive and protective effects of *Opuntia elatior* fruit against Chemotherpy-induced toxicity in ovarian cancer pre-clinical models. AYUSH, 2024-2025, 37.6 Lakhs, PROJ011/247/2023

Member of Society

1. Life Member, The Indian Science Congress Association, Kolkata-700017, India
2. Life Member, Chemical Research Society of India, Indian Institute of Science. Bangalore 560 012, India.
3. Life Member, Indian Society of Chemists and Biologists, CSIR-Central Drug Research Institute, Lucknow-226031, India

Dr. Rashmi Gaur, Scientist
Group Members: Ritisha Ghosh, DST-INSPIRE; Subhasundar Maji, Project JRF
Collaborators: Dr. Amit. K. Srivastava, CSIR-Indian Institute of Chemical Biology, Kolkata; Dr. Umesh. P. Singh, CSIR-Indian Institute of Chemical Biology, Kolkata; Dr. N.P. Yadav, CSIR-Central Institute of Medicinal and Aromatic Plants, Lucknow.

Dr. Sanjay Dutta and his group members

Targeting Nucleic acids with Quinoxaline and Indoloquinoline small molecules

Research Activities

Structural information of nucleic acids with small molecule or ligands can be useful for designing DNA/RNA targeting therapeutics. Recent work from our laboratory shows that the DNA superstructure formation by mono-quinoxaline derivatives is highly entropically favored and predominantly driven by hydrophobic interactions. Furthermore, over supercoiling of DNA and base-destacking cumulatively induces histone eviction from *in-vitro* assembled nucleosomes at lower micromolar concentrations implicating biological relevance. Furthermore, some of the designed quinoxaline amines were shown to cleave abasic sites in DNA and potentiate the therapeutic ability of known anticancer drugs in colon cancer cells.

Recognizing the significance of hydrophobicity-driven modulation of DNA structure, we were motivated to design a novel series of mono-quinoxaline-based DNA intercalators. This involves the modification of the π-surface by introducing different substitutions of the benzyl moiety, thereby amplifying the hydrophobicity of the compounds. We also showed that quinoxaline-induced changes in DNA structure induce ZBP1-mediated necroptosis in RIP3-expressing cells (HT-29).

Our laboratory also developed a concise two-step one-pot synthesis method for N-6-functionalized norcryptotackieine, achieved through a Pd-catalyzed double annulation reaction offering broad flexibility for substitution at the N-6 position, enabling access to diverse scaffolds, including two natural products: norcryptotackieine and neocryptolepine.

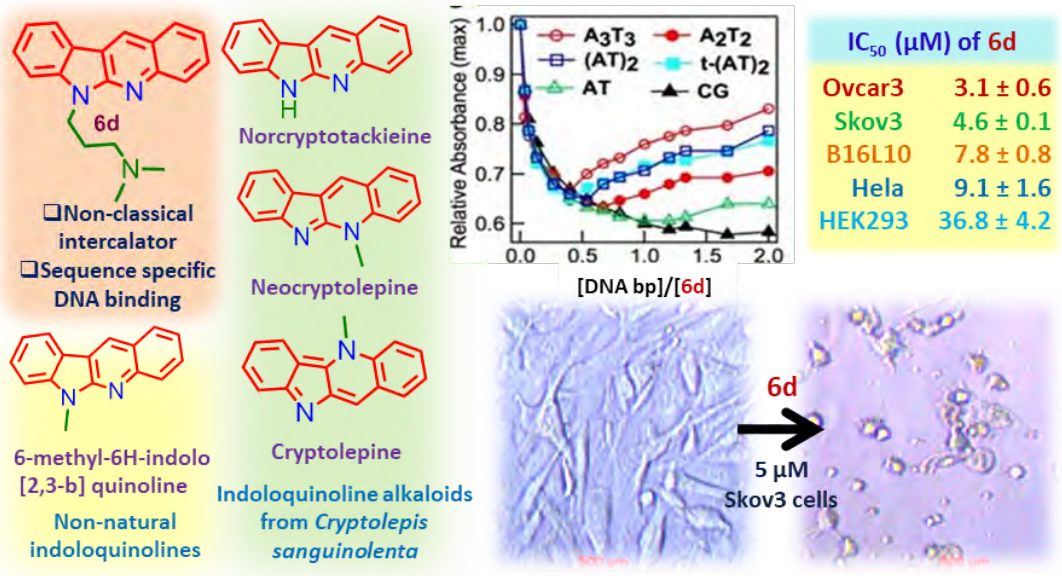
Additionally, we also examined the effect of substitutions at the N-6 position of norcryptotackieine on the cytotoxicity, as well as structure-activity relationship studies pertaining to sequence-specific DNA binding affinities. The representative compound binds DNA in a non-intercalative/ pseudo-intercalative fashion, in addition to non-specific stacking on DNA, in sequence selective manner. The indoloquinolines were screened in different cancer cell lines to assess their cytotoxicity and compared with that of the natural compounds Cryptolepine and Neocryptolepine to shed light on the effect of substitution at N-6 position in relation to their cytotoxicity.

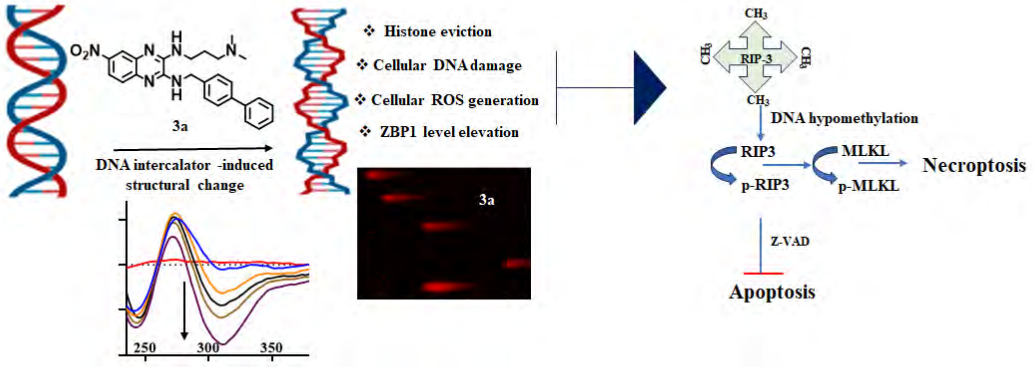
1. Sequence-specific dual DNA binding modes and cytotoxicities of N-6 functionalized norcryptotackieine alkaloids

Norcryptotackieine (1a) belongs to the indoloquinoline class of alkaloids isolated from Cryptolepis sanguinolenta, a plant species which has been traditionally used as an antimalarial agent. Additional structural modifications of 1a can enhance its therapeutic potency. Indoloquinolines such as cryptolepine, neocryptolepine, isocryptolepine and neoisocryptolepine show restricted clinical applications owing to their cytotoxicity deriving from interactions with DNA. Future development of norcryptotackieine analogs, as therapeutic agents with diminished cytotoxicity, will rely on the understanding of mode, selectivity and mechanism of their binding to specific sequences of nucleic acids. Here, we examined the effect of substitutions at the N-6 position of norcryptotackieine on the cytotoxicity, as well as structure-activity relationship studies pertaining to sequence specific DNA binding affinities. The representative compound 6d binds DNA in a non-intercalative / pseudo-intercalative fashion, in addition to non-specific stacking on DNA, in a sequence selective manner. The DNA-binding studies clearly establish the mechanism of DNA binding by N-6 substituted norcryptotackieines and neocryptolepine. The synthesized norcryptotackieines 6c-d and known indoloquinolines were screened in different cell lines (HEK293, OVCAR3, SKOV3, B16F10 and HeLa) to assess their cytotoxicity. Norcryptotackieine 6d (IC_{50} value of 3.1 µM) showed a two-fold less potency when compared to the natural indoloquinoline-cryptolepine 1c (IC_{50} value of 1.64 µM) in OVCAR3 (ovarian adenocarcinoma) cell lines.

2. Mono-quinoxaline-induced DNA structural alteration leads to ZBP1/RIP3/MLKL-driven necroptosis in cancer cells

Abstract: Evading the cellular apoptosis mechanism by modulating multiple pathways poses a sturdy barrier to effective chemotherapy. Cancer cell adeptly resists the apoptosis signaling pathway by regulating anti and pro-apoptotic proteins to escape cell death. Nevertheless, bypassing the apoptotic pathway through necroptosis, an alternative programmed cell death process, maybe a potential therapeutic modality for apoptosis-resistant cells. However, synthetic mono-quinoxaline-based intercalator-induced cellular necroptosis as an anti-cancer perspective remains under-explored. To address this concern, we undertook the design and synthesis of quinoxaline-based small molecules (3a-3l). Our approach involved enhancing the π-surface of the mandatory benzyl moiety to augment its ability to induce DNA structural alteration via intercalation, thereby promoting cytotoxicity across various cancer cell lines (HCT116, HT-29, and HeLa). Notably, the potent compound 3a demonstrated the capacity to induce DNA damage in cancer cells, leading to the induction of ZBP1-mediated necroptosis in the RIP3-expressed cell line (HT-29), where Z-VAD effectively blocked apoptosis-mediated cell death. Interestingly, we observed that 3a induced RIP3-driven necroptosis in combination with DNA hypomethylating agents, even in the RIP3-silenced cell lines (HeLa and HCT116). Overall, our synthesized compound 3a emerged as a promising candidate against various cancers, particularly in apoptosis-compromised cells, through the induction of necroptosis.



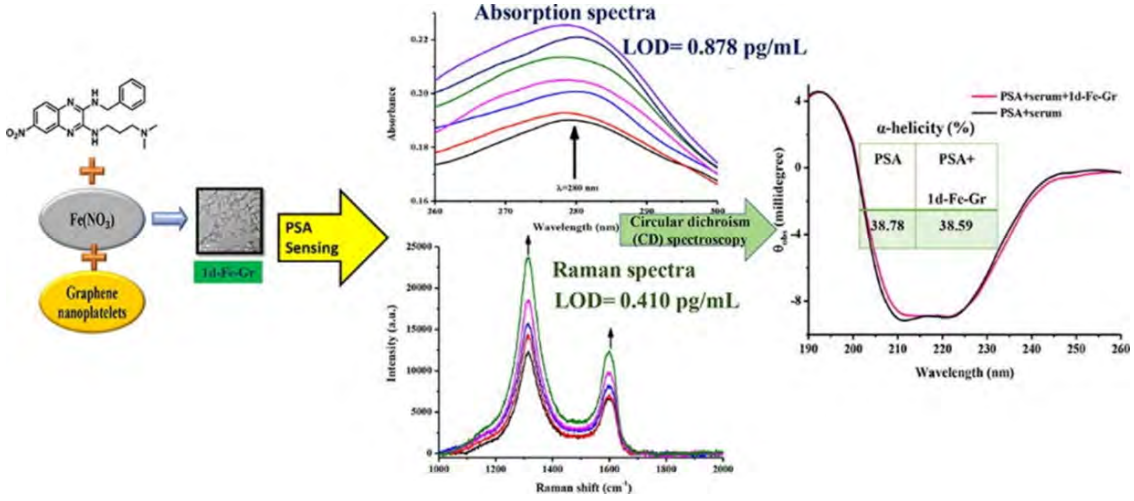


3. A multispectroscopic approach for ultra-trace sensing of prostate specific antigen (PSA) by iron nanocomposite fabricated on graphene nanoplatelet

Herein we report an easy, rapid and cost-effective method for spectroscopic sensing of a prostate cancer biomarker prostate specific antigen (PSA) using a novel nanocomposite. The material is a synthetic quinoxaline derivative-based iron nanocomposite fabricated on graphene nanoplatelet surface (1d-Fe-Gr). Presence of graphene enhanced the efficacy of synthesized 1d-Fe-Gr to sense PSA in serum medium with an impressive limit of detection (LOD) value of 0.878 pg/mL compared to 1d-Fe alone (LOD 17.619 pg/mL) using UV–visible absorption spectroscopy. LOD of PSA by 1d-Fe-Gr using Raman spectroscopy is even more impressive (0.410 pg/mL). Moreover, presence of interfering biomolecules like glucose, cholesterol, bilirubin and insulin in serum improves the detection threshold significantly in presence of 1d-Fe-Gr which otherwise cause LOD values of PSA to elevate in control sets. In presence of these biomolecules, the LOD values improve significantly as compared to healthy conditions in the range 0.623-3.499 pg/mL. Thus, this proposed detection method could also be applied efficiently to the patients suffering from different pathophysiological disorders. These biomolecules may also be added externally during analyses to improve the sensing ability. Fluorescence, Raman and circular dichroism spectroscopy were used to study the underlying mechanism of PSA sensing by 1d-Fe-Gr. Molecular docking studies confirm the selective interaction of 1d-Fe-Gr with PSA over other cancer biomarkers.

Future Research Plans

Development of quinoxaline-based small molecules which can target Hepatitis C Virus RNA and decrease translation. Development of quinoline-based small molecules which are less cytotoxic mTOR inhibitors having antilipidemic activities. Development of small molecules which target DNA abasic sites to enhance PARP inhibitor efficacy in cancer cells.



Publications

1. Basu, S.; Das, D.; Ansari, Z.; Rana, N.; Majhi, B.; Patra, D.; Kanungo, A.; Morgan, D.; ay Dutta, S. and Sen, K.* (2023). A multispectroscopic approach for ultra-trace sensing of prostate specific antigen (PSA) by iron nanocomposite fabricated on graphene nanoplatelet. *Spectrochim Acta A Mol Biomol Spectrosc*. Nov 15; 301:122955.
2. Majhi, B.;# Ganguly, S.;# Palit, S.;# Parwez, A.; Saha, R.; Basu,G.* and Dutta, S.* (2023) Sequence-specific dual DNA binding modes and cytotoxicities of N-6 functionalized norcryptotackieine alkaloids" *Journal of Natural Products*, 86, 7, 1667–1676.
3. Saha, R.;# Pal, R.;# Ganguly, B.; Majhi, B. and Dutta, S.* (2024). Mono-quinoxaline-induced DNA structural alteration leads to ZBP1/RIP3/MLKL-driven necroptosis in cancer cells. *Eur J Med Chem.* Apr 15; 270:116377.

Patents

Quinoline compounds for the treatment of fatty liver disease and process for preparation thereof. Subhadeep Palit, Tanushree Das, Bhim Majhi, Partha Chakrabarti, Sanjay Dutta, filing date 07/03/2024, PCT 0204NF2023/IN

Extramural / CSIR Funding

1. Project Title: "Targeting RNA driven processes: Novel Chemical Biology Approaches to Identify New Classes of RNA Modulators" CSIR Project (Co-PI, Five year project; April 2020-March 2025). MLP-139. Sanctioned Budget Rs. 4.1 crore.
2. Project Title: "Non-alcoholic Fatty Liver Disease (NAFLD): Novel Pathogenetic mechanism and therapeutic development", CSIR Project. (Co-PI, Five year project; April 2020-March 2025). MLP-138. Sanctioned Budget Rs. 4.99 crore.

Dr. Sanjay Dutta, Senior Principal Scientist
Group Mamber: Chandra Sova Mandi, SRF; Bhim Majhi, SRF; Achyut Bora, SRF; Aymen Parwez, SRF; Dr. Abhi Das, DST Women Scientist; Rimita Saha, DBT SRF; Mayank Gardia, JRF; Devojyoti Sadukhan, JRF; Bhaskar Ganguly, JRF; Biswadip Chakraborty, JRF; Niloy Biswas, JRF; Rounak Patra, Project Associate
Collaborators: Prof. Gautam Basu, Bose Institute; Prof. Kamalika Sen, CU; Dr. Partha Chakraborty, CSIR-IICB

Prof. Vibha Tandon and her group members

Discovery of a new target to combat antimicrobial resistance and understand the mechanism of radiosensitizers as well as radioprotectors for cancer therapy

Research Activities

Our laboratory focuses on two key areas: addressing antimicrobial resistance and safeguarding normal cells during cancer treatment to minimize damage while targeting cancer cells.

The development of antimicrobial resistance by bacterial strains is a serious and growing threat worldwide. It may reduce the ability to prevent and treat infections in human. World Health Organization (WHO) surveillance report concedes that resistance in common human Infectious disease-causing pathogens like *Acinetobacter spp., Pseudomonas spp*. and various *Enterobacteriaceae spp*., and *Staphylococcus aureus* as one of the biggest threats for mankind. In our lab, we could achieve type IA DNA topoisomerase as target for the antibacterial agents.

Lung cancer is among the most frequently occurring cancers (11.6%) and the foremost cause of death (18.4% of all cancer-related deaths), followed by breast (11.6%) and colorectal cancer (9.2%). GLOBOCAN2018 estimated approximately 2.09 million new cases and 1.76 million deaths with lung cancer. 85% of lung cancer patients have the non-small cell lung carcinoma (NSCLC) histological subtype. NSCLC resistance to radiotherapy is a clinical challenge, contributing to increased recurrence, progression, and mortality in patients. Alteration in multiple oncogenic driver were discovered in the last decade, and each represents a potential therapeutic target. K-Ras, a GTPase protein, is responsible for cell growth, proliferation, differentiation, and cell survival. In our lab, we took initiative on repurposing of drugs as radiosensitizers against radioresistant KRAS mutant tumors.

Aims and Objectives of our research are as follows:

- To develop radioprotectors for the protection of normal cells during cancer radiotherapy.
- To develop therapeutic agent against multidrug resistant clinical pathogens

The following work has been achieved so far:

Polydispersity-mediated high efficacy of an in-situ aqueous nanosuspension of PPEF.3HCl in methicillin resistant Staphylococcus aureus sepsis model

Our work focuses on an in-situ nanosuspension of PPEF.3HCl (IsPPEF.3HCl-NS) with enhanced efficacy against methicillin-resistant S. aureus in a septicemia model. The nanosuspension

demonstrated over 90% precipitation efficiency, an average particle size under 500 nm, and improved macrophage uptake. IsPPEF.3HCl-NS significantly outperformed free PPEF.3HCl in reducing bacterial loads and improving survival in septicemia mice, positioning it as a promising formulation against antimicrobial resistance.

Unraveling topoisomerase IA gate dynamics in presence of PPEF and its preclinical evaluation against multidrug-resistant pathogens

Type IA topoisomerases regulate DNA topology by cleaving ssDNA and relaxing negative supercoils. Inhibiting this activity prevents DNA processes, leading to bacterial cell death. Using this concept, two bisbenzimidazoles, PPEF and BPVF, were synthesized to inhibit bacterial TopoIA and TopoIII. PPEF stabilizes the topoisomerase-ssDNA complex and shows high efficacy against 455 multi-drug-resistant bacteria. Accelerated MD simulations indicate PPEF binds and stabilizes the closed TopoIA conformation with -6 Kcal/mol binding energy, disrupting ssDNA binding.

Prochlorperazine enhances radiosensitivity of non-small cell lung carcinoma by stabilizing GDP-bound mutant KRAS conformation

Lung cancer, with high mortality, often involves KRAS mutations, which drive poor prognosis and radioresistance. A high-throughput screen of FDA-approved drugs identified Prochlorperazine (PCZ) as a potential radiosensitizer for KRAS-mutant lung carcinoma. PCZ binds the GTP-binding pocket of mutant KRAS, stabilizing its inactive GDP-bound state. In combination with radiation, PCZ reduced clonogenic survival, activated DNA damage response (p-ATM, p53, p21), and increased apoptosis in KRAS-mutant but not wild-type cells.

Pixantrone confers radiosensitization in KRAS mutated cancer cells by suppression of radiation-induced prosurvival pathways

Through drug repurposing, in-silico screening identified pixantrone, an antineoplastic drug, with high affinity for KRAS G12C and G12D mutants. Pixantrone radiosensitized these KRAS mutant cells, enhancing DNA damage, ATM expression, and apoptosis.

DMA, A Bisbenzimidazole to take it to Early-Phase Human Phase Trials as a Radiomodulator /Radioprotector to Normal Cells for Cancer Radiotherapy in Patients

Survival, recurrence, and xerostomia are major challenges in treating oral squamous carcinoma. This study evaluated DMA as a salivary gland cytoprotectant in a patient-derived xenograft model. DMA treatment significantly increased saliva secretion and, when combined with radiation, showed a synergistic effect on survival and tumor reduction.

Future Research Plans

In future, we will characterize the molecular mechanism of Topoisomerase I of *Staphylococcus aureus* and establish different organoid/ spheroid development methods and study the effect of radiation alone and radiation along with radio protectors.

Extramural Funding (ongoing)

1. *Functional characterization of patient derived single cell spheroids from Oral Squamous Cell Carcinoma to decipher clinical heterogeneity: A Tool for drug screening.* Lady Tata Memorial Trust, 2023-26, 96.8 lakhs, (5-1(592)/2018-PD).
2. Synthesis of Novel 1,1'-Disubstituted C-nucleosides/nucleotides as potential antiviral drug candidates targeting RNA dependent RNA Polymerase. DST-SERB, 2022-2025, 51.18 lakhs (SPG/2021/004179)
3. Identification and characterization of cancer stem cell heterogeneity in head and neck cancer patients and their response to chemotherapy and radiation: A prospective study. ICMR, 2022-2025,63.9 lakhs (2021-13818/SCR/ADHOC-BMS)

Publications

1. Cardoza, S., Singh, A., Sur, S., Singh, M., Dubey, K. D., Samanta, S. K., Mandal, A., & Tandon, V. (2024). Computational investigation of novel synthetic analogs of C-1'β substituted remdesivir against RNA-dependent RNA-polymerase of SARS-CoV-2. *Heliyon*, *10*(17), e36786.
2. Chaudhari, T. Y., Bisht, S., Chorol, S., Bhujbal, S. M., Bharatam, P. V., & Tandon, V. (2023). Bronsted Acid-Catalyzed Regioselective Carboxamidation of 2-Indolylmethanols with Isonitriles. The Journal of organic chemistry, 88(15), 10412–10425.
3. Lokhande, A. S., Maurya, V., Rani, K., Parashar, P., Gaind, R., Tandon, V., & Devarajan, P. V. (2024). Polydispersity-mediated high efficacy of an in-situ aqueous nanosuspension of PPEF.3HCl in methicillin resistant

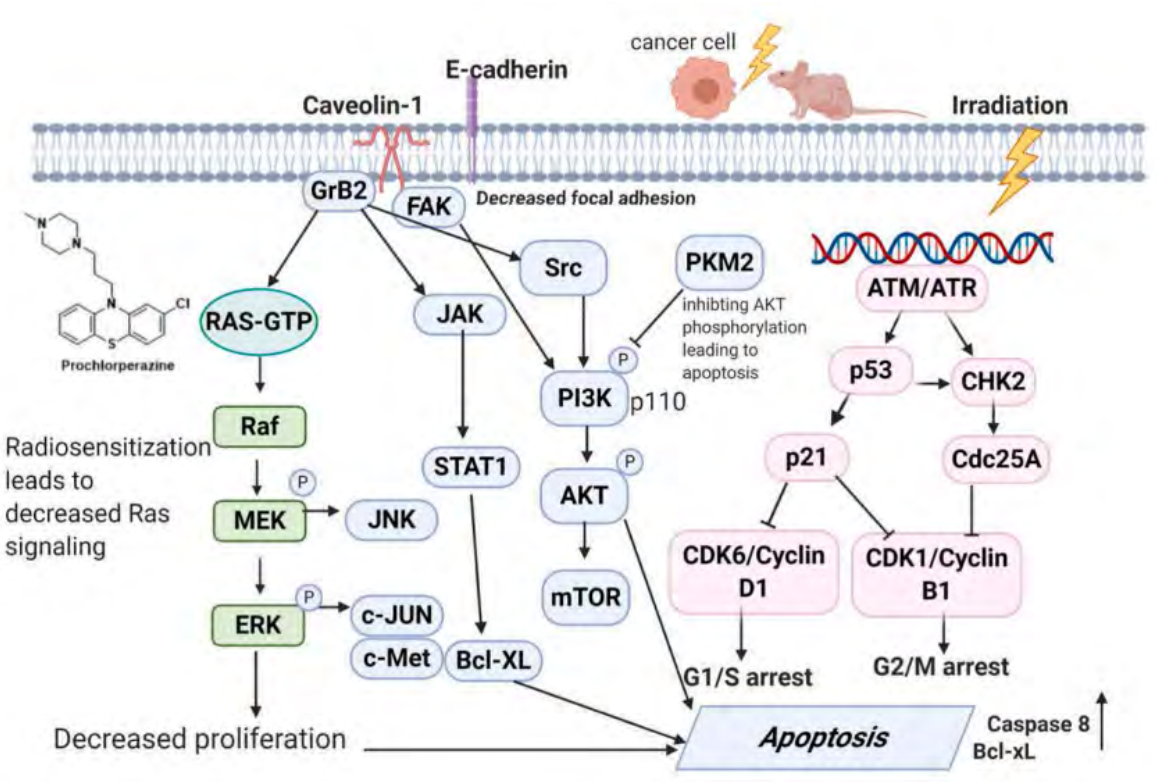
Staphylococcus aureus sepsis model. International Journal of Pharmaceutics, 655, 123982

Conferences attended

International symposium entitled "Nature Inspired Initiatives in Chemical Trends (NIICT-2024)" held at CSIR-Indian Institute of Chemical Technology, Hyderabad from 7th to 9th March 2024.

Awards

1st A. V. Rama Rao award for Women in Chemical Sciences by 33rd CRSI and CRSI-ACS lectures, 2024.

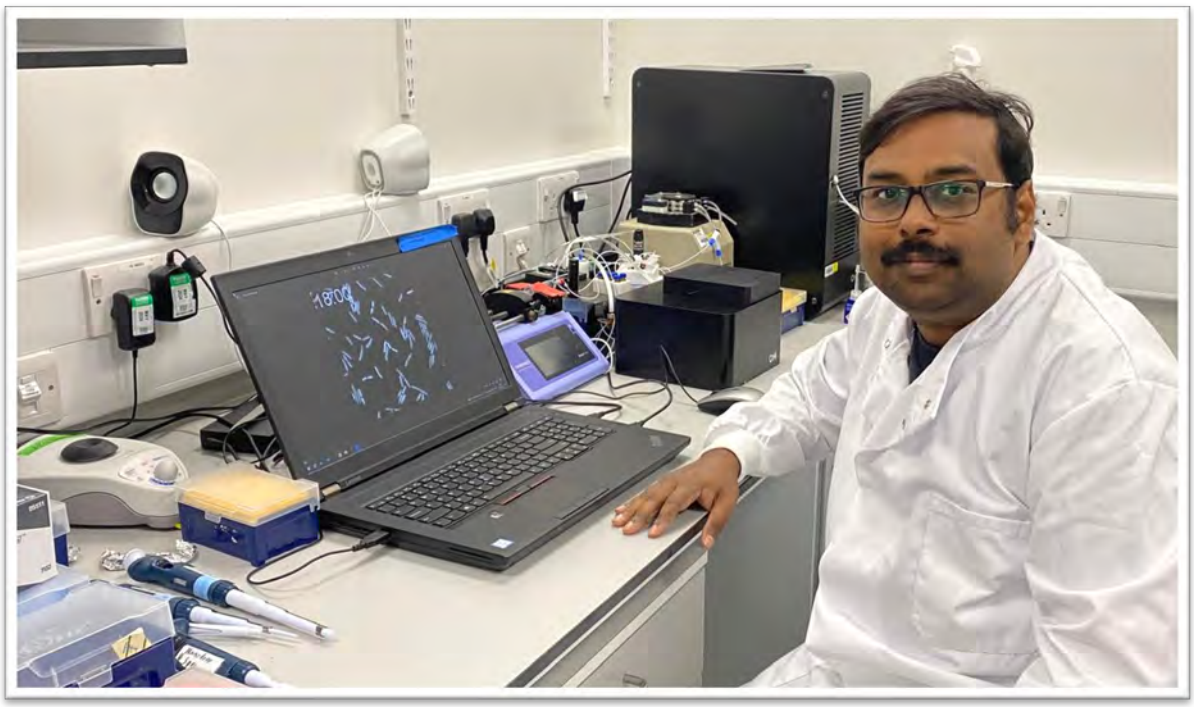


The proposed model describes that PCZ with irradiation activates ATM, resulting in increased dsDNA damage, cell cycle disruption, and downregulates the Ras pathway proteins. Overall PCZ along with radiation increase apoptosis in irradiated cells.

Prof. Vibha Tandon, Director, CSIR-IICB
Group Members: Palak Parashar, Vikas Maurya, Hungharla Hungyo, Antra, Komal Rani, Leena Saini, Vikas Kumar Singh, Naba Kumar Biswas, Mintu Singh and Shruti Jain
Collaborator(s): Prof. Rajni Gaind, VMMC & associated Safdarjung Hospital, New Delhi, Dr. Tejinder Kataria, Medanta-The Medicity, Prof. Padma V. Devarajan, ICT Mumbai, Dr. Vipin Arora, Director Professor of ENT, Head & Neck Surgery, University College of Medical Sciences & GTB Hospital, India and Prof. Sujata Mohanty, DBT-Centre of Excellence for Stem Cell Research, All India Institute of Medical Sciences, India.

Structural biology & Bioinformatics Division

With a view to understand cellular function and dysfunction in human health and disease, researchers at the Structural Biology & Bioinformatics Division 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 are being carried out on protein structure, functions, protein-protein interactions and protein-nucleic acid interactions, applying state-of-the-art technologies like X-ray crystallography, Nuclear Magnetic Resonance (NMR), Cryo-EM, single molecule fluorescence measurements and Fluorescence Correlation Spectroscopy, 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, multiple 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 novel software tools for NGS data mining, pathway analysis and other big data analysis and (xii) design and development of biological knowledgebase of clinical/societal relevance.



Dr. Abhishek Mazumder

Investgating the assembly and dynamics of coupled molecular machines

Research Activities

In bacteria transcription and translation occur in the same compartment and have been shown to be physically coupled by small protein factors like NusG/RfaH etc. As transcription is linked with DNA-repair and translation is linked with protein folding, both fundamentally important processes, a coupling between them likely constitutes a key mechanism that underpins gene regulation. Traditional approaches for deciphering the detailed mechanism of biochemical reactions rely on high-resolution structures and ensemble biochemical experiments. But accurate determination of the detailed mechanism often remains shrouded in mystery due to lack of information on the sequence of events, missing intermediates, and the heterogeneities involved in the process. To address this problem, we are using a complementary approach of following structural transitions in single active complexes by looking at specific signatures from fluorescent probe-labelled molecules during a biochemical reaction in real-time. Detail progress made on different fronts of this project is as below:

1. Interaction of NusG with partner proteins: We have made constructs and purified the reagents for studying a NusG-coupled transcription-translation system including RNAP core/holo enzyme, 70S ribosome particles, wild type NusG, NusG single cysteine mutants, and single fluorescent probe labelled (Atto532 or Alexa 647) NusG. Using Alexa 647 labelled NusG we performed fluorescence correlation spectroscopy (FCS) experiments to estimate the binding affinity of NusG with individual potential interaction partners like RNAP core enzymes, and 70S ribosome particles.
2. Role of NusG in initial transcription and early elongation: We investigated the stage at which NusG recruitment to a transcribing complex occur by systematically probing the effect of NusG on transcription initiation and elongation using photoisomerization dependent fluorescence enhancement (PIFE; Fig. 1a) and FCS. Surprisingly, these studies have led to the discovery of a novel role of NusG in early elongation – which is likely to have a significant impact on our understanding of sigma dependent pausing in bacteria. In a small diversion to these studies, we also discovered interesting effects of macromolecular crowding on promoter unwinding and escape (Fig. 1b). These results were summarised in a research

letter and was published in *Febs Letters* early this year.

3. Lifetime of NusG bound to a transcription elongation complex (TEC): To investigate the lifetime of a bound NusG to a TEC we performed single molecule measurements on a TIRF microscope at Prof. Padmaja Mishra's Lab at SINP, Kolkata. We have now successfully setup all analysis pipeline for analysing these movies at our lab in CSIR-IICB. We could detect transient binding events and estimate the on- and off-rates of NusG binding (Fig. 2). The initial results are quite interesting, and we hope to move quickly to the next planned single molecule experiments in the coming months.

Future Research Plans

In the next two years we target to execute the following projects:

1. Study the conformational dynamics of NusG in a TTC: We will generate a smFRET construct for probing the conformational dynamics of NusG using a double Cysteine containing NusG protein and stochastic labelling of donor and acceptor dynamics. Following which I will evaluate the conformational dynamics of NusG in solution as well as when bound to TEC and TTC. I will use both confocal and TIRF smFRET assays to conduct this work.
2. Mechanism of assembly of a RfaH bridged TTC: I will initiate preparation of RfaH constructs containing unnatural amino acids (Azido phenyl alanine) and label them with donor and acceptor probes via copper free click chemistry. These proteins will be used in smFRET assay for monitoring conformational dynamics of RfaH in solution and when bound to a TEC containing ops-pause element.

Extramural / CSIR Funding

Single molecule studies of transcription-translation coupling in bacteria. DBT/Wellcome Trust India Alliance, 2023-2027, 357 lakhs, (IA/I/21/2/505898).

Publications

1. Mukherjee, P., and Mazumder, A. (2024) Crowding results in opposite effects on two critical sub-steps of transcription initiation. *FEBS Letters*, 598, 1022-1033
2. Ploetz, E., Ambrose, B., Barth, A., Börner, R., Erichson, F., Kapanidis, A.N., Kim, H.D., Levitus, M., Lohman, T.M., Mazumder, A., Rueda, D.S., Steffen, F.D., Cordes, T., Magennis, S.W., Lerner, E. (2024) A new twist on PIFE: photoisomerisation-related fluorescence enhancement. *Methods Appl Fluoresc*. 12, 012001.

Conferences Attended

Indian Biophysical Society meeting, March 15-17, TIFR, Hyderabad.

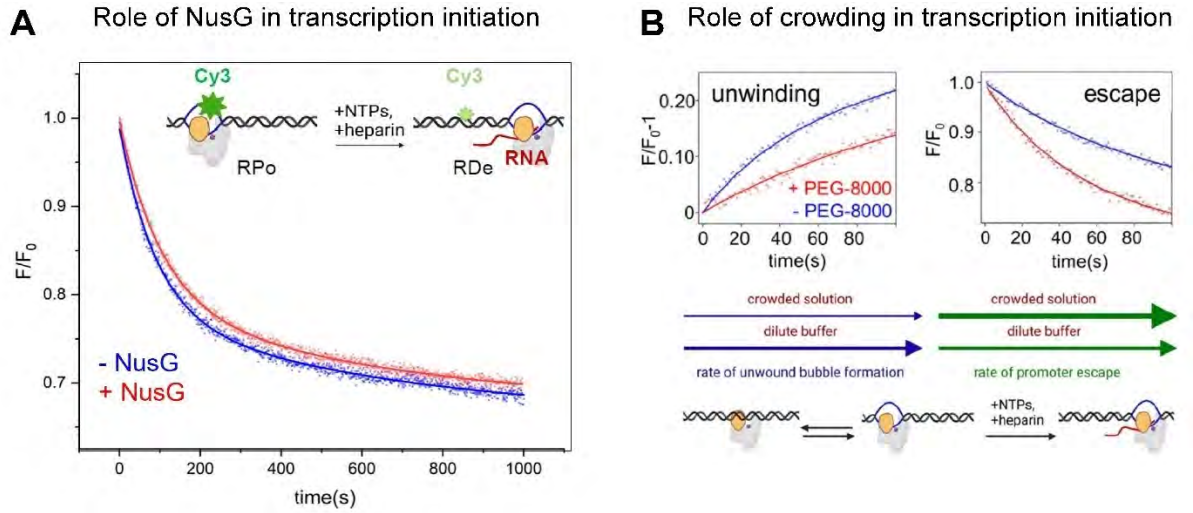


Figure 1: A. Photoisomerization induced fluorescence enhancement (PIFE) assay for monitoring the role of NusG in transcription initiation. B. (top) PIFE assay monitoring promoter unwinding (left) and promoter escape (right), in absence (blue) and presence (red) of 10% PEG-8000. (bottom) Proposed model showing the effect of macromolecular crowding on the two sub-steps of transcription initiation.

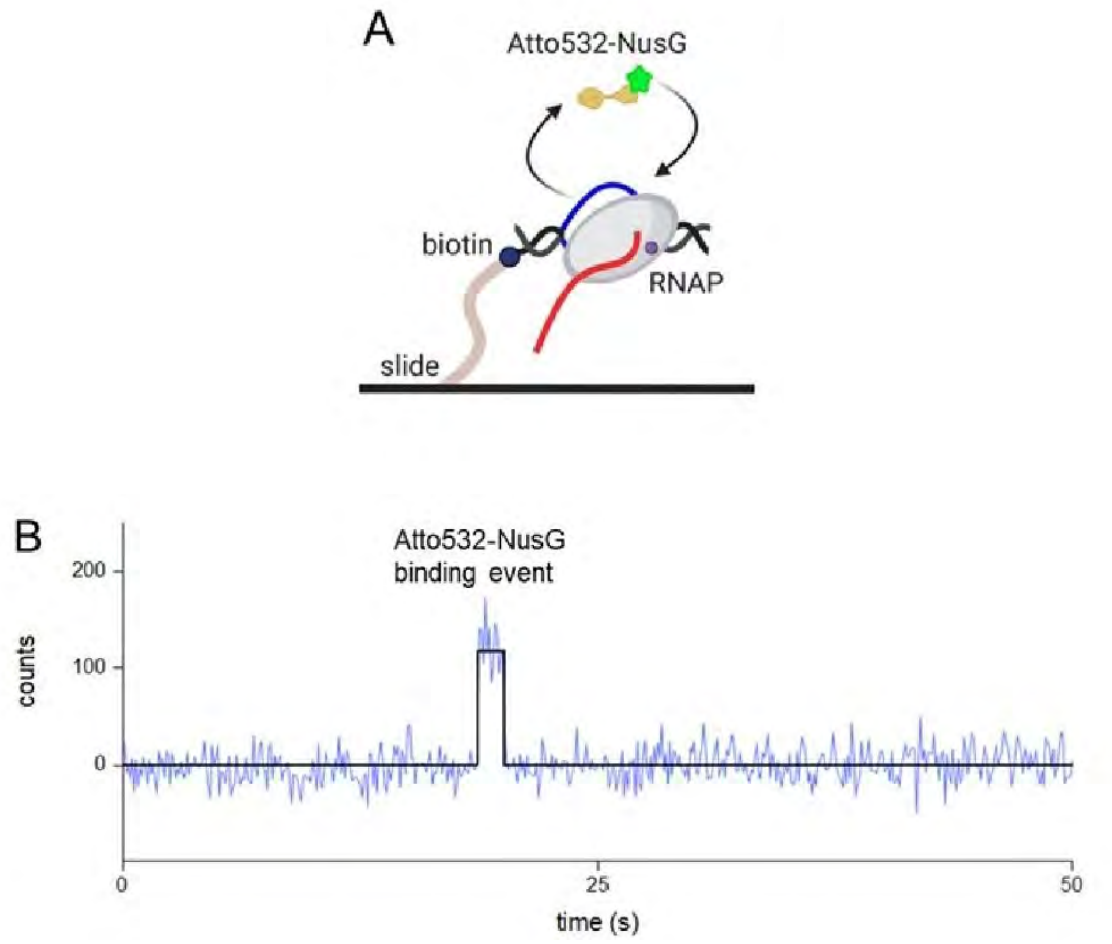


Figure 2: A. Schematic representation of a single molecule TIRF experiment: a transcription elongation complex is immobilised via biotin to a glass slide and Atto-532 labelled NusG is added to the solution. B. Binding and unbinding of a fluorescence probe labelled NusG can be detected from the appearance and disappearance of a fluorescence signal. Imaging was performed using a 532 nm laser with a time resolution of 100 ms per frame.

Dr. Abhishek Mazumder, DBT/Wellcome Trust India Alliance Intermediate Fellow
Group Members: Pratip Mukherjee, UGC-JRF; Saradindu Mandal, JRF; Dr. Sk. Alim, RA-1
Collaborators: Prof. Achillefs Kapanidis, University of Oxford, UK; Dr. Ranjan Sen, CDFD, Hyderabad, India; Dr. Padmaja Mishra, SINP, Kolkata, India; Dr. Mahipal Ganji, Indian Institute of Science, Bengaluru, India

Dr. Ashim Paul and his group members

Elucidating protein aggregation pathways in neurodegenerative diseases: Towards effective therapeutic approaches

Research Activities

Our primary focus is unveiling the molecular mechanisms of protein aggregation in neurodegenerative diseases (NDDs) such as Alzheimer's, Parkinson's, and Amyotrophic Lateral Sclerosis diseases. We employ a multifaceted approach, examining these diseases through the frameworks of Protein-Protein Interactions (PPIs), Protein-Lipid Interactions (PLIs), and Post-Translational Modifications (PTMs). In addition, our work extends to investigating the accumulation of metabolites associated with inborn errors of metabolism, specifically lysosomal storage disorders.

For the past few months (since Sep 2023), we are working on identifying different putative sites of PTMs available on tau proteins and designing short tau derived model peptides to understand the role of site specific PTMs on tau aggregation associated with Alzheimer's disease. In addition, we have identified few key domains of amyloidogenic proteins associated with NDDs and using computational tools (based on binding energies). We designed several peptide-based inhibitors that effectively binds with those domains and plausibly inhibit the amyloid formation and slow down the disease progression. We have procured all the starting materials and soon we will perform all the necessary experiments to execute our proposed plans.

- Submitted ICMR small extramural grant as a PI, jointly with Dr. S.C. Biswas (Co-PI).
- Submitted few CSIR internal grant applications including CSIR-FBR (as PI), CSIR-RDSF (Co-PI) and CSIR-mission mode project on neurodegenerative diseases (Co-PI).
- Attended three conferences on neuroscience, including Neuroupdate Nov 2023 (at IICB, Kolkata), SCAN annual symposium Jan 2024 (at IIT Bombay) and CHINTA inaugural symposium Jan 2024 (at RMIC, Kolkata).
- Reviewed a research paper of a prestigious journal, Advanced Science (IF 15.1).

Future Research Plans

Our long-term research plan is to understand the mechanism of protein aggregation associated with neurodegenerative diseases primarily at early onset of disease progression focusing mainly on protein-protein and protein-lipid interactions. One of the specific future research plan is to understand how different metabolites (primarily sphingolipids) interact with various intrinsically disorder proteins (such as α-Synuclein and tau protein) that are associated with neurodegenerative diseases, and exploring avenues for potential cross talk between these distinct yet interrelated conditions. Another plan is to develop peptide based therapeutic molecules towards neurodegenerative diseases.

Conferences Attended

1. Neuroupdate 2023 (November 25-26, 2023) at CSIR-IICB, Kolkata, India.
2. SCAN Annual Symposium 2024 (January 9-10, 2024): Recent Trends in Neurodegeneration at IIT Bombay, Mumbai, India.
3. CHINTA INAUGURAL SYMPOSIUM 2024 (January 18-20, 2024), Ramakrishna Mission, Golpark, Kolkata, India.
4. CSIR-IICB Annual Research Conclave 2024 (January 25, 2024), IICB Kolkata, India.

Extramural / CSIR Funding

Selected for the prestigious Ramanujan Fellowship on 3rd January, 2024 (SQUID-1987-AP-0477, file number-RJF/2023/000030). I declined it as I joined CSIR-IICB before the declaration of the result.

Dr. Ashim Paul, Senior Scientist
Group Members: Sangramjit Biswas, UGC-JRF
Collaborators: Dr. Subhas C. Biswas, Chief Scientist; Dr. Manish Debnath, Scientist; Prof. Daniel Segal, Emeritus Professor, Tel-Aviv University, Israel

Dr. Dhabaleswar Patra and his group members

Understanding the Structural and Functional Mechanism of Proteins involved in Cardiovascular and Neurodegenerative Diseases

Research Activities

Cardiovascular disease (CVD) is the leading cause of death in the developed as well as in the developing world. The annual mortality of CVD is expected to reach 23.6 million by 2030. Parallelly, the incidence of neurodegenerative diseases is expected to rise with the increasing life expectancy in most countries. About 50 million people are currently affected by dementia, which is estimated to increase to 130 million by 2050. Dementia is a leading cause of disability, dependency, and mortality globally.

AEBP1 belongs to metallocarboxypeptidase family and contains discoidin, carboxypeptidase (CP) domain and C-terminal transcriptional repressor region. High expression of AEBP1 due to injury in the arterial wall results in the inhibition of PPARγ1 (Peroxisome proliferator-activated receptor gamma1) and LXRα (Liver X receptor alpha) activating NFκB (Nuclear factor kappa-light-chain-enhancer of activated B cells) via inhibition of IκB (Inhibitory kappa-light-chain-enhancer of activated B cells). This activates the expression of proinflammatory molecules while decreasing downstream signalling factors such as ATP-binding cassette A5 (ABCA5) expression. Also, it has been reported that during atherosclerosis the expression of ATGL decreases and this protein is regulated by PPARγ. ATGL is a rate limiting lipase that hydrolyses Triacylglycerol into Diacylglycerol and non-esterified fatty acids.

Our lab research interests are in understanding molecular mechanisms of cardiovascular and neurodegenerative disease. Our principal approach is to determine cryo-EM or X-ray structures of proteins involved in such diseases and their downstream signalling components alone and in complex with key-regulators, and then test structure -derived hypotheses via a battery of functional assays. The underlying rationale is that a better understanding of the molecular and cellular mechanisms that underlie the regulation of these proteins will accelerate development of novel therapeutics. A major focus of our lab has been the structure and function of ABCA5, PNPLAs and

AEBP1, which are dysregulated in chronic disease such as heart failure (ABCA5, PNPLA2) and neurodegenerative diseases (ABCA5, AEBP1, PNPLA 6,7,8,9). The main focus is to study disease biology and empower medicine to achieve a more optimal view towards therapeutic interventions by elucidating the structures and functions of the proteins involved in cardiovascular diseases and neurodegenerative disease like ABCA5, PNPLA2 and AEBP1.This structural and functional analysis will further help us to promote wellness against some globally alarming diseases like atherosclerosis and Alzheimer's Disease by drug development as a long-term aim.

Aims and Objectives:

- Elucidate the crystal structure of the various domains of Extracellular domain 1 (ECD1) of ABCA5.
- Expression and purification of AEBP1.
- Cloning and Expression of PNPLA2.

In previous studies it is known that ABCA5 effluxes cholesterol; but the molecular intricacies of ABCA5 still remains to be elusive. The way cholesterol binds to ABCA5 is still unknown. To understand the binding site of ABCA5 with cholesterol, we have performed in silico Docking studies using PrankWeb, HADDOCK & Prodigy (PrankWeb: Prediction of Ligand binding site; HADDOCK: for ligand-Protein docking, Prodigy: to predict the binding energy of the structure) ABCA5 with cholesterol to confirm the interaction between ABCA5 & Cholesterol (Figure.1A). The probable residues that interact with cholesterol has also been indicated (Figure.1B). We have also cloned, overexpressed and purified the extracellular domain 1 (ECD1) of ABCA5 in bacterial system (Figure.2)

- We have cloned, overexpressed and purified AEBP1 full length (Figure.3A,B) and its structured region in bacterial system (Figure.3C,D) and also, they are confirmed by Western blot analysis using Anti-His and Anti-AEBP1 antibody. The full-length clone is still under process of improvisation towards its purity.
- Cloning of ATGL: Mouse ATGL from pCDNA 3.1(b) is cloned into bacterial vector pGEX using Gibson cloning. Firstly, PCR was performed using respective primers and copy numbers of both the full length and only the patatin domain as well as the vector backbone. After, gel purification the insert and the vector were set up for ligation using Gibson mix. Then the ligated DNA was electroporated in DH5α cells and plated in Ampicillin containing agar plates. After, incubation the colony achieved was streaked in another plate. The PCR products showed 4997bp, 1475bp and 787bp lengths of the vector backbone, ATGL full-length and patatin domain respectively(Figure.4).

  Purification and Expression of ATGL: DNA was purified and transformed in Rossetta cells and induced for protein expression. To confirm the expression western blot was performed using specific antibody. The expression of the protein was checked with western blot using specific antibody and a clear band was seen in near 48kDa (Figure.5).

Future Research Plans

- Structural and Functional analysis of AEBP1, ABCA5 and ATGL.
- Testing and identifying small molecule interventions against these proteins.
- As a long-term plan, structural analysis of all the members of PNPLAs.

Publications

Madasu, PK., Maity, A., Patra, D., Chandran, T. (2023). Betacoronaviral lectins: Identification through a genomic search-A structural and evolutionary biology perspective. *Journal of Carbohydrate Chemistry.* 42, 112-34.

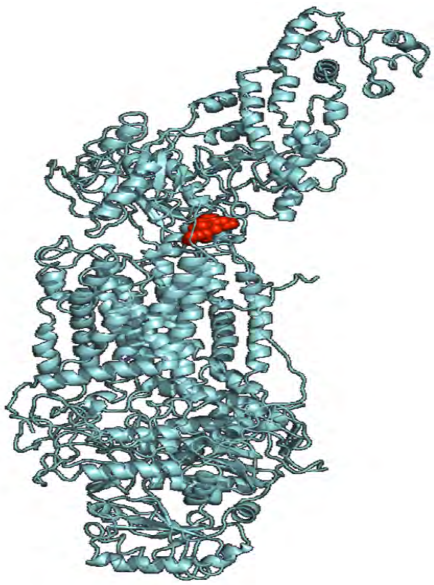


Figure.1A: Docking of ABCA5 with Cholesterol

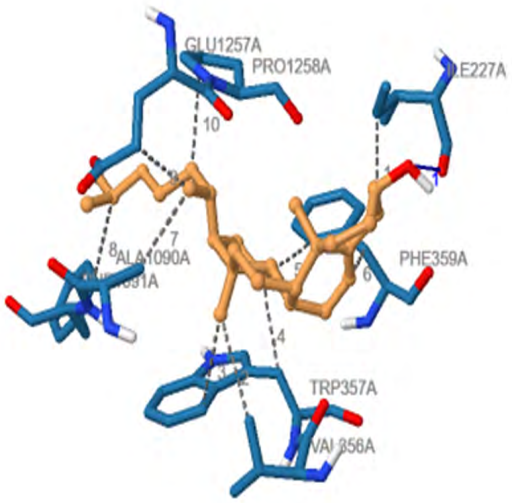


Figure.1B: Interacting residues of ABCA5 with Cholesterol

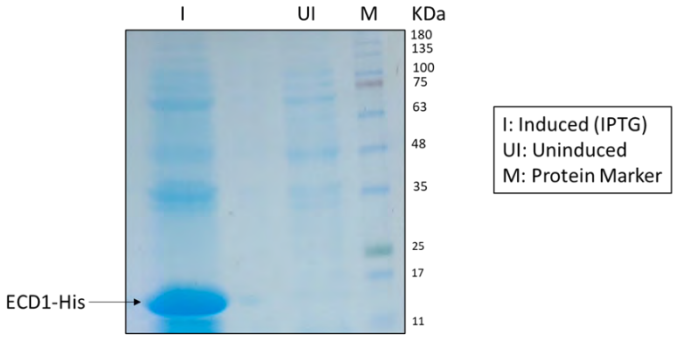


Figure.2: Expression of Extracellular Domain (ECD1) of ABCA5

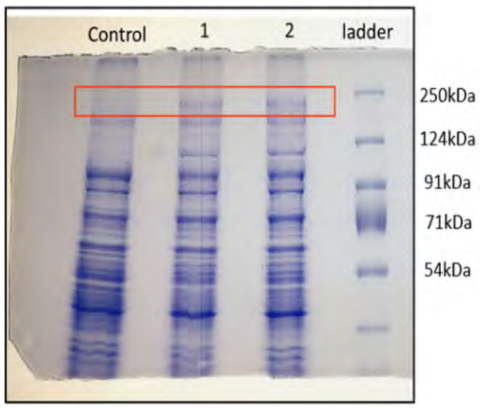


Figure.3A Expression of AEBP1 full length

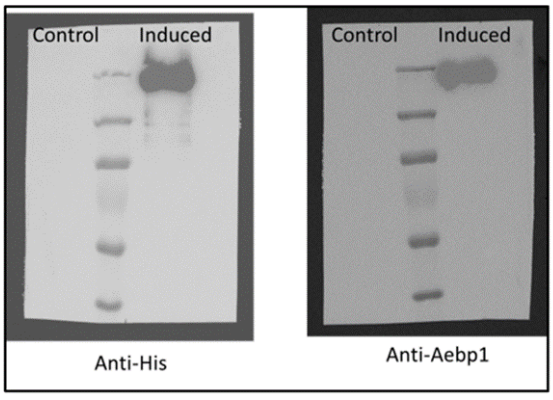


Figure.3B Western Blot with Anti-His and Anti-AEBP1 showing the expression of Full length AEBP1

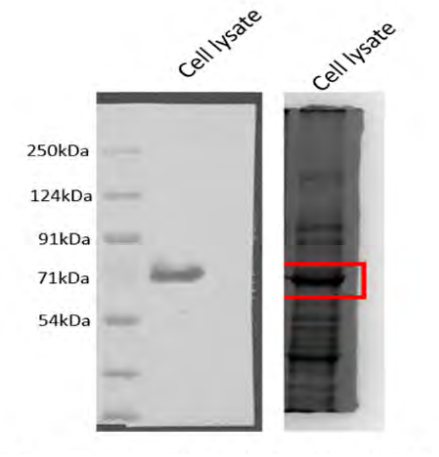


Figure.3C Expression of AEBP1 structured

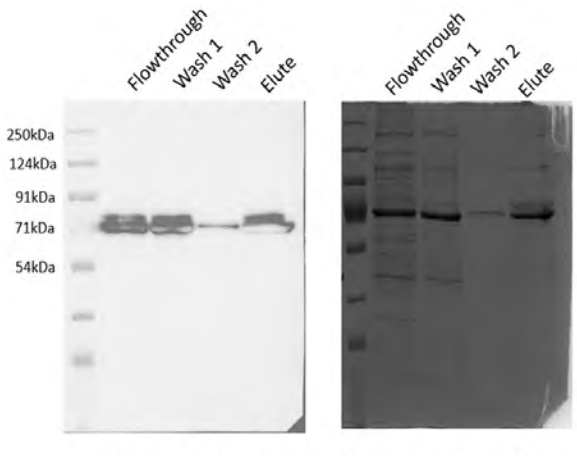


Figure.3D Purification of AEBP1 structured region

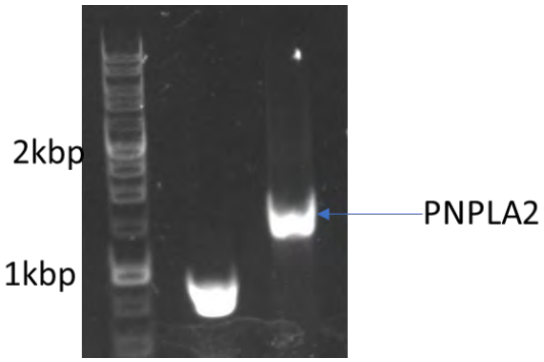


Figure.4: Cloning of PNPLA2

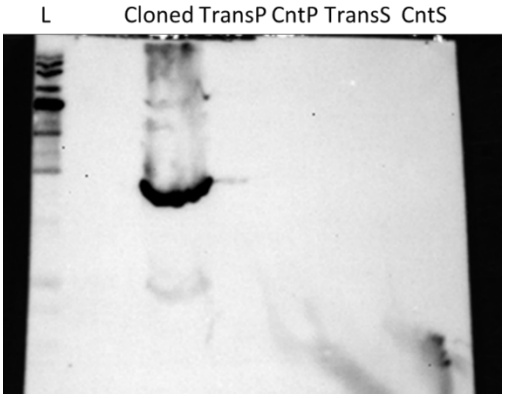


Figure.5: Western Blot of PNPLA2 using specific antibody

Dr. Dhabaleswar Patra, Senior Scientist
Group Members: Bhaskar Bhattacharya, JRF; Ela Lepcha, JRF; Soumyajit Nandy, JRF; Teasha Biswas, JRF
Collaborators: Dr. Thyageshwar Chandran, National Institute of Technology, Warangal; Dr. Aditya Kumar, Tezpur University, Assam; Dr. Md. Jahangir Alam, CSIR-Indian Institute of Chemical Biology

Dr. G. Senthil Kumar and his group members

Unlocking Therapeutic Avenues: Computational Insights into Ferroptosis-Related Genes and Inhibitors for Managing Diabetic Retinopathy

Research Activities

Diabetic retinopathy (DR) is a leading cause of blindness worldwide, characterized by retinal microvascular damage and neurodegeneration. Emerging evidence suggests that ferroptosis, a regulated form of cell death driven by iron-dependent lipid peroxidation, may contribute to the pathogenesis of DR. This study aims to identify potential ferroptosis-related genes and inhibitors for DR using a multidisciplinary computational approach integrating single-cell RNA sequencing (scRNA-seq) dataset analysis, molecular docking, and simulation studies.

We have employed the comprehensive computational analysis of publicly available single-cell RNA sequencing datasets. We have successfully determined Differentially Expressed Genes (DEGs) and Differentially Expressed Marker Genes (DEMGs) specific to diabetic retinopathy. Subsequent investigation led to the identification of Ferroptosis-Associated DEGs (FA-DEGs), Ferroptosis-Associated DEMGs (FA-DEMGs), and Ferroptosis-Associated Hub Genes (FAHGs). Moreover, our investigation extended to FDA-approved drugs targeting these specific proteins, with a meticulous assessment of their ADMET properties. Employing molecular docking and simulation techniques, we examined the stability of interactions between compounds and target proteins.

In conclusion, our analysis highlighted 63 FA-DEMGs, notably enriched in Peroxiredoxin activity, Ferroptosis, Mitophagy, and Autophagy pathways. Subsequent predictive modeling identified PRDX1 and UBC as promising candidate target proteins. Our molecular docking endeavors unveiled Pazopanib, Thiazolopyrimidine, and Dexamethasone as compounds demonstrating a high binding affinity with PRDX1 and UBC. Furthermore, molecular dynamics simulation underscored the stability of Pazopanib, the top performer from the docking

analysis, in its interaction with PRDX1 and UBC, affirming its potential therapeutic efficacy.

Future Research Plans

Evaluate the therapeutic efficacy of pazopanib in modulating PRDX1 and UBC expression/activity and mitigating ferroptosis in vitro and in vivo models of diabetic retinopathy. Elucidate the mechanisms underlying pazopanib's protective effects against ferroptosis, including its impact on cellular redox balance, iron metabolism, and lipid peroxidation.

Extramural funding

1. Evaluation of Insulin-Like Growth Factor 2 (IGF2) as a potential epigenetic biomarker and therapeutic target to abolish the metabolic memory in diabetic retinopathy. ICMR, 2022-2024, 39 Lakhs, (5/4/6/8/OPH/2020-NCD-II)
2. Evaluating the epigenetic adaptation of COL4A1, COL4A2 as a potential therapeutic target for early pathological events in diabetic retinopathy. ICMR, 2023 –2026, 40 Lakhs, (5/4/6/30/OPH/2021-NCD-II)

Publications

Kar, A., Ghosh, P., Gautam, A., Chowdhury, S., Basak, D., Sarkar, I., Bhoumik, A., Barman, S., Chakraborty, P., Mukhopadhyay, A., Mehrotra, S., Ganesan, S. K., Paul, S., and Chatterjee, S. (2024) CD38-RyR2 axis-mediated signaling impedes CD8+ T cell response to anti-PD1 therapy in cancer. *Proc Natl Acad Sci U S A*. 121, e2315989121

Dr. G. Senthil Kumar, Senior scientist
Group Members: Ms. Nidhi Kumari, CSIR-SRF; Ms. Aditi Karmakar, UGC-SRF; Ms. Chirasmita Das, DBT-JRF; Mr. Shubhrajit Barman, DBT-JRF; Mr. Maqsood Ahamad Khan, ICMR- Project Fellow
Collaborators: Dr. Krishna Pada Baidya, MBBS, MD, Professor, Department of Ophthalmology, Nil Ratan Sircar Medical College & Hospital (NRSMC&H), Kolkata

Dr. Jayati Sengupta and her group members

Elucidating cryo-electron microscopy structures of mycobacterial ribosomal complexes to understand the functional mechanisms

Research Activities

Structural investigation on the mechanism of HflX-mediated erythromycin resistance in mycobacteria.

HflX is a conserved ribosome-associated GTPase (RA GTPase) that plays a regulatory role in multiple stress responses in bacteria. Mycobacterial HflX is known to play a crucial role in mediating antibiotic resistance, including macrolide and lincosamide antibiotics, although the mechanism was unknown. In this study, we have investigated this mechanism underpinning antibiotic resistance by mycobacterial HflX. We report here the first cryo-EM density map of *M. smegmatis* (Msm) HflX-50S subunit complex at a global resolution of ~3 Å. A critical nucleotide A2286 (2062 in *E. coli*) at the gate of Nascent Peptide Exit Tunnel (NPET), which usually remains in dynamic (preferably non-swayed) conformation, was observed to interact with HflX in a swayed conformation. Our assays revealed that HflX binds to the 50S subunit with enhanced affinity and acts as a potent anti-associator. Remarkably, this swayed conformation of the gate residue is associated with the binding of NPET targeting antibiotic erythromycin and its derivatives. The conformation likely acts as an erythromycin sensor for HflX, which leads to enhanced binding, ribosome sequestration and protection from futile translation.

Future Research Plans

Our lab is one of the first few labs in India to start 3D cryo-electron microscopy (cryo-EM) of biological molecules. Our research particularly focuses on the translational machinery of pathogenic bacteria. We aim at identifying hitherto unknown ribosome-associated factors instrumental in various stress-related mechanisms of pathogenic bacteria and characterizing the ribosome-factor interactions using high-resolution3D cryo-EM.

We have been successfully elucidating ribosome-associated mechanisms in pathogenic bacteria primarily using high-resolution cryo-EM, with the aim to identify species-specific potential drug targets.

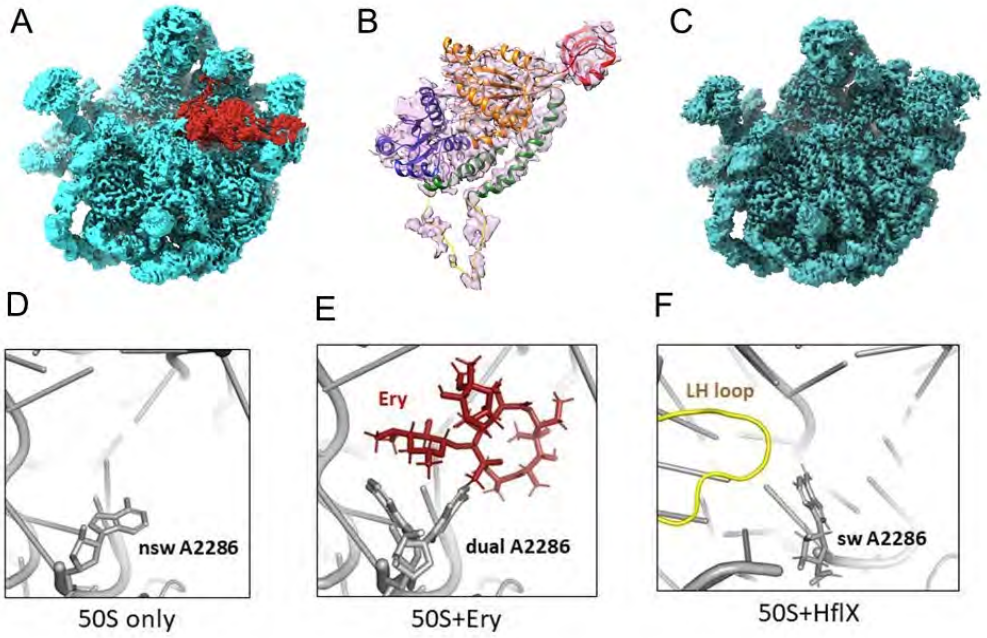


Figure 1: LH loop of Mycobacterial HflX senses erythromycin via the conformation of gate residue. (A) Cryo-EM map of the HflX-bound mycobacterial 50S ribosomal subunit. (B) Density corresponding to the HflX protein is shown (different domains are colour coded). (C) Cryo-EM map of the erythromycin-bound mycobacterial 50S ribosomal subunit. (D) Close-up view of the conserved base A2286 in the ligand-free 50S subunit showing non-swayed (nsw) conformation. (E) Close-up view of the conserved base A2286 in the erythromycin-bound 50S subunit showing both swayed (sw) and non-swayed (nsw) conformation. (F) Close-up view of the conserved base A2286 in the HflX-bound 50S subunit showing both swayed (sw) conformation

Extramural / CSIR Funding

In quest of novel drug targets: Investigation on structural dynamics of the mycobacterium ribosome using high-resolution cryo-electron microscopy. SERB Power Fellowship, Department of Science & Technology (DST), 2022-2025, 38.1 Lakhs, (SPF/2021/000141)

Publications

Baid, P., Sengupta, J. (2023) Cryo-EM captures a unique conformational rearrangement in 23S rRNA helices of the Mycobacterium 50S subunit. *Int J Biol Macromol.* 253,126876.

Book Chapters

Dhur, A., Banerjee, A., Srinivasan, K., Sengupta, J. (2023) Cryo-EM structures of ribosomes from human pathogens: Implications for drug targeting. Cryo-Electon Microscopy in Structural Biology (CRC Press), Editor: Prof. Krishnarao Appasani.

Invited Lectures

A ribosome exit tunnel gate nucleotide acts as a sensor to confer HflX-mediated erythromycin resistance in mycobacteria, Indian Institute of Technology Bombay, 7-9 March, 2024

Conferences Attended

Understanding the Breathing of Biomolecules: Recent Advances in Cryo-EM and Chemical Biology, A symposium organized on the occasion of setting up a Cryo-EM facility, Indian Institute of Technology Bombay, 7-9 March, 2024

Dr. Jayati Sengupta, Senior Principal Scientist
Group Members: Mr. Ankit Dhur, UGC-SRF; Mr. Aneek Banerjee, DBT-SRF; Mr. Krishnamoorthi Srinivasan, CSIR-SRF (SPM Fellow); Ms Priya Baid, CSIR-SRF (Thesis submitted)

Dr. Krishnananda Chattopadhyay and his group members

To use the spectroscopy at ensemble and single molecule resolution to study protein folding/aggregation and its implications in Neurodegenerations and Infections

Research Activities

We have been studying the early and unexplored events of protein aggregation and its implications in neurodegenerations and infections. We first showed using spectroscopy at single molecule resolution that a protein at the early microsec fluctuates between conformers of different radii and forms oligomers (JBC 2010, JBC 2012, JBC 2015). We then combined FRET and FCS to develop methodology to detect the formation of early oligomers, which contribute maximally to the cellular toxicity of neurodegeneration (Langmuir 2014). We then followed up using cryo-EM to report for the first time the structural understanding of toxicity induced by alpha synuclein oligomers in Parkinson's Disease, in which targeting a crucial histidine residue of alpha synuclein arrests fibril propagation (Communications Biology 2021).Our applications of chemical biology tools on spectroscopy in vitro and in live cells show that, the nature of fluctuations of a protein and its ability to form early oligomers can have profound implications on how this protein would form amyloid at the late stage (ACS Chem Neurosci 2014; Sci. Rep 2018), Recently, using more than 140 mutants of superoxide dismutase (SOD1) we have developed a cofactor based membrane association model of ALS, and provided experimental validations (eLife 2021).

Protein conformational changes during protein-lipid interactions play ubiquitous roles in governing a number of cellular events. Using two proteins of unknown functions, we investigated the role of protein-lipid interactions to define the mechanistic pathway regarding infectious disease progression. Our findings suggested that KMP-11-membrane interaction is modulated by the cholesterol content of lipid bilayer which is directly linked with the mechanism of parasite survival strategy (J. Phys. Chem. B 2017) in leishmaniasis. On the other hand, environment-dependent binding events between immunogenic KMP-11 and membrane ergosterol resolved the missing link between ergosterol biogenesis and immune suppression. In another context, we established that MPT63, a protein of M.Tb with immunoglobulin like fold, loses its immunogenic responses through surface binding and this happens through the environment-sensitive conformational switching from native beta sheet to helical conformation (Langmuir 2018). Nevertheless, this environment-dependent switch event of MPT63 is also responsible for host cell death through membrane pore formation. Our investigation has revealed that the helix conformer of MPT63 creates toxic oligomers in order to perforate host membranes (ACS Chemical Biology, 2019). Using the understanding of the conformational switch of a protein towards the productive infections as a dark side of nature, we investigated the unexplored binary combination of the sequences of SARS COV2 spike protein and the similarity with diverse pathogen derived proteins, which may provide novel molecular insights into the process of infection (Communications Biology 2021a).

Ongoing Research Questions:

- Developing the molecular understanding of the roles of aggregation intermediates in neurodegeneration
- Studying the role of protein-membrane interactions in infections

Using computational and spectroscopic techniques, we have reported the liquid liquid phase separation (LLPS) of SOD1. The formation of droplets was modulated by the cofactors, Cu and Zn. Using ALS disease mutants, we have shown that the droplet formation and the subsequent maturation into the solid fibril formation can be implicated in the pathology of the disease. The characterization of the SOD1 droplets were carried out using spectroscopy at the ensemble and single molecules resolution. In addition, we have been collaborating with the Department of Physics, Indian Institute of Science, Bangalore study the growth kinetics of SOD1 droplets formation. Using a collaboration with Tata Institute of Fundamental Research (TIFR)-Hyderabad, we have studied how molecular crowding modulates the liquid phase separation of model proteins.

Future Research Plans

Our lab would continue to use a combination of chemical biology, biophysics and mathematical biology to work towards developing a molecular grammar, which applies to key aspects of complicated human diseases. While we have made some progress in our in vitro studies, we are now applying our experimental methodologies in live cells measurements.

Publications

1. Kundu, S., Jana, P., Sahoo, P., Nandi, SK., Mishra, S., Begum, R., Dutta, M., Seikh, A H., Chattopadhyay, K*, and Ghosh, CK* (2024). Curcumin-based Nanoformulation for the Pyroptotic Death of MDA-MB-231 Cells. *ACS Applied Nano Materials*. 7, 4895
2. RoyChowdhury, S & Chattopadhyay, K* (2023). A tale of (disordered) tail. *Communications Biology*, 6, 411
3. Sahoo, P., Jana, P., Kundu, S., Mishra, S., Chattopadhyay, K., Mukherjee, A., Ghosh, CK. (2023) Quercetin@Gd3+ doped Prussian blue nanocubes induce the pyroptotic death of MDA-MB-231 cells: combinational targeted multimodal therapy, dual modal MRI, intuitive modelling of r1–r2 relaxivities, *J. Materials Chemistry B*. 11, 6646
4. Tiwari, A., Pradhan, S., Sannigrahi, A., Mahakud, AK., Jha, S., Chattopadhyay, K., Biswas, M., Saleem, M. (2023) Interplay of lipid-head group and packing defects in driving Amyloid-beta mediated myelin-like model membrane deformation, *J. Biol. Chem.* 299, 104653

Invited Lectures

1. Conformational fluctuations of proteins: from test tubes to neurodegenerative diseases, TIFR-Hyderabad, 46th Indian Biophysical Society Meeting, March 15-17, 2024
2. Protein conformation, dynamics and aggregation: from test tubes to human diseases, Kenilworth, Goa; The Indo German conference on Sustainability Organized by IIT-Indore, Feb 20-22, 2024
3. Protein conformation, dynamics and aggregation: from test tubes to human diseases, Colloquium at the Presidency College, Kolkata, Aug 23, 2023
4. Water pollution and neurodegeneration: is there a connection? NIT Nagaland, Apr 06, 2023
5. Conformation fluctuations in phase separation, Pre-conference workshop at Compflu, IIT-Madras, Dec 16-23, 2023
6. Protein conformation, dynamics and aggregation: from test tubes to human diseases, Dr. Bishnu Pada Mukerjee Memorial Award Lecture, Sustainability and Interdisciplinary in Chemical Sciences, IISER-Kolkata, Jul 15, 2023
7. Protein conformation, dynamics and aggregation: from test tubes to human diseases, New Horizons in Biotechnology, Haldia Institute of Technology, March 16, 2023

Member of Society

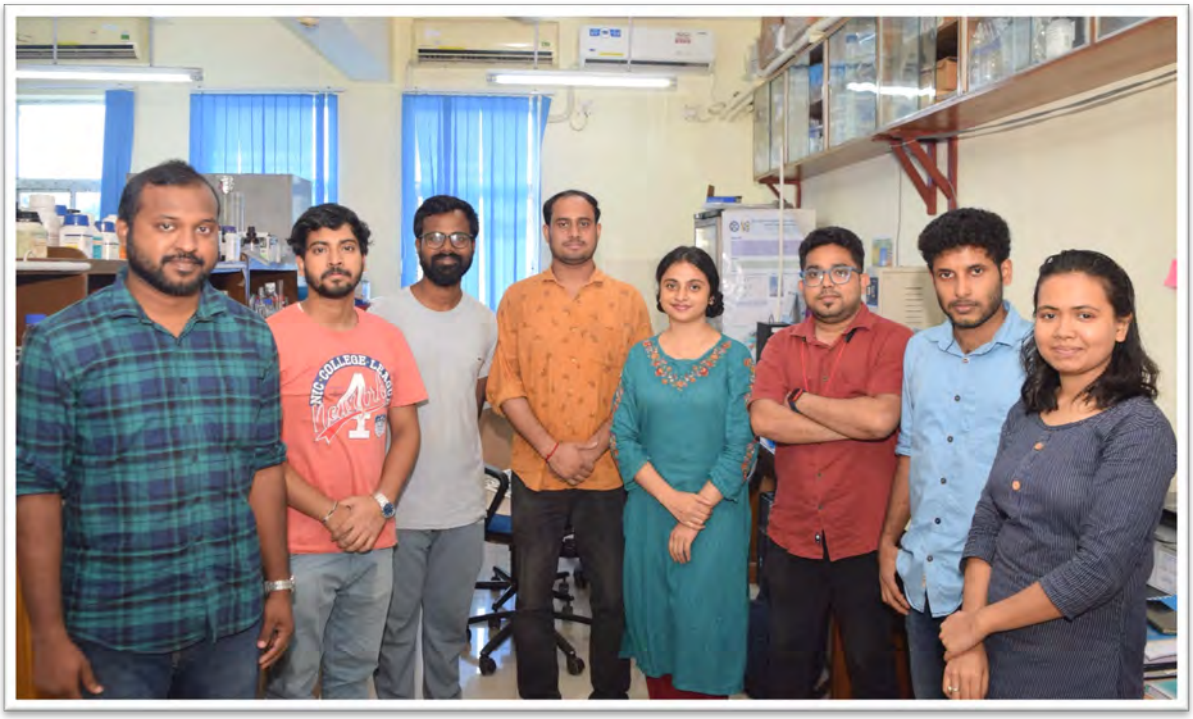
1. Fellow, National Academy of Sciences, India (NASI)
2. Fellow, Indian Academy of Sciences (IASc)

Awards

Dr. Bishnu Pada Mukerjee Memorial Lecture Award, Awarded by the Indian Photobiology Society

Dr. Krishnananda Chattopadhyay, Chief Scientist

Group Members: Sayantani Chall, RA; Dwipanjan Sanyal, DST-INSPIRE-SRF; Bidisha Das, CSIR-SRF; Sumangal Roychowdhury, UGC-SRF; Rajeev Jain, CSIR-SRF; Pulak Jana, CSIR-SRF; Souradip Paul, DBT-SRF; Rajdip Roy, DBT-JRF; Ahana Banerjee, DST-INSPIRE-JRF; Pratip Mukherjee, UGC-JRF; Sampa Mondal, DBT-JRF; Ashmita Mukherjee, ICMR-SRF



Dr. Nakul Chandra Maiti and his group members

Protein conformation linked human diseases and metal nano-formulation for therapy

Research Activities

Certain instability inside the cellular microenvironment for both the disorder and ordered protein cause misfolding which often become a starting point of amyloid formation and, cause of several conformations linked human diseases. Structural intricacies of disease linked intrinsically disordered proteins (IDPs) such as amyloid beta (Aβ), α-synuclein and functional enzyme such as insulin, serine proteases from viruses causing human diseases are therefore, are the prior field of investigation and research. Understanding membrane less organelles and phase transition are also gaining momentum in this regard. Application of biological Raman spectroscopy, fluorescence spectroscopy and molecular dynamics simulations to understand the aggregation and phase transition of protein solution and structure/function accepts of important proteins and enzyme is indeed very helpful. Raman spectroscopy was discovered in our next door at Indian Association for the Cultivation of Science and about a century ago, very recently we could house the indigenous biological Raman instrument at CSIR-IICB and idea is to engage to know about the protein structure and function with greater emphasis on neurodegenerative diseases.

Raman spectroscopy is increasingly becoming a popular technique in several areas of science and technology including biology and medicine. The technique can be used for structural quantification of biomolecules, molecular imaging of cells and tissue, medical diagnosis, understanding of diseases sate in Parkinson's and Alzheimers. and similar many other fields. Our focus is to use the technique for understanding protein structure and function. Particularly those proteins which are linked to diseases formation. We are trying to address issues like this: (i) explored the dengue NS2B/NS3serine protease dynamics to identify conserved loops/residues with specific motions and probe their effect on the enzyme kinetics; (ii) we are also studying serine protease. (iii) Additional focus is on nanoparticles/quantum dots and their role in protein aggregation. Further we are also investigation the role of mutation on alpha syncline stability and folding. We showed how the naringenin-embedded nanostructure effectively retards aggregation and fibril formation of α-synuclein, the protein which is strongly associated with the pathology of Parkinson's-like diseases. (ii)We further explored the role of Ser 129 residue in alpha synclein unique residue and associated structure in aggregation behavior of α-synuclein in an ambient solution

condition. (iii) initiation of hydrophobic zipping of syuclein caused the transformation of IO into thermodynamically stable β-sheet rich amyloid fibril. On the other hand, the presence of molten globule like conformation in LO, rendered greater toxicity to cultured neuronal cells. We prepared two recombinant artificial single point mutants of aS: S129W and S129A and investigated the protein secondary structure of the mutant proteins by CD and Raman spectroscopic methods. (iv) Our studies show coomassie brilliant blue G-250 (CBBG) as a promising chemical chaperone that stabilises the α-helical. nnative human insulin conformers, disrupting its aggregation. Furthermore, it also increases the insulin secretion. (v) Modulatory role of copper on hIAPP aggregation and toxicity in presence of insulin. (vi) We have introduced a unique in vitro noninvasive perturbation method on dengue main proteases using solvent exchange and cold stress to study the motions in the enzyme and link the motions to its activity. (vii) In collaboration, we also established the binding affinity of secretion effector protein Pem B for phosphoinositides through isothermal calorimetric titrations (viii) We also showed that the oligomeric bovine insulin maintained the orientation/conformation of the disulfide bonds. However, in the fibrillar state, the disulfide linkages became more strained and preferred to maintain a single conformation state. (ix) Further we established the mechanism of metal-free activation of molecular oxygen by quaternary ammonium-based Ionic liquid

Future Research Plans

Designing nano-platform for better understanding protein and cellular event by Raman spectroscopy. Detail understanding of virus protein, mainly main proteases linked to Dengue and Covid-2. Detail understanding of protein oligomers and their assembly structure by Raman and other computational methods such as DFT and molecular dynamics. Associated research interest is to target allosteric site (that include protein disorder region) of enzymes with small natural and synthetic molecules to modulates their activity, function and overall molecular mechanics. The allosteric modulators can fine-tune protein mechanics. Besides, allosteric sites are evolutionarily less conserved/more diverse even in very similarly related proteins, thus, provides high degree of specificity in targeting a particular protein. Therefore, targeting of allosteric sites is gaining attention as an emerging strategy in rational drug design. However, the experimental approaches provide a limited degree of characterization of new allosteric sites. Computational approaches are useful to analyze and select potential allosteric sites for drug discovery. We use molecular docking, which has become an integral part of the drug discovery process, to predict the drug- ability of novel allosteric sites as well as the active site on target proteins (e.g Dengue and COVID main proteases) by ligand screening and subsequent analysis by Raman microscopy We also established the method of preparation of green fluorescence quantum dot and we will explore its different biological application. Also long term goal to early detection of Parkinson/Alzheimer's by Raman spectroscopy

Publications

1. Khamaru, K., Pal, U.; Shee, S., Lo, R., Seal, K., Ghosh, P., Maiti, N. C*., Banerji, B* (2024). Metal-free Activation of Molecular Oxygen by Quaternary Ammonium-based Ionic Liquid: A Detail Mechanistic Study, *J. Am. Chem. Soc.,* 146, 10, 6912–6925.
2. Mondal, A., Dolui, S,, Dhabal, S., Kundu, S., Das, L ., Bhattacharjee, A., Maiti, N.C. (2023). Structure specific neuro-toxicity of α-synuclein oligomer, *Int. J. Biol. Macromol.,* 253, 126683.
3. Maity, A., Mandal, A., Kundu, S., Shome, G., Misra, R., Maiti, N. C (2023). Naringenin-Functionalized Gold Nanoparticles and Their Role in Synuclein Stabilization, *Langmuir*. 39, 7231-7248.
4. Misra, R., Maity, A., Kundu, S., Bhunia, M., Nanda, B., Maiti, N. C*., Pal, U* (2023). Loop Dynamics And Conformational Flexibility in Dengue Serine Protease Activity: Noninvasive Perturbation by Solvent Exchange. *Journal of Chemical Information and Modeling*., 63, 2122-2132.
5. Pandit, E., Das, L., Das, AK., Dolui, S., Saha, S., Pal, U., Mondal, A., Chowdhury, J., Biswas, S., Maiti, N.C (2023). Single Point Mutations at S129 Residue of α-Synuclein and Their Effect on Structure, Aggregation and Neurotoxicity. *Frontiers in Chemistry. 11, 1145877.*
6. Pariary, R., Dolui, S., Shome, G., Mohid, SA., Ratha, BN., Harikishore, A., Jana, K., Mandal, A.K., * Bhunia, A.,* Maiti, N .C* (2023). Coomassie brilliant blue G-250 acts as a potential chemical chaperone to stabilize therapeutic insulin; *Chemical communication*, 59, 8095-8098.
7. Debsharma, S., Pramanik, S., Bindu, S., Mazumder, S., Das, T., Pal, U., Saha, D., De, R., Nag, S., Banerjee, C., Maiti, N. C., Ghosh, Z., Bandyopadhyay, U (2024). NSAID targets

SIRT3 to trigger mitochondrial dysfunction and gastric cancer cell, iScience, 27, 109384.
8. Rudra, DS., Chatterjee, S., Pal, U., Bhunia, M., Maiti, N.C., Jaishankar, P., Swarnakar, S (2023). Newly synthesized 3-Indol Furanoid Inhibits Matrix Metalloproteinase-9 Activity and Prevents Nonsteroidal Anti-inflammatory. *J. Med. Chem*. 66, 8917-8928
9. Choudhury, A., Saha, S., Maiti, N.C., Dutta, S (2023). Exploring Structural Features and Potential Lipid Interaction of Pseudomonas aeruginosa PemB by S Spectroscopic and Calorimetric Experiment, *Protein Science*. 32, e4627.
10. Kumar, S., Maiti, A., Ratha; BN., Biswas, R., Maiti, N.C., Mandal, A.K., Bhunia, A (2023). Modulatory role of copper on hIAPP aggregation and toxicity in presence of insulin, *Int. J. Biol. Macromol.* 241, 124470.

Member of Society

Elected to the West Bengal Academy of Science & Technology (WAST) as Fellow, 2024

Invited Lectures

1. Attended International Conference from 14th to 16th September, 2023 with Pre-Conference Workshop from 8th to 13th September, 2023. NEHU, Shilong
2. Attended and was a part of organizer of 17th Neuro Update meeting 'Neuro-update meeting 2023' at CSIR-IICB, November 25-26, 2023
3. Invited Speaker, 14th National Workshop on Fluorescence and Raman Spectroscopy, followed by a National conference. Organized jointly by the Indian Institute of Science Education and Research Mohali (IISER Mohali) and Institute of Nanoscience and Technology (INST) from December 9 to December 18, 2023.
4. Served as chairperson in a scientific seassion, the 46th Indian Biophysical Society Meeting, March 15-17, 2024, Tata Institute of Fundamental Research Hyderabad (TIFRH), Hyderabad

Dr. Nakul Chandra Maiti, Senior Principal Scientist
Group Members: Esha Pandit, SRF; Banadipa Nanda, SRF; Rajdip Misra, SRF; Shubham Kundu. SRF; Anupam Maity, SRF; Mrinmay Bhunia, JRF; Ananya Adhikari, JRF; Sauman Saha, DBT-RA
Collaborators: Dr. Achinta Kumar Saha, Professor, University of Calcutta, Kolkata; Dr. Anirban Bhunia, Professor, Bose Institute, Kolkata; Dr. Biswadip Banerji, CSIR-IICB; Dr. Subhas Biswas, CSIR-IICB

Dr. Saikat Chakrabarti and his group members

Understanding the molecular mechanisms underlying systemic diseases using computational systems biology and machine learning approaches

Research Activities

Over the years we have managed to set up an unique infrastructure and human resource group where state-of-the-art computational analysis including data science and data mining, mathematical modelling and graph theory, molecular modelling and dynamics analysis, in silico drug screening, machine and/or deep learning, image processing and analysis based findings are complemented with experimental verifications using cell culture based RNA and protein expression studies and other relevant biochemical and molecular biology experiments. Our unique skills and expertise in various strata of bio-medical research has gained national and international attentions and accolade. Similarly, this expertise has benefitted many of my colleagues with whom we have done successful collaboration leading to numerous high quality scientific findings and subsequent publications.

We utilize large-scale genomics, transcriptomics, proteomics, and metabolomics data to construct disease or context specific bio-molecular interaction networks and further study them to understand and decipher their biological significance using meta-interactome analysis. Our group also develops various computational tools, techniques and web servers, which are freely available for users and are beneficial to the scientific community throughout the world. Recently, we have also ventured into developing image processing and machine learning / deep learning based software packages to process and analyze brain MRI and CT images for detection of early features of Alzheimer's disease and stroke, respectively.

Please visit our lab website (http://www.hpppi.iicb.res.in/saikatlab/) for more detailed overview and description of the previous and ongoing projects and to use various tools (servers and databases) that we have developed over the years. The objectives of our laboratory are:

- Computational systems biology analysis of cancer interactome network using patient

derived multi-omics data in order to identify diagnostic and/or prognostic markers for women centric cancers.

- Detection of Alzheimer's disease using brain magnetic resonance image (MRI) processing and machine learning techniques.
- Detection of novel method and device for brain haemorrhagic stroke followed by 3D reconstruction of the identified stroke regions using computer tomography (CT) image processing and machine learning techniques.
- Development of tools and techniques for protein-ligand docking and novel machine learning-based method to evaluate protein-ligand docking results.
- Computational systems biology analysis of cancer interactome network

Identification of cancer signature markers using machine learning-based multi-omics analysis

Revealing cancer stage-specific alterations and their associated networks holds great potential for precise diagnostics, advancing precision medicine. High-throughput multi-omics technologies enable comprehensive molecular profiling, providing insights into cellular mechanistic complexity networks in cancer biology. We employ an exhaustive machine learning pipeline including multiple algorithms like Support Vector Machines (SVM), Random Forest (RF), and eXtreme Gradient Boosting (XGBoost), and artificial neural networks (ANN) to extract stage-specific patterns across multi-omics data including genomics (CNV and SNV), transcriptomics (RNA and miRNA), and epigenomics, respectively derived from cervical cancer cohorts.

Feature selection techniques aim to identify key elements within datasets. Our study identified reduced features that exhibited heightened predictive accuracy at single omics level, and extending this to multi-omics, reduced feature sets demonstrated even greater predictive power, highlighting the strength of multi-omics over single omics data (Figure 1).

Detection of Alzheimer's disease (AD) using brain magnetic resonance image (MRI) processing and machine learning techniques

Alzheimer's disease (AD) imposes a growing burden on public health due to its impact on memory, cognition, behavior, and social skills. Early detection using non-invasive brain magnetic resonance images (MRI) is vital for disease management. We introduce CCADD (Corpus Callosum-based Alzheimer's Disease Detection), a user-friendly webserver that automatically identifies and segments the corpus callosum (CC) region from brain MRI slices. Extracted shape and size-based features of CC are fed into Support Vector Machines (SVM), Random Forest (RF), and eXtreme Gradient Boosting (XGBoost) classifiers to predict AD or Mild Cognitive Impairment (MCI). Exhaustive benchmarking on publicly available ADNI data reveals high prediction accuracies for different AD severity levels (Figure 2). CCADD empowers clinicians and researchers for AD detection. This server is available at: http://www.hpppi.iicb.res.in/add.

Combination of structural MRI (sMRI) and functional MRI (fMRI) derived image analysis may provide unique ability to capture the dynamic state of change in the degenerating brain. Hence, to capture the overall structural and functional anomalies of brain tissues caused by AD an exhaustive combinatorial system has been developed using structural and/or functional MRI data followed by rigorous image processing and deep learning based algorithms to diagnose AD and/or MCI patients. Whole brain sMRI and fMRI slices are processed and brain pixel based intensity features are fed into a deep learning based convoluted neural network (CNN) algorithm to calculate the AD/healthy probability of each MRI slice. We achieved very high accuracy (>90%) in detecting AD and/or MCI patients. This embedded system could easily be synced with the clinically used MRI/fMRI machines. This detection system (Figure 3) can aid clinical diagnostics of AD and AD like symptoms in an efficient manner. A provisional patent has been approved (Ref. No. 0071NF2023) for this system.

Evaluation system for protein-ligand docking/binding complex using machine learning techniques

Accurate prediction of protein-ligand binding affinity is crucial in drug discovery and molecular biology. Molecular docking simulations have become a standard tool for predicting binding modes and affinities, but their accuracy can vary significantly. In this study, we present a novel machine learning-based approach to evaluate protein-ligand docking results. Our method leverages a diverse set of physico-chemical and protein-ligand interaction based features extracted from docking poses and employs SVM, RF, and XGBoost to classify native and non-native protein-ligand complexes using large number protein-ligand complexes utilizing curated protein-ligand complexes, active/inactive ligand bound complexes, and similar/dis-similar compound

complexes, respectively. We developed multiple models containing various types of native and non-native complexes and further trained and validated the models, which offer more than 90% accuracy in differentiating true/native-like complexes from the false/non-native ones. Comparison analysis further demonstrated superior performance of our models and features compared to traditional scoring functions and other available machine learning based approaches. Our invention offers a valuable tool for the rapid and accurate evaluation of protein-ligand docking results, facilitating more efficient drug discovery and molecular modeling efforts.

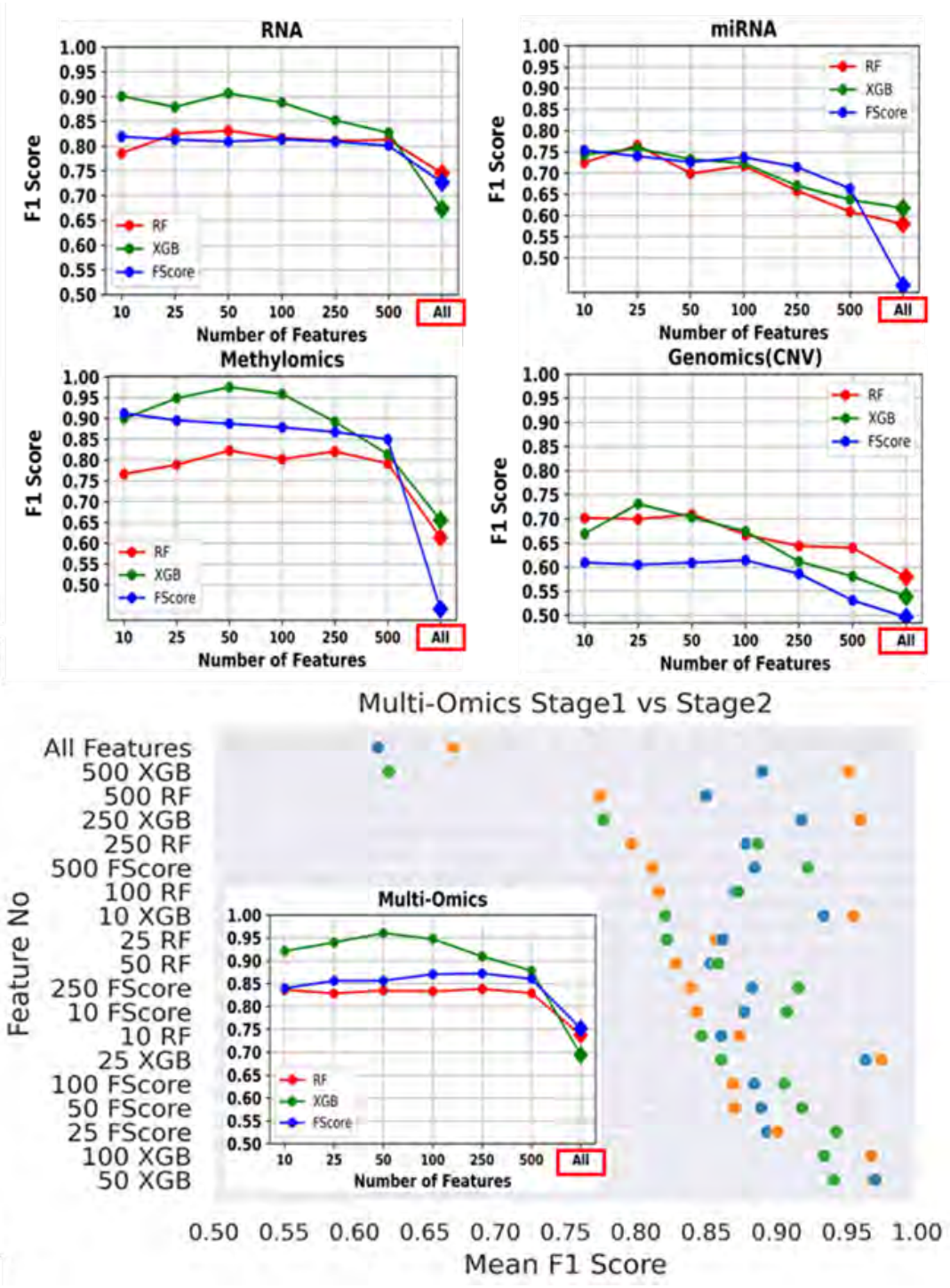


Figure 1: Performance of machine learning-based multi-omics analysis for cervical cancer stage differentiation. F1 score is a machine learning evaluation metric that measures a model's accuracy by balancing precision and recall. Three different feature reduction protocols (RF, XGB, and Fscore/ANOVA) were utilized.

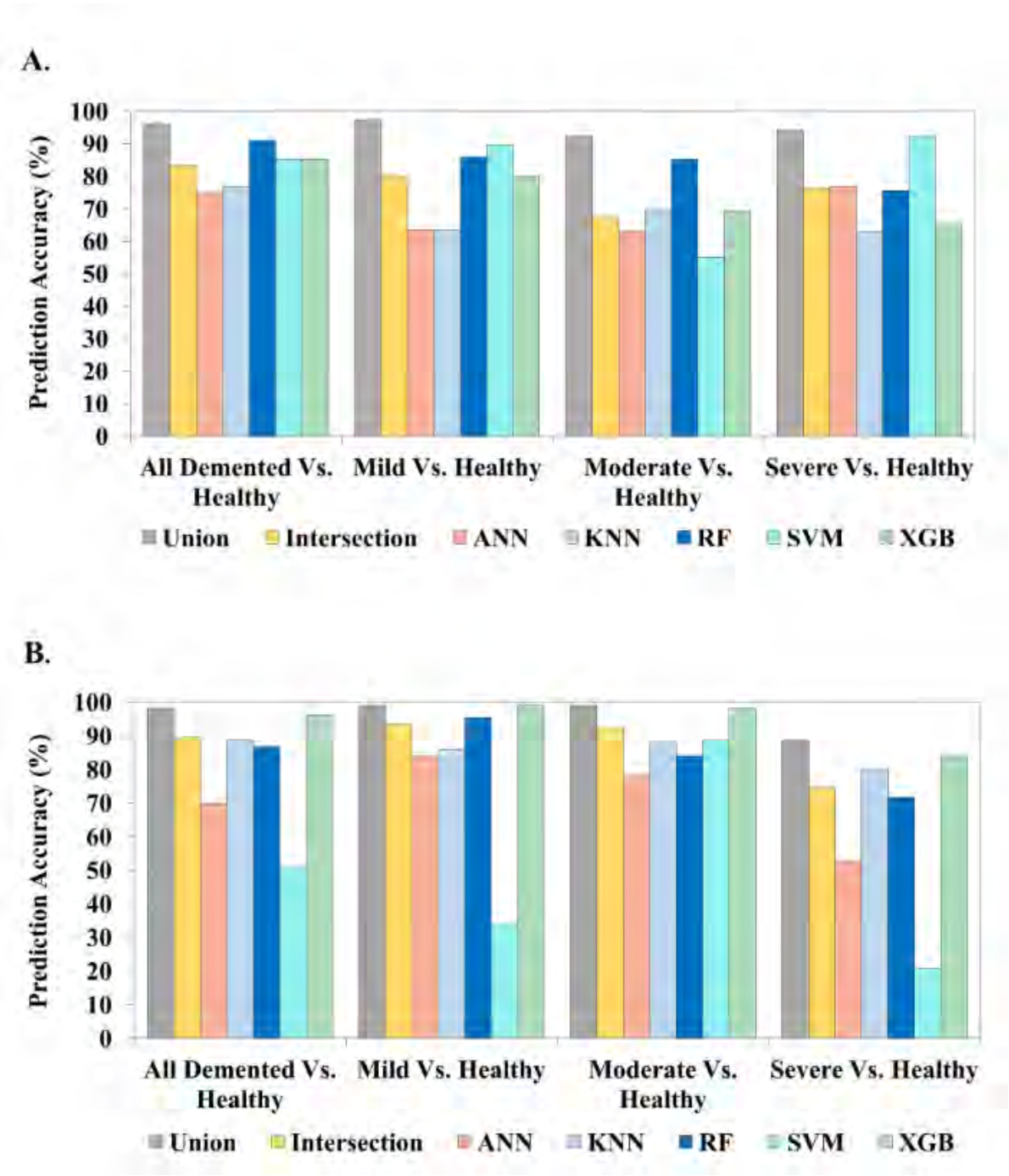


Figure 2: Performance of the different machine learning models embedded within the CCADD server. Panel A shows the average percentage of accurate (y-axis) identification of all demented samples across various AD categories while panel B plots the average accuracy of identification of all healthy samples.

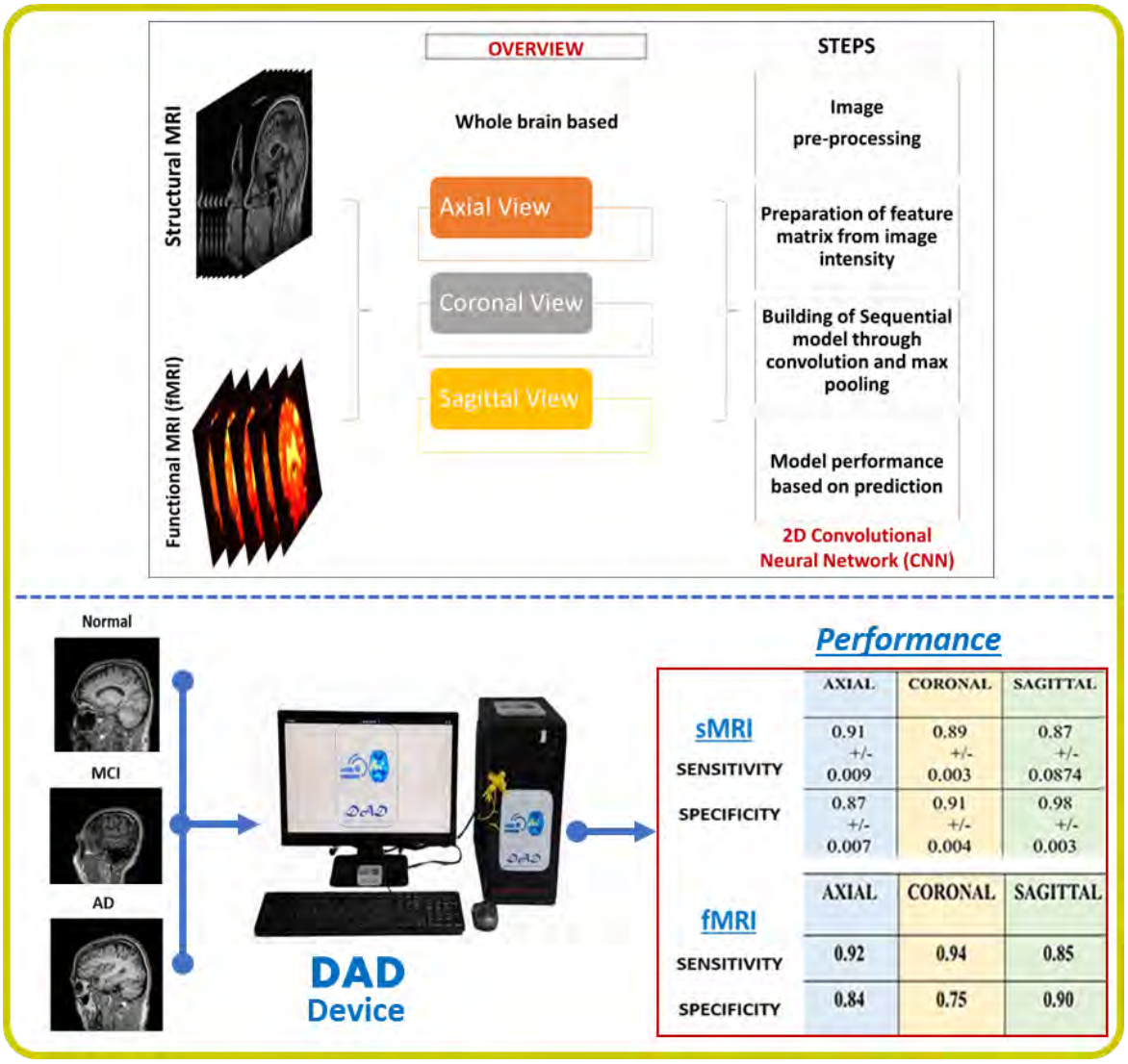


Figure 3: Overview of the protocol and the prototype of the detection system for Alzheimer's disease using brain structural and/or functional magnetic resonance image processing and machine learning techniques.

Future Research Plans

1. Development of detection system for automatic identification and 3D-reconstruction of haemorrhagic stroke regions using brain computer tomography (CT) image processing and deep learning techniques.
2. To identify novel ER-mitochondria cross-talk proteins under ER stress condition. Investigating the probable roles of novel ER stress and UPR pathway genes in progression of female specific cancers.
3. Exploring the role of androgen receptor (AR) as of novel player in regulating cervical cancer progression using meta-interactome network analysis and experimental validations.

Extramural / CSIR Funding

Platform integration for high Through-put multi omics data analysis and text processing. Department of Biotechnology, 2022 – 2027, 227.21 Lakhs, (BT/PR40137/BTIS/137/35/2022).

Publications

1. Kamal, I.M., Das, A., Datta, S., Paul, K., Chakrabarti, S., Chakrabarti, S*., Bhattacharjee, P. (2023) A Novel spice-antioxidant-based nano-vehicle as a putative green alternative of synthetic AChE inhibitor drugs. *J Biomol Struct Dyn.* 28:1-18.
2. Bandyopadhyay, D., Basu, S., Mukherjee, I., Chakrabarti, S., Chakrabarti, P., Mukherjee, K., Bhattacharyya, S.N. (2023) Accelerated export of Dicer1 from lipid-challenged hepatocytes

buffers cellular miRNA-122 levels and prevents cell death. *J Biol Chem.* 299,104999.
3. Kumar, K., Bhowmik, D., Mandloi, S., Gautam, A., Lahiri, A., Biswas, N., Paul, S., Chakrabarti, S*. (2023) Integrating Multi-Omics Data to Construct Reliable Interconnected Models of Signaling, Gene Regulatory, and Metabolic Pathways. *Methods Mol Biol.* 2634,139-151.
4. Bandopadhyay, S., Kamal, I.M., Padmanaban, E., Ghosh, D.D., Chakrabarti, S., Roy, S.S. (2023) Oncogene-mediated nuclear accumulation of lactate promotes epigenetic alterations to induce cancer cell proliferation. *J Cell Biochem.* 124, 495-519.
5. Kamal, I.M., and Chakrabarti, S*. (2023) MetaDOCK: A Combinatorial Molecular Docking Approach. *ACS Omega*. 8, 5850-5860.
6. Som Chaudhury, S., Nandi, M., Kumar, K., Ruidas, B., Sur, T.K., Prasad, P., Chakrabarti, S., De, P., Sil, J., Das Mukhopadhyay, C. (2023) Rodent Model Preclinical Assessment of PEGylated Block Copolymer Targeting Cognition and Oxidative Stress Insults of Alzheimer's Disease. *Mol Neurobiol.* 60, 2036-2050.
7. Garg, A., Goel, N., Abhinav, N., Varma, T., Achari, A., Bhattacharjee, P., Kamal, I.M., Chakrabarti, S., Ravichandiran, V., Reddy, A.M., Gupta, S., Jaisankar, P. (2023) Virtual screening of natural products inspired in-house library to discover potential lead molecules against the SARS-CoV-2 main protease. *J Biomol Struct Dyn*. 41, 2033-2045.
8. Saha, G., Sarkar, S., Mohanta, P.S., Kumar, K., Chakrabarti, S., Basu, M., Ghosh, M.K. (2023) USP7 targets XIAP for cancer progression: Establishment of a p53-independent therapeutic avenue for glioma. *Oncogene*. 41, 5061-5075.
9. Das, R., Das, S., Chakrabarti, S., Chakrabarti, O. (2022) CMT2A-linked mitochondrial hyperfusion-driving mutant MFN2 perturbs ER-mitochondrial associations and Ca2+ homeostasis. *Biol Cell.* 114, 309-319.

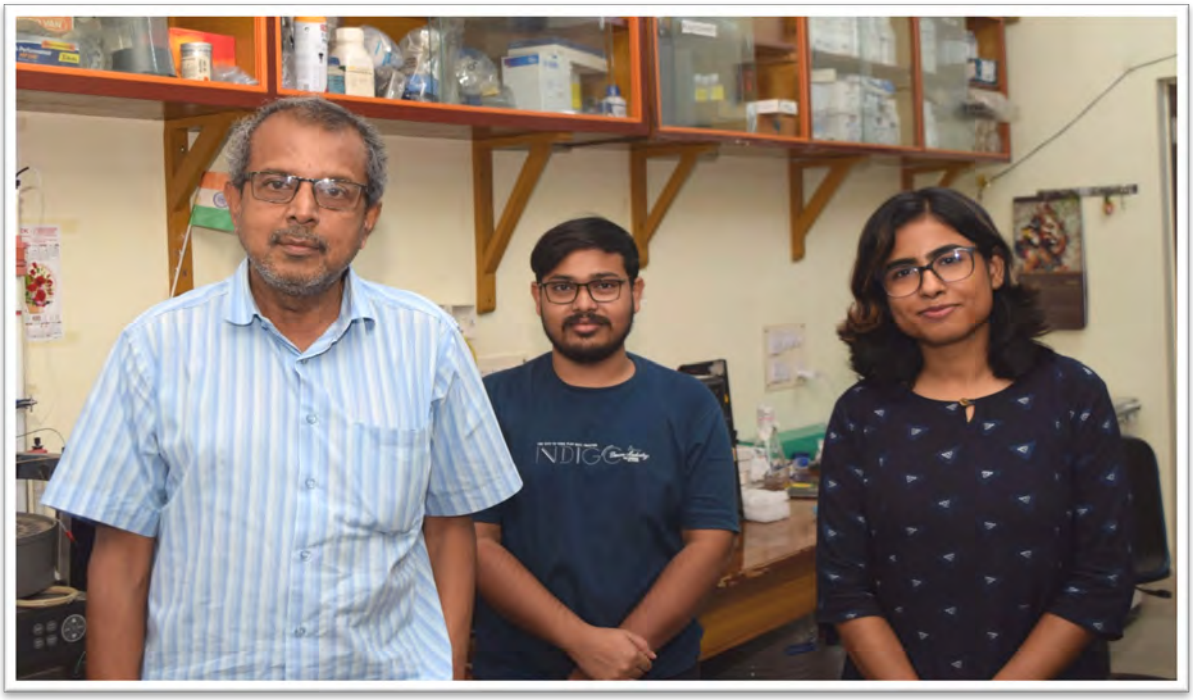
Patents

1. Detection system for Alzheimer's disease using brain structural and/or functional magnetic resonance image processing and machine learning techniques. Saikat Chakrabarti, Subhrangshu Das, Priyanka Panigrahi, filing date 09/06/2023, application number: 202311039559 (provisional).
2. A non-invasive system and method for automatic identification of haemorrhagic stroke regions' has been filed. Saikat Chakrabarti, Subhrangshu Das, Priyanka Panigrahi, filing date 24/03/2024, application number: 0017NF2024 (provisional).

Invited Lectures

1. AIDIAS: Artificial Intelligence based Diagnostic and Analytical Systems; Invited; Bose Institute / National Workshop on Bioinformatics: AI in Healthcare; Kolkata; India; January 2024.
2. AIDIAS: Artificial Intelligence based Diagnostic and Analytical Systems; Plenary; Brainware University / Brain Healthcon-2023; Barasat; India; December 2023.
3. AIDIAS: Artificial Intelligence based Diagnostic and Analytical Systems; Keynote; JIS Institute of Advance Studies and Research (JISIASR) / Bioinformatics and AI in Healthcare – An Introduction; Kolkata; India; August 2023.

Dr. Saikat Chakrabarti, Senior Principal Scienctist
Group Members: Raktim Chowdhury, JRF; Sangita Bose, JRF; Izaz Monir Kamal, SRF; Priyanka Panigrahi, SRF; Anindita Choudhury, SRF; Sarpita Bose, SRF; Priyanka Mullick, SRF; Subhangshu Das, RA; Dr. Parna Kanodia, RA; Dr. Ankur Chaudhuri, RA
Collaborators: Sudipto Roy, IMCB, Singapore; Sourav Ghosh, Yale University, USA; Oishee Chakrabarti, SINP, Kolkata; Jaya Bandyopadhyay, MAKAUT, India; Sandip Paul, JIS, Kolkata; S N Bhattacharyya, IICB, Kolkata



Dr. Saumen Datta and his group members

Structural and functional insights of itaconyl-CoA hydratase from Pseudomonas aeruginosa highlight a novel N-terminal hotdog fold

Research Activities

Itaconic acid (methylene succinic acid) is an unsaturated 1,4 dicarboxylic acid, the most promising organic acid found in soil. This compound is mainly produced by fungi like Aspergillus terreus as well as some other organisms such as Escherichia coli, and Ustillago spp. It is also produced by mammalian macrophages during active infection. Itaconate (methylenesuccinate) is also known as a potent inhibitor of isocitrate lyase of bacterial glyoxylate cycle which is required for assimilation of acetyl-CoA as a carbon source for bacteria upon degradation from fatty acids. Many pathogenic bacteria like Pseudomonas spp., Yersinia spp., Micrococcus spp., Salmonella spp. used itaconate as a sole carbon source and catabolized into acetyl-CoA and pyruvate for their survival in human host cells. Some non-pathogenic bacteria like Burkholderia spp. also metabolize itaconate. Itaconate utilization gene

cluster was previously identified in those organisms. In this itaconate catabolic pathway, itaconate is first activated to its corresponding CoA-ester by succinyl-CoA: itaconate CoA transferase (Ict), then itaconyl-CoA is hydrated to (S)-citramalyl-CoA by (R)-specific itaconyl-CoA hydratase (Ich) and at last (S)-citramalyl- CoA is cleaved by (S)-citramalyl-CoA lyase (Ccl) to acetyl-CoA and pyruvate. In Pseudomonas aeruginosa PAO1 strain, these three enzymes are encoded by genes named PA0882 (Paict), PA0878 (Paich), and PA0883 (Paccl) respectively. Similarly, the gene for PaIch product in PA14 strain was named PA14_52910. Later, it was identified some virulence factors in PA14 strain by genome-wide screening of P. aeruginosa expression library based on yeast growth phenotype. Of them, PA14_52910 gene product was shown to have increased cellular toxicity toward macrophages and the Caenorhabditis elegans model. So, they called this gene product PA14_52910 (PaIch) as P. aeruginosa effector candidate 1 (Pec1) based on showing virulence in eukaryotic host cells. we have found that sequence of Pec1 is identical to previously described itaconyl-CoA hydratase from P. aeruginosa (PaIch) of itaconate catabolic pathway by blastp analysis. Thus, a crucial role of PaIch in itaconate degradation pathway as part of bacterial defense weaponry from macrophages was established in previous work.

Despite this significance, structural and mechanistic insights regarding PaIch and hydration of itaconyl-CoA remain undetermined. So, In this work, we report the first three-dimensional structure of PaIch at 1.98 Å resolution. The crystal structure of PaIch shows that it is dimeric in nature confirmed by also in-solution by mass spectrometry analysis. The structure resembles MaoC-like hydratases/dehydratases consisting of N- and C-terminal domains connected by a long stretch of flexible loop. Herein, each domain represents a "hotdog fold" found previously in other (R)-specific enoyl-CoA hydratases. Although C-terminal hotdog fold of PaIch was found similar to other hydratases, the N-terminal hotdog fold carries unique characteristic features which were not observed previously in any other hydratases. Unlike other hydratases, structural dynamicity is not restricted to helix/loop region but is also present in main frame β-sheet of PaIch. Based on multiple sequence alignment and structural superposition of C-terminal domain of PaIch with other DHF-containing hydratases delineate the conserved hydratase motif with catalytic residues followed by mechanistic point of view in catalysis. A remarkably long substrate binding tunnel predicts the binding of C5 or more acyl chains of CoA derivatives. We found that it shows a significant binding affinity towards acetoacetyl-CoA like in crotonase and mitochondrial enoyl-CoA hydratase of bovine and rat liver respectively. So, this study provides the first atomic-level insights of PaIch which fulfills the missing nexus of itaconate degradation pathway in P. aeruginosa.

Full-length N-terminal His_6-tagged PaIch (~ 32 kDa) was heterologously produced in E. coli and purified to apparent homogeneity using affinity chromatography method which was further analyzed by SDS/PAGE. In size exclusion chromatography method, the protein eluted as a dimer (~ 64 kDa) which was further confirmed by mass spectrometry analysis. Here, we report the first crystal structure of itaconyl-CoA hydratase from P. aeruginosa (PaIch) at 1.98 Å resolution. An initial attempt to get phase by molecular replacement method was not successful probably due to very low sequence similarity (< 20%) with other hydratases/dehydratases family of enzymes. Eventually, the structure was solved by multiple isomorphous replacement with anomalous scattering (MIRAS) method using heavy atom derivatives (Au and Hg).

The crystallographic asymmetric unit (ASU) of PaIch consists of four copies (chain A, B, C and D) of a monomeric unit forming two dimers (A–C and B–D) where each dimer represents a biologically active form (Fig. 1A,B). In ASU, two dimers are oriented at 90° to each other and each monomer of this dimer was related to each other by two-fold symmetry. The overall structure of PaIch resembles the structure of MaoC-like hydratases/dehydratases (PDB ID: 1PN2, 3KH8, and 5I7N) composed of two domains, the N-terminal half and the C-terminal half connected by an intervening bridge (Fig. 1C). As mentioned earlier, PaIch has two dimers in the crystallographic asymmetric unit where chains A-C make one dimer and chains B-D form another dimer. The whole PaIch dimeric unit shows like a crab's shell with a dimension of ~ 77.5 × 60.8 × 54.2 Å. The most noticeable feature observed in this dimeric assembly was that each monomer consists of two b-sheets with variable number of strands as well as their arrangement (Fig. 1B). However, no significant R.M.S.D. value was observed between the monomers. Each monomer contains a total of 275 amino acid residues consisting of 6 α-helices and 11 strands of parallel β-sheet in chain A while 7 helices and 10 strands of β-sheet in its complementary chain C (Fig. 1B). Each helix and β-strand of a monomer was sequentially numbered on the basis of their arrangement (Fig. 1B, C). These strands of β-sheet range from 3 to 13 residues in length. The order of their arrangement is 1-4-5-6-7-8-9-14-15-16-17 found in chain A while β4 strand is not present in chain C (R.M.S.D value over C_α atoms between chain A and C is 0.207; Fig. 1B).

It has been stated earlier that C-terminal domain was found to be similar with other (R) specific enoyl-CoA hydratases but N-terminal domain showed distinguished characteristic features which were not present in other hydratases. A common characteristic feature of all hotdog fold-containing hydratases exemplified a 9–17 residues long central helix represented as sausage properly wrapped by β-sheet as a bun. This characteristic feature is distributed through all domains of life until the revelation of a new kind of hotdog fold as observed in PaIch. It is first noticed in the N-terminal domain of PaIch that a very short 4-residues helical segment α3 (Trp_{47}-Ala_{50}) which we named as an eaten sausage is not properly placed inside the core of its hotdog fold (Fig. 2A,B). Top view representation of PaIch showed that α3 characterized as an eaten sausage has been slipped away from the β-sheet scaffold (Fig. 2B). The extended loop region (~ 7 residues) succeeding helix α3 is the missing region of sausage seen in other hydratases. The reason for

appearance of very short helical segment α3 is the presence of α2 and α10 helices from its dimeric counterpart. α2 and α10 helices of each monomer interact with the extended loop region (Phe_{51}-Gly_{65}) of the other monomer. Mainly α2 rather than α10 helix takes part in this interaction due to α2 being situated in close proximity to extended loop region (Phe_{51}-Gly_{65}). Around 69% of residues of this extended loop region (Phe51-Gly65) are of hydrophobic in nature. So, a strong hydrophobic interaction is seen between α2/α10 and the extended loop region (Phe_{51}-Gly_{65}) between each dimer which ultimately gives overall dimeric stability.

Future research plans

My laboratory is working on several T3SS proteins which are putatively annotated as effector proteins. We are working on to characterize those proteins by several biophysical techniques.

Publications

Choudhury A, Saha S, Maiti NC, Datta S. (2023). Exploring structural features and potential lipid interactions of Pseudomonas aeruginosa type three secretion effector PemB by spectroscopic and calorimetric experiments. *Protein Sci.* 32, e4627.

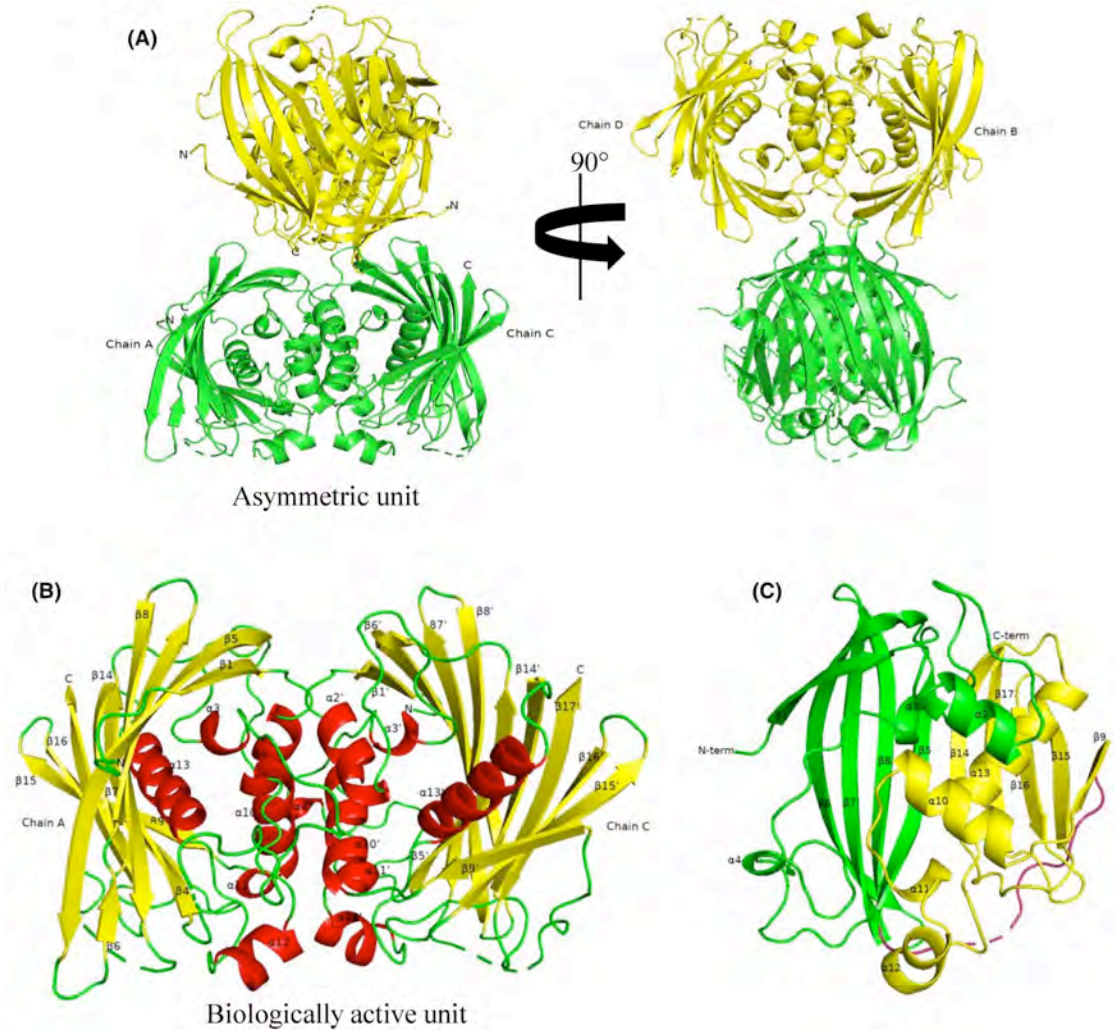


Figure 1: Overall structure of itaconyl-CoA hydratase from Pseudomonas aeruginosa (PaIch). (A) The whole asymmetric unit of PaIch consists of a tetrameric assembly in which two dimers are positioned around 90° from each other. Chain A and chain C formed one dimer (green) whereas chain B and chain D made another dimer (yellow). A 90° rotation about y-axis of whole unit is shown here. (B) Overall structural view of a dimeric assembly (chain A–chain C) is represented here as a functional unit of PaIch. Each α-helix and parallel β-pleated sheet are colored red and yellow respectively and they are labeled sequentially in order of their arrangement. (C) Cartoon representation of monomeric unit (chain C) showing the N-terminal and C-terminal domain comprised of a double hotdog fold. The N-terminal and C-terminal domains are colored green and yellow respectively and the intervening highly flexible segment is colored warm pink. All structural representations were made through PYMOL v2.5.4.

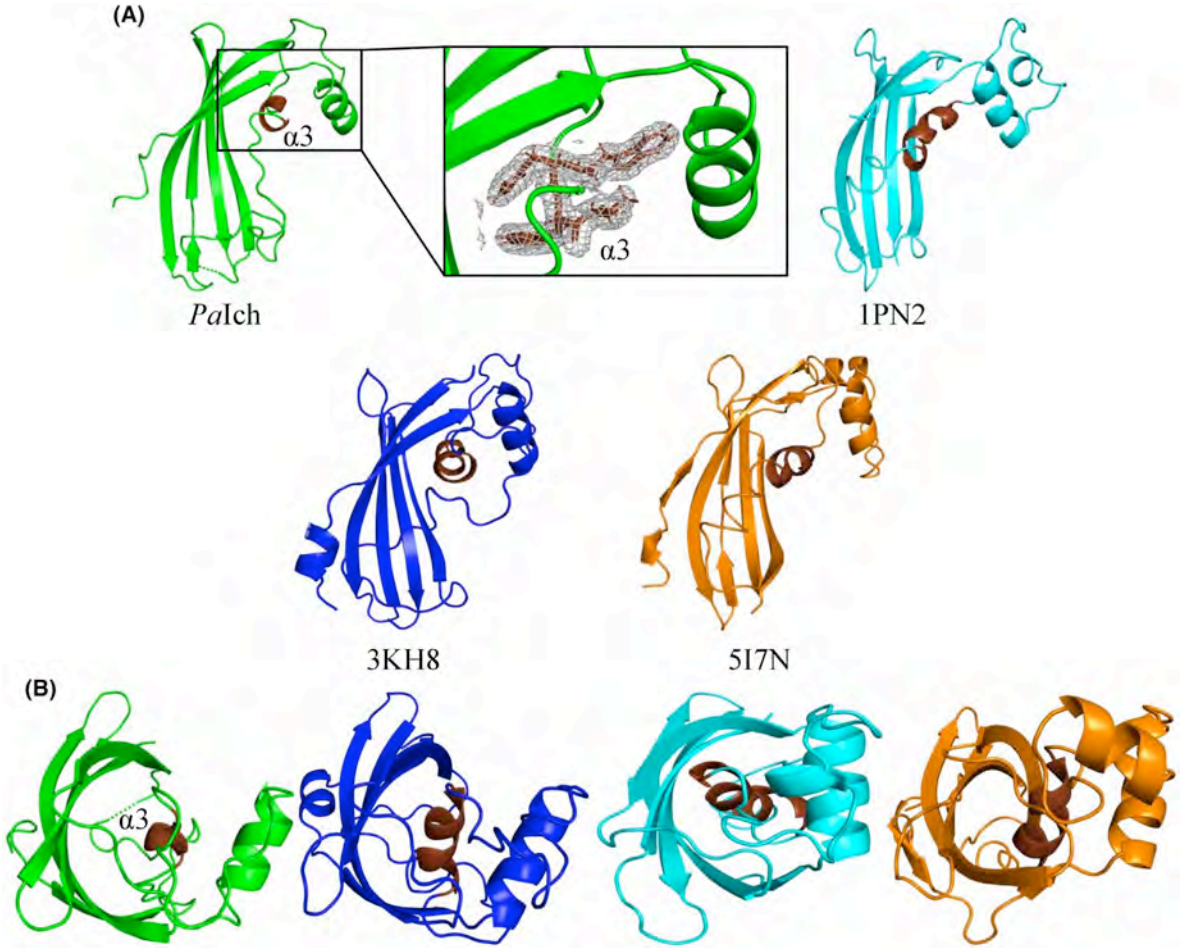


Figure 2: A unique N-terminal hotdog fold of PaIch and model structure of itaconyl-CoA hydratase from Yersinia pestis (YpIch). (A) Cartoon representation of side view of N-terminal hotdog fold. The β-sheets represented here as buns of PaIch from Pseudomonas aeruginosa, eukaryotic hydratase 2 from Candida tropicalis (PDB ID: 1PN2) and MaoC-like dehydratases from Phytophthora capsici (PDB ID: 3KH8) and Mycobacteroides abscessus (PDB ID: 5I7N) are shown in green, cyan, blue and orange color respectively whereas all central helices of those β-sheets of so-called "hotdog fold" represented as sausage are shown in chocolate color. A 9–17 residues long central α-helix (chocolate) represents the sausage of hotdog fold as seen in 1PN2, 3KH8, 5I7N and other DHF-containing hydratases where a 4-residues short helical segment α3 (Trp47-Ala50) named as an eaten sausage of PaIch resemble the sausage counterpart shown in other hydratases. Inset: Final $2F_o$-F_c map showing that central helix "α3" (chocolate) of PaIch is in right fit (contoured at 1.0 σ). (B) Top view of N-terminal hotdog fold of PaIch (green) showing that central helix (α3; chocolate) is slipped away from the β-sheet scaffold (bun) while central helices (sausage) of other (R)-specific enoyl-CoA hydratases (PDB ID: 1PN2, 3KH8, and 5I7N) are properly wrapped by their respective hotdog folds. All structural representations were made through PYMOL v2.5.4.

Dr. Saumen Datta, Chief Scientist
Group Members: Gourab Basu Choudhury, DBT-SRF; Atanu Pramanik, UGC-SRF, Bidisha Chakraborty, CSIR-SRF; Angira Saha, ICMR-SRF; DEbyan Saha, UGC-JRF
Collaborators: Saumya Ray Chaudhuri, CSIR-Institute of Nicrobial Technology, Chandigarh, India

Dr. Siddhartha Roy and his group members

Understanding the structural landscape of chromatin: Chromatin regulators and histone chaperons

Research Activities

TONSOKU or TONSL was first reported as a protein involved in the DNA damage response pathway along with its interacting partner MMS22L. TONSL consists of four domains- N-terminal tetratricopeptide repeat (TPR) domain, Ankyrin repeat (ANK) domain, Ubiquitin-like (UBL) domain, and C-terminal Leucine-rich repeat (LRR) domain. TONSL-MMS22L complex was shown to be involved in homologous recombination by loading RAD51 onto the ssDNA, thus mediating the survival of cells after replication fork collapse. Moreover, TONSL acts as a histone chaperone and binds H4K20me0, the epigenetic mark of newly synthesised histones, which are incorporated during DNA replication and marks post-replicative chromatin until the G2/M phase of the cell. This chromatin-dependent binding is essential for the DNA repair functions of TONSL. It has also been reported that in TONSL overexpressed cell lines, basal DNA repair functions are more active, and thus, it acts as an oncogene. Recently, it was found that mutations in the TONSL gene are responsible for SPONASTRIME Dysplasia, a rare autosomal-recessive skeletal dysplasia first reported in 1983. These mutations span the entire protein length and lead to various DNA damage responses and homologous recombination problems. These mutations were reported from patient samples from all over the world, including India. However, how these mutations, especially those present in the histone interacting domain(s) of TONSL, correlate to the disease phenotype is not yet known. These mutations might also hinder global genome stability by preventing the proper functioning of TONSL and affecting its homo-oligomerization. Hence, characterising these mutations is essential to better understanding the disease, which may lay the groundwork for tackling this disease soon. List important mutations found in SPONASTRIME Dysplasia patients in different domains of TONSL are as follows— p.(Arg42His), p.(Ser174Asn), p.(Glu199Lys), p.(Asp364His), p.(Gln430Arg), p.(Arg934Trp), p.(Gly973Arg) etc.

Our preliminary work suggests that TONSL homo-oligomerizes in vivo by its UBL domain. UBL domain itself homo-oligomerizes in vitro as evident from size-exclusion chromatography and cross-linking assay (Figure-1). Secondly, we have also identified that the TONSL-TPR domain binds to histone H3 in vitro. We

also observed that the TPR domain binds the N-terminal tail of histone H3. Currently, we have purified the TPR domain up to homogeneity and set up a crystallization screen using the sitting drop vapor diffusion method. Finally, we have expressed, purified, and successfully crystallized the UBLR934W p. (Arg934Trp) mutant which is directly associated with SPONASTRIME Dysplasia (Figure-2). This mutation was also reported to be embryonic lethal in mice models. X-ray diffraction data collection and structure solution of this disease mutant domain are currently ongoing.

Future Research Plans

By completing this project, we will address how TOSNL homo-oligomerization regulates its DNA repair related functions and global genome stability; characterize its novel histone-binding domain both structurally and functionally. Furthermore, we will comprehensively elucidate of how disease specific TONSL mutants affect the global genome stability and lead to disease pathogenesis of SPONASTRIME Dysplasia. This study will bridge the gap between structure-function research on TONSL and the overall disease mechanism of SPONASTRIME Dysplasia, which is currently unknown.

Extramural / CSIR Funding

1. Structural characterization of Zinc finger MYND domain containing protein with GATAD2A subunit of NuRD complex implicated in Neural Differentiation. Department of Biotechnology (DBT), 2023-2026, 74.329 Lakh, (BT/PR45090/MED/122/319/2022).
2. Elucidating the structural and functional role of TONSL, a novel histone chaperone and chromatin dependent DNA damage response protein in SPONASTRIME Dysplasia, a rare skeletal dysplasia in human. SERB Board, Department of Science & Technology (DST), 50.2 Lakh, (CRG/2022/001895).

Publlications

1. Das, C., Adhikari, S., Bhattacharya, A., Chakraborty, S., Mondal, P., Yadav, SS., Adhikary S., Hunt, CR., Yadav, KK., Pandita, S., Roy, S., Tainer, JA., Ahmed, Z., Pandita, TK. (2023) Epigenetic-Metabolic Interplay in the DNA Damage Response and Therapeutic Resistance of Breast Cancer. *Cancer Res.* 83, 657-666.
2. Singh V, Nandi S, Ghosh A, Adhikary S, Mukherjee S, Roy S, Das C. (2024) Epigenetic reprogramming of T cells: unlocking new avenues for cancer immunotherapy. *Cancer Metastasis Rev.* 43, 175-195.

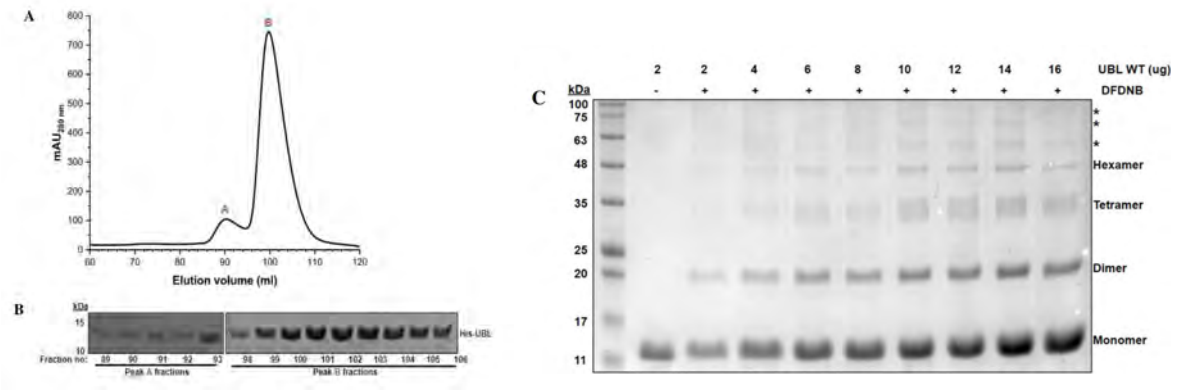


Figure 1: TONSL-UBL domain homo-oligomerizes in vitro A. Size-exclusion chromatogram of TONSL-UBL domain shows presence of two distinct peaks (Peak A & B) B. SDS-PAGE of fractions from both the peaks show presence of UBL. C. DFDNB-mediated cross-linking assay of UBL domain in increasing concentration

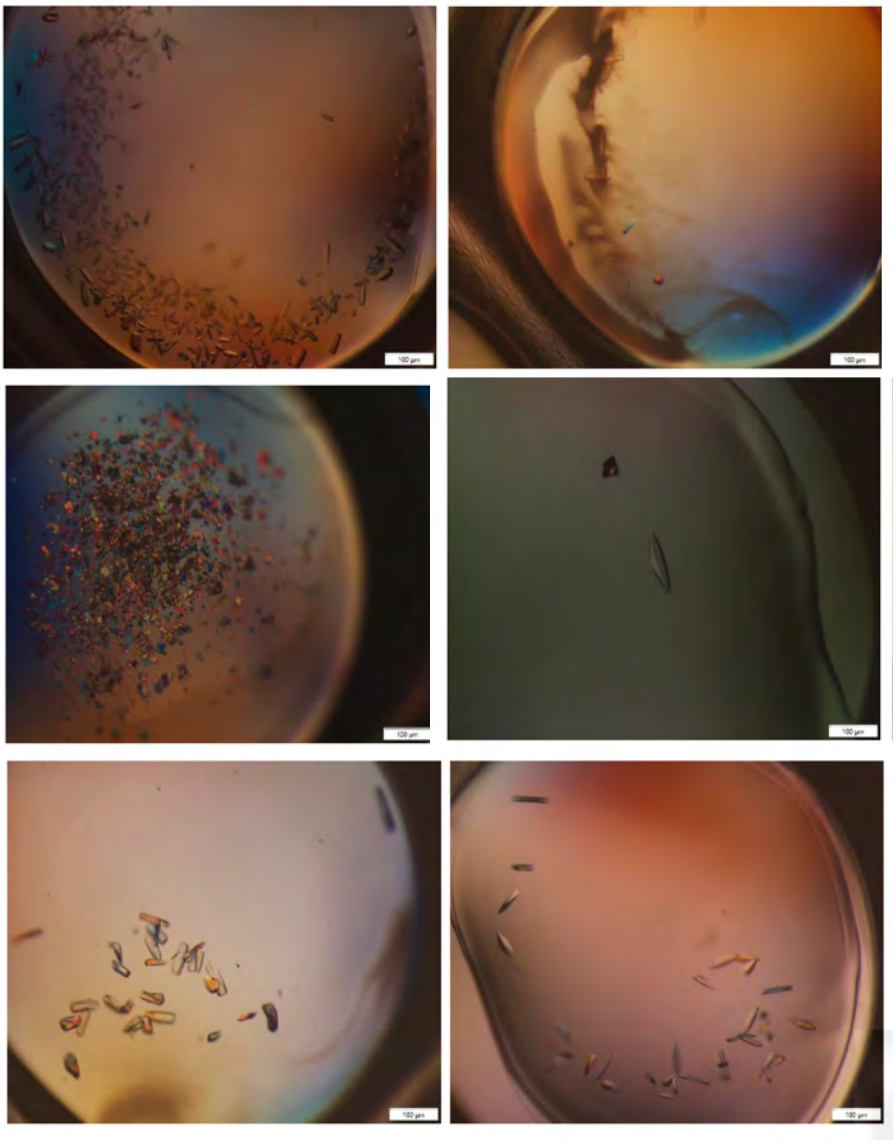


Figure 2: Crystal of UBLR934W obtained from crystal screening

Dr. Siddhartha Roy, Senior Principal Scientist
Group Members: Sinjini Dhang, UGC-SRF; Avradeep Karmakar, CSIR-SRF; Deep Basu, UGC-JRF; Sayan Gupta, ICMR-JRF; Bhaskar Das, UGC-JRF; Bonodip Chowdhury, UGC-JRF
Collaborator: Dr. Chandrima Das, Saha Institute of Nuclear Physics, Kolkata

Dr. Subrata Adak and his group members

Uncover the mechanism for the regulation of leishmanial PAS domain-containing phosphoglycerate kinase activity by its PAS domain at the molecular level

Research Activities

PAS (Per-Arnt-Sim) domain within sensory proteins makes up one of the most flexible classes of regulatory domain in the biological science regarding their functions, including signal transfer, sensing stimuli, and protein/protein interaction. PAS domain can either function as a signal directly via small molecule binding or interact with a cofactor that permits sensing of the environment like redox potential, visible light, and dissolved gases. Furthermore, several groups of researchers have reported that the PAS domains within numerous sensory proteins binds divalent Mg^{2+} cation at neutral pH 7.5 for sensing the environment.

Human pathogen *Leishmania* spp have three isoforms of phosphoglycerate kinase (PGK) those are PGKB, PGKC and PAS-PGK. Out of these three isoforms, PAS-PGK protein contains ~115 amino acids long regulatory PAS domain at the N-terminus that is attached to the C-terminal catalytic PGK domain. Recently we have suggested from our comparative studies with overexpression, gene knockout, and complement cell lines that LmPAS-PGK displays a key role in cell survival through autophagy. Localization study suggests that LmPAS-PGK is present in the glycosome (single-membraned peroxisome-like organelle) as well as the lysosome. By comparing Mg^{2+} ion dependent PGK activity between PAS domain containing PGK protein (full length LmPAS-PGK) and PAS domain deleted PGK protein (Δ115 LmPAS-PGK) at neutral pH 7.5, we have reported two unique observations: (a) ~10 μM Mg^{2+} ion is sufficient for optimum PGK activity of full length protein, which is ~100 fold lower compared to PAS deleted proteins (~1.0 mM); (b) full length protein is inhibited by millimolar level of Mg^{2+} ions at neutral pH 7.5 but this repression is absent in PAS deleted protein. Above results suggest that PAS-PGK has two Mg^{2+} binding site; first high affinity binding site is at PGK domain, which is required for catalytic PGK activity via nucleotide binding; second low affinity binding site is at the PAS domain that represses cofactor Mg^{2+} dependent-PGK activity in the PAS-PGK proteins at neutral pH 7.5.

Using the Protein Data Bank [PDB, http://www.rcsb.org] and a cognate ligand domain mapping for enzymes (PROCOGNATE), several groups show the atomic resolution of octahedral coordination geometry of Mg^{2+} binding sites in proteins, where water molecules, carboxyl groups of Asp/Glu residues and carbonyl oxygen atoms of the protein backbone are involved. Even though it is known that Mg^{2+} cations are regulated by His-57 at PAS domain of LmPAS-PGK but which specific acidic (Asp/Glu) residue is responsible for cofactor Mg^{2+} binding is still unclear.

Objectives

1. Identification of the specific acidic residues, which is involved in Mg^{2+} binding at PAS domain.
2. What is the mechanism for the regulation of PGK activity by PAS domain at the molecular level?

Work Achieved

Twelve acidic residues (D4, D16, D22, D24, D29, D43, D44, D60, D63, D77, D87, and E107) are present in the primary sequence of the PAS domain of LmPAS-PGK. To examine the possibility of deprotonated form of one or more of the acidic residues in Mg^{2+} ions binding, all acidic residues were separately mutated to alanine and all twelve Ala point mutant proteins were verified for divalent Mg^{2+} ion-dependent enzymatic activity at various pHs. The PGK activity of wild-type proteins and mutants of all acidic residues in the PAS domain showed optimum PGK activity at a limited concentration of Mg^{2+} (30 µM) ions at neutral pH 7.5. To compare the K_D value of Mg^{2+} ions at catalytic site among wild type and D4A, we measured Mg^{2+} ion dependent enhancement of catalytic activity at pH 7.5. These results indicate that none of the acidic residues in the PAS domain are involved in enhancement of the Mg^{2+} binding affinity for the catalytic PGK domain at neutral pH 7.5. However, the PGK activity of the D4A (with or without His-tag) mutant out of the twelve acidic residue mutants was not inhibited by a higher (1 mM) concentration of Mg^{2+} ions at neutral pH 7.5, suggesting that the loss of the carboxylic side chain of aspartate at position 4 by alanine disrupts the repressed state. Taken together, the presence of an Asp at position 4 is mandatory for maintaining suppressed state of wild type LmPAS-PGK at neutral pH via Mg^{2+} binding in PAS domain.

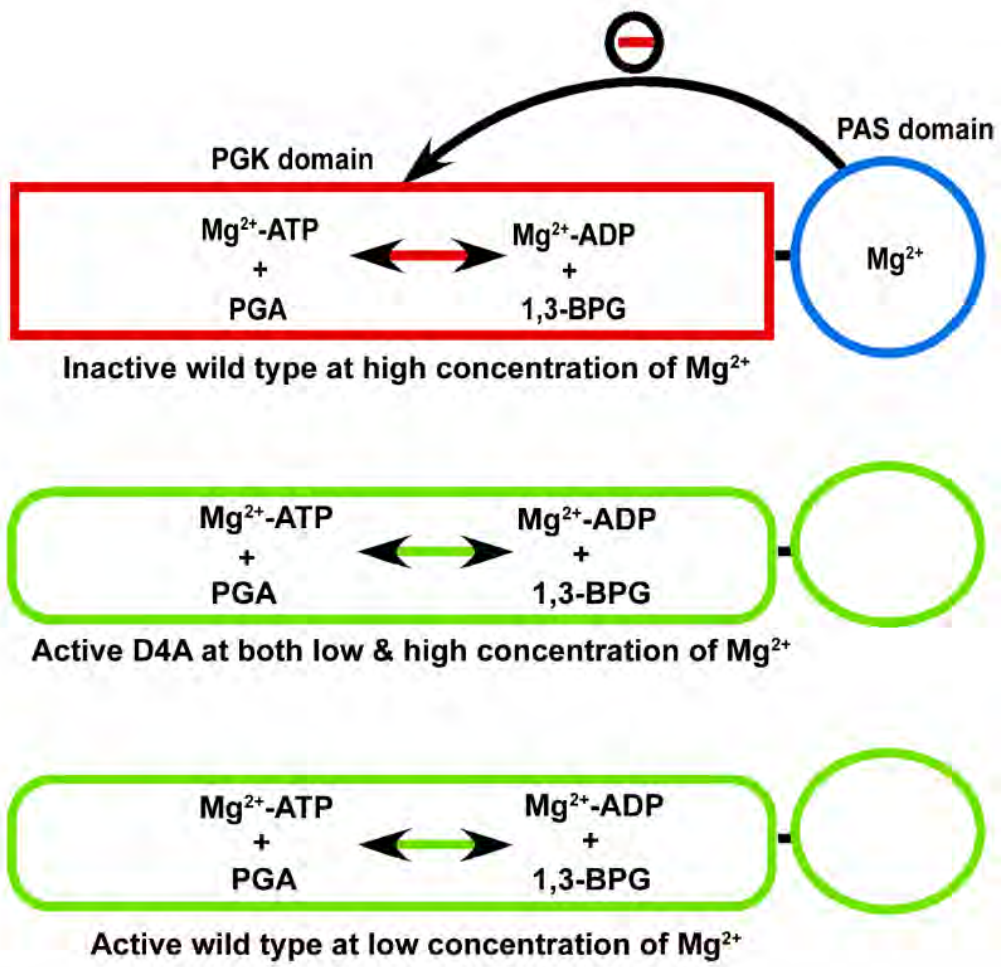


Figure 1: The PAS domain-containing phosphoglycerate kinase from *Leishmania major* (LmPAS-PGK) contains an N-terminal sensory domain (PAS) and a C-terminal catalytic phosphoglycerate kinase domain (PGK). In a Mg^{2+}-limited environment (low), the conformation of LmPAS-PGK favours its PGK activity and produces ATP at neutral pH. At millimolar (high) concentrations of Mg^{2+}, Mg^{2+} ion binds to PAS domain through Asp-4 and the altered conformation of LmPAS-PGK inhibits its PGK activity.

Future Research Plans

From the mechanistic viewpoint, the immediate question arises why LmPAS-PGK needs limited Mg^{2+} ions for PGK activation. So, the main future objective is why Mg^{2+} binding affinity in PGK domain of PAS-PGK protein is very high. For achieving our goal, we will do following works

1. We will predict the Mg^{2+} binding residues in catalytic PGK domain by homology modelling.
2. We will make the mutation for the Mg^{2+} binding residues in catalytic PGK domain.
3. We will characterize all mutant proteins.

Extramural / CSIR Funding

1. Translocation and regulation of an unusual novel PAS domain containing phosphoglycerate kinase in *Leishmania*. SERB, Department of Science & Technology (DST) 2021-24, 35.748 Lakhs, (CRG/2021/000421)
2. Leishmaniasis: Target specific approaches to affect host-pathogen interaction and disease process. CSIR, 2020-2025, 300 Lakhs, MLP-136

Publications

Chowdhury, G., Biswas, S., Dholey, Y., Panja, P., Das, S. (2024) Adak S Importance of aspartate 4 in the Mg2+ dependent regulation of Leishmania major PAS domain-containing phosphoglycerate kinase. *Biochim Biophys Acta* 1872, 140964.

Conferences Attended

92nd Annual Meet of the Society of Biological Chemists, BITS Pilani K K Birla Goa Campus, 18-20th Dec 2023

Dr. Subrata Adak, Chief Scientist
Group Members: Yuthika Dholey, UGC-SRF; Puja Panja, UGC-SRF; Gaurab Chowdhury, CSIR-SRF; Namrata Dhara, DBT-JRF; Swastik Biswas, UGC-JRF; Ritwick Modak,DBT-JRF; Dr. Swati Pal, Senior Project Associate

Dr. Sucheta Tripathy and her group members

Piecing together genomes of microbes for exploring the biological treasure trove

Research Activities

India is a major mega diverse nation with most of its microbial populations lying under explored. We work on a plethora of organisms belonging to different phylogenetic clades towards solving the biological riddles encoded in their genomes and exploiting them for beneficial purposes. We use existing and in house softwares in joining the shorter reads generated by the nextgen sequencing methods into larger contiguous segments. We use these contigs in predicting genes and assigning biological functions into them. We have already sequenced the genomes and transcriptomes of prokaryotic and eukaryotic organisms in discovering major genes including anti-freezing genes in endophytes that helps them sustain in sub-zero temperatures. These genes have huge economic significance. We have been able to over produce cell wall degrading enzymes in some fungal species that can have major implications in paper industry. We have predicted novel effectors that lie in the repeat rich regions of the genomes that evolve much faster than other regions of the genomes - re-iterating the two-speed genome evolution concept in pathogens. We have created computational resources for genomic data analysis in forms of lightweight genome analyzers. Our interest in prokaryotes centers on photosynthetic Cyanobacteria that grow in extreme environment. These organisms are shown to be extremely rich in signalling molecules that help them adapt quickly to changing environments. They also produce a range of secondary metabolites that has huge commercial significance. In future, we would like to use this information for commercial level production of bio-enzymes and metabolites and bio-remediation agents. The objectives of our laboratory are:

- Analyzing complex genomes in understanding the genomic re-arrangements for adaptations.
- Harvesting genes for metabolic re-engineering for commercial exploitation.
- Developing biological softwares for data analysis.

Our lab focuses on analyzing genomes and transcriptomes of extremophile and pathogenic microbes that are exclusively isolated from India. Our main goal is to understand their adaptation and

localized evolution. In this context, we have already sequenced several genomes of Cyanobacteria to unearth their genetic components.

We have uncovered the mechanism of heterocyst pattern formation in a hotspring species isolated from Eastern India. This species, *Mastigocladus laminosus* has reduced fitness during prolonged exposure to Nitrogen. In other words, Nitrogen induces stress in these organisms, which could implicate that exposure to Nitrogenous fertilizers in the field may cause harm to the naturally inhabiting Cyanobaceria in the Agricultural fields, thereby reducing the productivity. In addition, we have shown that a genetic mutation leading to an altered motif formation "QGNGH" in place of "RGSGR" reduces the binding affinity of HetN to HetR. The global expression change in the organism in response to Nitrogen stress and Nutrition stress clearly indicates Nitrogen to be a fitness reducer to the Nitrogen fixing organisms. We work on host pathogen interactions involving oomycetes pathogens. We have used machine learning approaches to predict the direction of horizontal gene transfer in 31 species of *Phytophthora sp* [fig 1].

Apart from this, we have been working on machine learning approaches in analysis and assembly of simple and complex genomes. We are now characterizing the genes of interest that are involved in production of metabolites.

Future Research Plans

We are now working towards over production of metabolites as well as other biologically active components from the Cyanobacterial cells. With the fungal dried cell wall, we wish to produce bio-materials that can be directly used for bio-remediation purposes.

Extramural / CSIR Funding

1. Platform integration for high Throughput multi omics data analysis and text processing. (DBT-Bioinformatics Center), 2022-2027, 227 lakhs, BT/PR40137/BTIS/137/35/2022.
2. Development of Genome Consortium Databank from plants and microbial population emerging from India. DBT (National Networking Program), 2023-2028, 169 lakhs, (BT/PR40243/BTIS/137/75/2023)
3. Development of Clinical Data Repository and Analysis Platform for Disease Detection and Prognosis. DBT, 2023-2028, 16 lakhs, BT/PR40233/BTIS/137/74/2023).

Publications

1. Comparative Genomic Analysis of 31 Phytophthora Genomes Reveals Genome Plasticity and Horizontal Gene Transfer, Kronmiller, B.A., Feau, N., Shen, D., Tabima, J, F., Ali, S, S., Armitage, A, D., Arredondo, F., Bailey, B, A., Bollmann, S, R., Dale, A., Harrison, R, J., Kelly Hrywkiw, Takao Kasuga, Rebecca McDougal, Charlotte F. Nellist, Preeti Panda, Sucheta Tripathy, Nari M. Williams, N, M., et. al., Molecular Plant-Microbe Interactions. 2023 36:1, 26-46.
2. Chakraborty, A., Prasad, S., Kant, S. et al. Thermally stable bioactive borosilicate glasses: Composition–structure–property correlations. Journal of Materials Research 38, 2969–2985 (2023).

Member of Society

1. Member of Research Advisory board of National Tea Research Foundation (2019-2022).
2. Associate Editor of Frontiers in Genetics and Microbiology (2020).
3. Senior Editor for Molecular Plant Microbial Interaction (An American Phytopathological Society Journal) Year: 2020-2023.
4. Life member of Biotech Research Society of India, BRSI Central office, Thiruvananthapuram (Year: 2014 onwards), membership ID: LM-1818.
5. Reviewer DST-SUPRA grants (2023-2024).
6. Life member of Proteomic Society of India, CCMB, Hyderabad, India. Membership ID: 593.
7. Life member of Electron Microscope Society of India, affiliated to international federation of societies for microscopy, CSIR-AMPRI, MP, India. Membership id: LM-1956
8. Elected member of West Bengal Academy of Science and Technology (WAST), Kolkata, 2024.

Conferences Attended

Plant Biology in the post genomics era: Strategies for crops and mankind, Sister Nivedita University, Feb 9th 24, Kolkata.

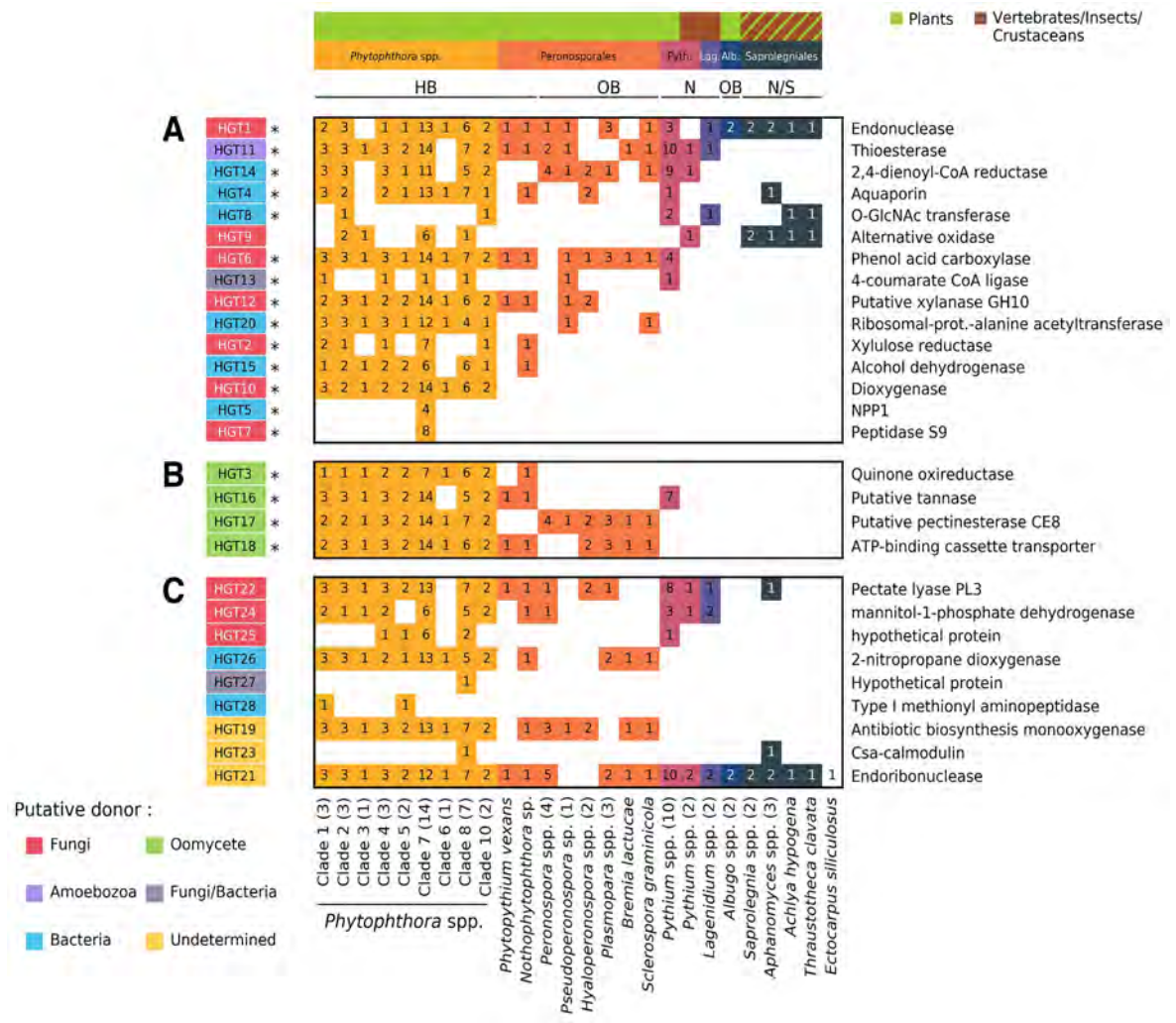


Figure 1: Conservation level of the 44 Phytophthora HGT candidates in oomycetes. Set of 19 horigzontal gene transfer (HGT) candidates for which a maximum likelihood phylogeny was reconstructed and alternate tree topologies were tested with the Shimodaira-Hasegawa test (asterisks indicate significant topological difference [P < 0.05] between the constrained alternate topology and the observed topology. A, HGT to oomycetes, B, HGT for the opposite relationships, i.e., transfers from oomycetes to fungi or bacteria, C, HGT candidates with no maximum likelihood phylogeny support. For each HGT candidate the number of sequence homologs identified among 37 Phytophthora and 30 oomycete transcriptomes (identified by reciprocal DIAMOND BLASTp, minimum E value of 1e-03, sequence subject coverage of 50% and sequence query coverage of 50%; a dash indicates the absence of a one-to-one ortholog) is reported. The filamentous brown alga Ectocarpus siliculosus (Ectocarpales, Ectocarpaceae) was used as an outgroup. Putative functions are indicated on the right. Top rows: Pyth. = Pythiales, Lag. = Lagenidiales, Alb. = Albuginales, HB = hemibiotrophic lifestyle, OB = obligate biotrophic, S = saprotrophic, N = necrotrophic. Species names, Phytophthora clade names and the group of species names are indicated on the bottom; numbers between brackets indicate the number of species considered in a group.

Dr. Sucheta Tripathy. Senior Principal Scientist
Group Members: Dr. Bornita Das, DST Women Scientist; Dr. Aditi Maulik, DBT BRC Scientist; Asharani Prusty, SRF; Aribam Geeta, SRF; Subhajeet Dutta, SRF; Kajal Mandal, SRF Aditya Upadhyay SRF; Sreyashi Das, JRF; Poulomi Ghosh, Project Assistant; Vaishnavi, Project Assistant; Sashikant, Project Assistant
Collaborators: Dr. Rays Jiang, Professor, UCSF, USA; Dr. Kaushik Biswas, Principal Scientist, CSIR-CGCRI, Kolkata, India

Dr. Tanaya Bose and her group members

Targeting bacterial ribosomes with a new class of antibiotics to overcome antibiotic resistance

Research Activities

Currently, our lab is engaged in growing bacteria which are a problem to mankind. We also have a library of antibiotics in the lab which will be tested against ribosomes of pathogens. We are currently studying the molecular docking of these compounds with our ribosomes to sort out the best-binding antibiotics to the ribosomes in silico which can be used later for testing on the ribosomes.

Future Research Plans

Antibiotic resistance has been a nuisance worldwide. While there has been no recent discovery of any class of antibiotics, mankind has already developed resistance to the antibiotics currently in the market. Therefore, developing new class of antibiotics is the need of the hour. 40% of the antibiotics currently in the market target ribosomes. Ribosomes are the protein synthesis unit of the cell. Therefore, targeting them to paralyze a cell is a wonderful strategy to overcome a disease. The new class of antibiotics that we aim to design are structure driven which will target the ribosomal RNA and hence disrupt ribosomal functions.

Extramural / CSIR Funding

Targeting bacterial ribosomes with a new class of antibiotics to overcome antibiotic resistance. DBT-Ramalingaswami fellowship, 2024-2027, 39 Lakhs

Conferences Attended

One-day International Symposium on “Recent Advances in Chemistry and Chemistry-Biology Interface” at the Department of Chemistry, Vivekananda Satavarshiki Mahavidyalaya, Jhargram on January 05, 2024. (chairperson of technical session).

Dr. Tanaya Bose, Senior Scientist
Group Members: Pranay Karmakar, UGC-JRF; Amar Pal, UGC-JRF

Central Instrumentation Facility

Central Instrumentation Facility Division (CIF)

Group members of Central Instrumentation Facility Division

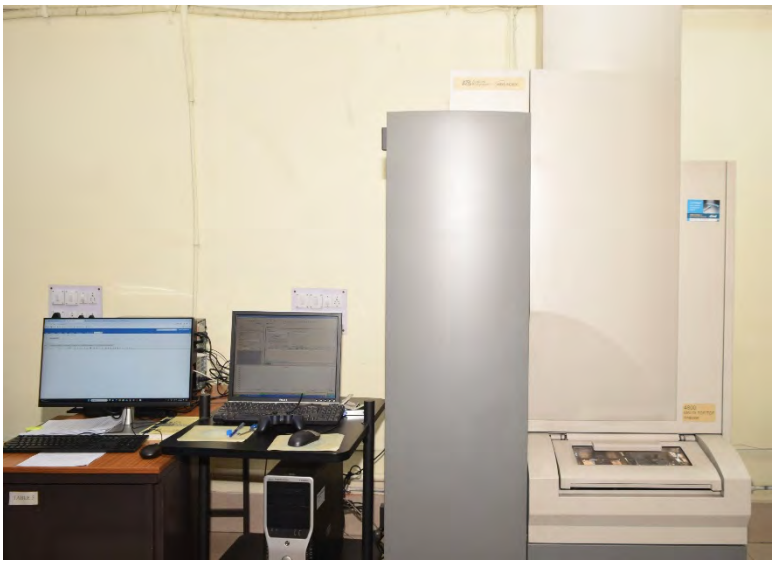
The facilities available at the Central Instrumentation Facilities (CIF) provides support to the researchers at CSIR-IICB along with different academic and R&D organizations, that includes Universities and Colleges of the country. CIF has more than thirty high-end and sophisticated instruments, which are run by well-trained operators and provide the data to the users. A few new equipment has been inducted to the facilities recently and procuring more high-end instruments are planned in the coming years to enrich our facility.

This division is also providing knowledge and information to the college and university students. For the PhD students of CSIR-IICB, Instrumentation and techniques course is imparted as a compulsory paper, where theoretical and practical aspects of relevant Instruments are imparted by the faculties and the technical operators. Through the relevant courses of the 'Skill Development Program' of CSIR, the faculties and technical officers of CIF train about different instruments to many candidates coming from all over the country. This Skill Development Program is happening in each quarter of the year. The facility of the CIF is taking care of extending support to the students and faculties under the science dissemination and popularization scheme of CSIR-IICB. During the CSIR-IICB open house program, the instrument facility is showcased to many students came from colleges and Universities and these instruments include NMR, LCMS, AFM, XRD, FACS, Confocal Microscope, etc. In the 'Jigyasa' program, the instruments of CIF are shown to the school students. In this year several school children were demonstrated the instruments of CIF.

The instruments list of CIF is available on the CSIR-IICB webpage along with their location and their operators. These facilities are distributed in both campuses of IICB. There are one or two faculty-in-charges of each instrument and their job is to look after the instruments on a day-to-day basis with the help of the designated operators. Besides, there is a CIF-advisory committee, which is advise and monitor the activities of CIF. As per the CSIR guidelines, booking for the instruments with AnalytiCSIR, a web-based portal is being done regularly. The CIF has been providing services to each and every user of our Institute as well as to external users throughout the country. The process of booking instruments is simplified that allow access to their required instruments. The data obtained from the CIF instruments are included in many papers to enrich their quality and published by scientists at IICB and other Institutes. Although CIF's objective is to provide satisfactory and accurate service to the users, in parallel our division is earning revenue. The CIF@IICB is committed to provide instrumental service and facilities towards all potential users of the country.

Instrumentation Facility

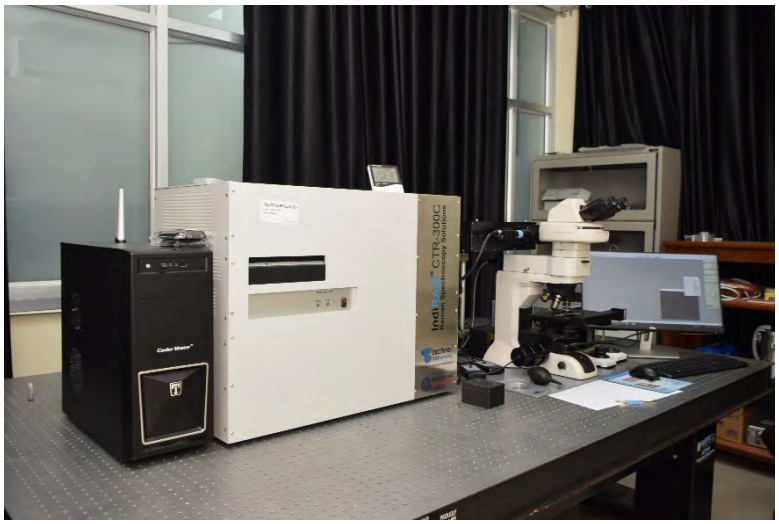
LC-MS ESIHRMS



MALDI

NIKON Fluoresence Microscope

NMR 400 mhz



RAMAN

STED

HPLC

XPN 100 Ultra centrifuge

Human Resource: Dr. Sib Sankar Roy, Chief Scientist & Head, Dr. Indu Bhusan Deb, Senior Principal Scientist & Deputy Head, Dr. Ramdhan Majhi, Principal Technical Officer; Dr. Ardhendu Kumar Mandal, Principal Technical Officer; Dr. E. Padmanaban, Principal Technical Officer; Mr. Binayak Pal, Principal Technical Officer; Mr. Sandip Chowdhury, Senior Technical Officer (2); Mr. Sandip Chakraborty, Senior Technical Officer (2); Mr. Jishu Mandal, Senior Technical Officer (1); Mr. Sounak Bhattacharya, Senior Technical Officer (1); Mr. Sandip Kundu, Senior Technical Officer (1); Mr. Santu Paul, Senior Technical Officer (1); Mr. M. Vigneshwaran, Senior Technical Officer (1); Mr. Soumik Laha, Technical Officer; Mrs. Arpita Maji, Technical Officer; Mr. Tapas Chowdhury, Senior Technician (3); Mr. Tarak Prasad Nandi, Senior Technician (2); Mr Anirban Manna, Senior Technician (2); Mr. Hari Shankar Beni, Technician (1); Mr Arijit Chowdhury, Mr. Nilaksha Swarnakar, Senior Technician (1); Mr. Bhaskar Basu, Lab Assistant; Mr. Nimai Charan Pradhan, Lab. Assistant

Support Divisions

Animal House

CSIR-IICB is associated with research in the area of chemical biology and its accomplishment vastly depends on animal experiments. CSIR-IICB Animal Facility had been established long back; however, it's been modernized time to time to keep pace with the evolving needs of research. The facility maintains high standards for animal husbandry and provides opportunity to conduct different experiments with a diverse range of animal species.

The animal facility of CSIR-IICB is registered to cpcsea (Registration No 147/GO/ReBi/S/99/ CPCSEA) and functions as per the guidelines of the CPCSEA. A uniform environment (Room temperature 24 $\pm$ 2^{o}C, relative humidity 55–60%, light and dark schedule 12:12hrs; illumination 200-400 lux at 1 mt above the floor) is maintained in the animal facility; the animals are housed in Individually Ventilated Cages (IVC). The 3Rs are strictly adhered to for animal experiments. All animals including transgenic and immune compromised strains of mice are bred and supplied from the in-house breeding colony. They are raised under strict health and genetic monitoring.

Besides catering the needs of the institute, CSIR-IICB animal facility extends necessary knowhow to other CPCSEA registered facilities. The facility acclaimed high appreciation from the representatives of CPCSEA, private entrepreneurs, and visiting scientists.

The species and strains of animals, routinely maintained in the facility are as follows:

Mice: Balb/C, C57BL/6J, Swiss Albino, FVBN and Transgenic strains, Immuno compromised mice strains.
Hamster: Golden.
Rabbit: New Zealand white.

A brief account of animal produced/supplied during this period is given in the following table:

Species	Stock on 1st April 2023	No. of animals		Total (A)	No. of animals issued		No. of animals		Total (B)	Stock on 31st March 2024
		Produced	Purchased		Produced	Purchased	died in-stock	Supplied to other R&D organization		
Mouse	1714	2126	160	4000	2164	160	136	0	2460	1540
Rat	304	131	0	435	183	0	0	0	183	252
Hamster	91	23	0	114	15	0	25	0	40	74
Rabbit	63	0	0	63	0	0	05	0	05	58

Human Resource: Dr. A. Konar, Chief Scientist & Head; Dr. R. Sarkhel, Scientist; Dr. S. Bhatiya, Scientist; Mr. S. S. Verma, MTS; Mr. R. Sarkar, MTS; Mr. J. Midya, MTS; Mr. P. Midya, MTS; Mr. Lalu Sardar, MTS; Mr. G. C. Sardar, MTS; Mr. S. K. Midya, MTS

Business Development Group (BDG)

Group members of Business Development Group

CSIR-Indian Institute of Chemical Biology is engaged primarily in research on diseases and certain biological problems of global interest and is continuously developing its knowledge base through world-class scientific research and innovation. The Institute is conducting basic research related to human health care with an intention to translate basic knowledge into technologies for the benefit of mankind.

In its constant endeavour to translate the research carried out at the Institute into meaningful products, the Business Development and Intellectual Property Management Group performs the dual functions of protecting the various aspects of the research as well as taking steps for early translation of the developed products and processes.

All innovations of the Institute, after an assessment of the potential for commercialization, are protected through the filing of patents or copyrights by its Intellectual Property Management (IPM) cell. The IPM cell of CSIR-IICB works in close co-ordination with the CSIR-Unit for Research & Development of Information Products (CSIR-URDIP) and 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 mankind. With the help of a new Comprehensive Patent Database prepared by this cell, now brief information about a patent filed by CSIR-IICB, since 1990 is just a click away.

This cell maintains liaison with Scientists of CSIR-IICB and IPU, CSIR to protect the Intellectual Properties of CSIR-IICB/CSIR. This cell functions with advice from the Head, BDG & IPM Cell, and Patent Advisory Committee whenever required. The IPM Cell extends co-operation to the inventors, CSIR-IICB in writing and filing patent applications and prosecution of the filed applications. This cell provides necessary information on technologies developed, patents filed and granted whenever required; provides information on patents and technology to IPU, CSIR regarding Audit and Parliamentary Question; prepares year-wise documents on total Patents of CSIR-IICB filed and granted.

Human Resource: Dr. Arindam Talukdar, Senior Principal Scientist & Head; Dr. Ranjan Jana, Senior Principal Scientist & Deputy Head; Mr. Sandeep Aggarwal, Scientist; Dr. Aparna Laskar, Senior Principal Technical Officer; Mr. Arupesh Majumder, Senior Principal Technical Officer; Mr. Saibal Giri, Junior Stenographer

Information Technology Division (IT)

Group members of Information Technology Division

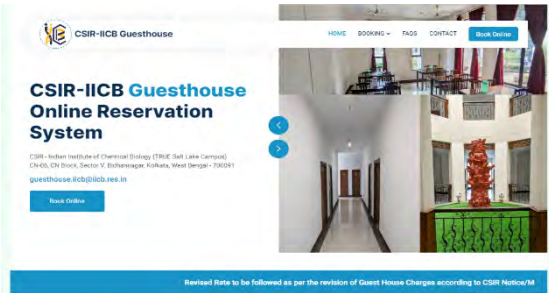
Information Technology Division of CSIR-IICB provides the essential IT services of the institute including scientists, students, and staff members. The IT group works towards maintaining uninterrupted IT services to both campuses of the institute. It has been at the forefront of deploying information technologies towards modernizing the IT infrastructure and facilities besides providing technical support services to the ongoing R&D projects. The Division has also extended its services to CSIR-IICB TRUE, Salt Lake campus through Point-to-Point connectivity.

Major Implementations and Achievements of the IT Division:

- Implementaion and Hosting of CSIR-IICB Guesthouse Online Reservation System.
- Upgradation of Digital Signage Display System Terminals at CSIR-IICB Jadavpur Campus including Installation of Updated Signage Editor Software.
- Upgradation of Point to Point Connection with 125 Mbps between Campuses of the institute for smooth running of inter campus IT & IT enabled services.
- CSIR-IICB represented at CSIR FITO (Forum of IT Officials) Meeting held on 26th & 27th October 2023 at CSIR HRDC New Delhi.
- The 57th meeting of the Management Council of CSIR-IICB approved the change of nomenclature of `Computer Division' to `Information Technology Division' reference to Office O.M. No. Admn6(36)/23/57th MC, Dated: 08.02.2024.

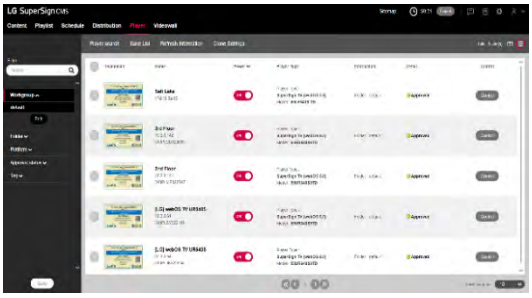
Jadavpur Campus Server Room

Salt Lake Campus Server Room

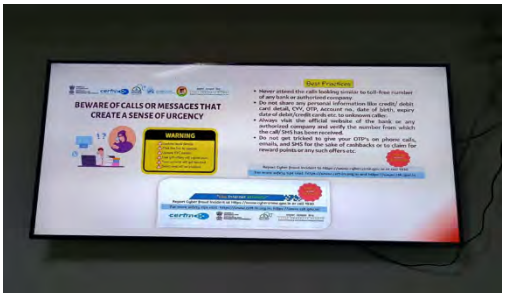


Upgraded Digital Signage Display System Terminals at Jadavpur Campus, CSIR-IICB

CSIR-IICB Guest House Online Reservation System inaugurated by Prof. Vibha Tandon, Director, CSIR-IICB



CSIR-IICB Guest House Online Reservation System hosted at CSIR-IICB Jadavpur Campus.



Upgraded Digital Signage Display System Editor Software installed at Server Room of Jadavpur Campus, CSIR-IICB.

CSIR-IICB Presenation at CSIR FITO Program held on 26th & 27th October 2023 at CSIR-HRDC, Ghaziabad, New Delhi.

IT Activities and Services of the Information Technology Division:

- IT and Network Infrastructure Management for both the campuses of CSIR-IICB.
- Primary ISP NIC(NKN) Link, Emergency Backup ISP (BSNL) Link and Point to Point Connectivity between campuses of the institute including Maintenance and Link Monitoring Services.
- Cyber Security and Gateway Services.
- CSIR-IICB Staff VPN Services.
- Administration and Maintenance of IT Division Servers and Server Infrastructure at both the campuses of CSIR-IICB.
- Implementation and Administration of Enterprise Client Server Architecture Antivirus System for the both campuses of the CSIR-IICB.
- Email Services for Staff and Students.
- Group Email Services for Staff, Scientists and Students.

- CSIR-IICB Website, Intranet and SDP Portal Maintenance & Content Management.
- Digital Signage Display System Services for Quick Information and announcements.
- Biometric Attendance System for Staff and Students.
- CSIR-IICB Guest House Online Booking Software Implemetation, Hosting and Maintanance Services.
- Ticketing System Job Cart Portal maintenance, Call Assignment & Monitoring Services.
- IT Facilities Arrangements and Hosting Hybrid Mode virtual meetings for Conferences, Events, and Institute Annual Programs like Foundation Day Celebrations, etc. including Internal Meetings, Administration Meetings, Colloquium lectures, Summer Trainee Programs, Skill Development Programs, Jigyasa Programs, etc.
- Technical Support Services, Call Assignment, and Monitoring Services to the users to provide support services for Desktops, Servers, Work Stations, Laptops, Printers, Scanners, Softwares, etc.
- Technical Documents and Other Special ICT Services from time to time.

Human Resource:
CSIR-IICB Jadavpur Campus: Dr. Sucheta Tripathy, Senior Principal Scientist, Head, Mr. Pradeep Sypureddi, Senior Technical Officer (1), Mr. Shiv Kumar Gupta, Technician (2)
CSIR-IICB TRUE Salt Lake Campus: Dr. Saikat Chakrabarti, Senior Principal Scientist, IT In-Charge

Engineering Services Unit (ESU)

Group members of Engineering Service Unit

The Engineering Services Unit (ESU) is comprised of Civil Engineering, Electrical Engineering and Air-conditioning & Refrigeration sections.

Civil Engineering Section

The Civil Engineering Divisionunder Engineering Services Unit of CSIR-IICB takes major role to render services in board areas of infrastructural development, new construction, renovation and up-gradation of laboratories and animal houses for Scientific Research Activities and common facilities, maintenance of campus, water supply, sewerage and drainage systems, cleaning and house-keeping work at both the campuses at Jadavpur as well as Salt Lake.

In addition to the above works, ESU Civil Section have been looking after the Gardening and Horticulture work, Audio-Visual works at Auditorium and Seminar Rooms as well as Conference Rooms in coordination with Electrical and Computer sections, Housekeeping and Conservancy works etc.

The major repair and renovation works taken up in the Financial year 2023-24 are as follows:

- Repair and Renovation of building, sanitary and water supply services.
- Repair and Renovation of different room (Phase-3) at CSIR-IICB Jadavpur Campus, Kolkata (Civil Work).
- Repair and Renovation of Animal House (Part) at CSIR-IICB, Jadavpur campus, Kolkata
- Repair and Renovation of Laboratory Room on the 4rt Floor floor at CSIR-IICB, Jadavpur campus, Kolkata
- Repair and renovation of canteen at CSIR-IICB at Jadavpur campus, Kolkata
- Construction of new shed besides underground water tank at CSIR-IICB, Jadavpur Campus, Kolkata
- Repair and Renovation of different room (Phase-4) at CSIR-IICB Jadavpur Campus, Kolkata (Civil Work).
- Construction of HT transformer platform with shed at CSIR-IICB, Jadavpur Campus, Kolkata
- Repair and renovation of Corridor at ground floor (near Admn wings), corridor at 1st floor (near Animal house) at CSIR-IICB, Jadavpur campus, Kolkata
- Repair and Maintenance of Air Handing Room above Auditorium Roof at CSIR-IICB, Jadavpur campus, Kolkata
- Replacement of PVC water tank in RL Block roof top at CSIR-IICB, Salt Lake campus, Kolkata.
- Painting and aluminium partition of Room No. 30 and 21 at CSIR-IICB, Jadavpur, Kolkata.

Electrical Engineering Section

Electrical Engineering Section under ESU has various activities and involvements towards overall management of Electrical Power Distribution systems installed at the Campuses of CSIR-IICB at Jadavpur and Salt Lake. In addition to this, ESU Electrical Section having regular activities for Estimation, Planning, Execution and Monitoring of all types of works related to Electrical Power and associated system including major modernization works. Different works like Provision of LED Lighting Fittings, Renovation and upgradation of Electrical systems of different Rooms and Working areas etc. were taken up during last financial year.

The major repair & renovation works taken up in the Financial year 2023-24 are as follows:

- Electrical and associated work for renovation of animal house (1st floor) at CSIR-IICB, Jadavpur Campus, (Phase-A).
- Renovation and upgradation of Electrical systems of different Rooms and Working areas at CSIR-IICB Jadavpur, Kolkata -700032.
- Renovation Electrical systems of different Rooms and Working areas at 1st Floor (West Side) at CSIR-IICB Jadavpur, Kolkata -700032.
- Upgradation of Electrical Systems of canteen hall at CSIR-IICB, Jadavpur.
- Provision of Energy Efficient and Emergency Lighting arrangement at CSIR-IICB, Salt Lake campus.
- AMC works for various electrical appliances like DG Sets, Capacitor panels, Fire Detection system, EPBAX System.

Air Conditioning and Lift Maintenance Section

This section has various activities at CSIR-IICB, Jadavpur and Salt Lake Campuses. The important activities performed by this section are as follows:

- Operation service and maintenance of Central Air Conditioning Plants of CSIR-IICB Jadavpur campus to ensure normal activities of the Auditorium and Library.
- More than 600 Split ACs are maintained round the clock by this section for Scientific and Research purpose.
- Lifts total 6 nos. are maintained round the clock at both the campuses of CSIR-IICB
- Cold Rooms two nos. at different floors of CSIR-IICB Jadavpur Campus are maintained properly throughout the year for different scientific purposes.
- Operation and maintenance service of Central Air Conditioning Plants HVAC system to ensure normal activities of the RL block of CSIR-IICB Salt Lake campus.
- Operation and Maintenance of state of Art Animal Resource Facility (ARF) for various animal experimentation for research purpose at CSIR-IICB Salt Lake campus.
- Operation and Maintenance of Ductable split AC for Mini Auditorium, Seminar room, Conference room at guest house CSIR-IICB Salt Lake campus.
- Operation and Maintenance of VRV system for comfort cooling purpose at guest house rooms.

Human Resource:
Civil Engineering Section: Dr. Nakul C. Maiti (Head), Mr. Sandip Saha, Mr. Susanta Ray, Mrs. Nirali Bage, Mr. Debashis Banik, Mr. Avijit Paul, Mr. S.R. Tudu and Mr. S.K. Ghosal.
Works Section under ESU: Mr. Sujit Kumar Majumder and Md. Muktar Ahmed.
Electrical Engineering Section: Dr. Nakul C. Maiti (Head), Mr. Susanta Ray, Mr. Ujjal Roy, Mr. Sourin Ghosh, Mr. Abhijit Paul, Mr. Samir Majumder, Mr. Anup Karmakar and Mr. Tanmoy Biswas
Air Conditioning and Lift Maintenance Section: Dr. Nakul. C. Maiti (Head), Mr. Prosenjit Gangopadhyay, Mr. Shubhendu Ghosh, Mr. Arijit Chowdhury and Mr. Monoranjan Adhikari

Human Resource Group (HRG)
Academic Affairs Division

Group members of Human Resource Group

Human Resource Group (HRG) of CSIR-IICB is involved in a wide range of activities towards the academic affairs of the doctoral students pursing their research work at CSIR-IICB. The major area where HR group contributes are: Activities related to Academic administration concerning PhD program, CSIR-IICB PhD course work, student affairs, post-graduate training programme, and different other program and activities of the institute. HRG provides assistance in the preparation of teaching and research materials and co-ordination of various programs critical to the mission of the Institute.

The functions include: Guidance and co-ordination for the CSIR-IICB PhD course work for the PhD students. Head, HRG serves as the co-ordinator of the Academic Affairs committee.

Activities, Guidance and Initiatives:

Student Affairs & Academic Affairs

- PhD course work: Management of Course work schedule, curriculum planning and course co-ordination, class schedule and attendance records, coordination with the teachers, management of semester examinations, evaluation, seminar, and publication of result, issuance of certificates and statement of marks.
- Scrutinization of applications for PhD registration and documents of research fellows related to their academic records and necessary applications. Maintenance of PhD registration related information.
- Scrutinization of academic records, selection and placement of post-graduate trainees at CSIR-IICB and co-ordination of the program.
- Coordination of Academic Affairs committee meeting and related documentations.
- CSIR-IICB JRF entrance interview: Information, web notification, vacancy for the number of JRFs. Maintenance of record of student strength under the guidance of the PhD supervisors at CSIR-IICB and associated activities.
- Content development for Research fellow's handbook, publication of course catalogue, Teacher's guideline, academic Calendar and

different guidelines related to PhD students at the institute and PhD course work.
- Organization of Orientation programme for PhD students.
- Interacting and required coordination with CSIR HRDG.

Human Resourses: PhD students (as on March 2024)
Number of existing Research Fellows: 262 (approx.) (CSIR/UGC/DST/DBT/ICMR)
Number of students awarded PhD degree during 2023-24: 41 (Doctorate degree received from AcSIR/University of Calcutta/ Jadavpur University)

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 the opportunity to do basic research in top-notch research areas, in a supportive learning environment with plenty of interaction with PhD research fellows and faculty members. Detailed guidelines are made available in CSIR-IICB website.

Number of Summer Trainee/Project Trainee carried their dissertation project work at CSIR-IICB during 2023-24: 48

Learning and instructional support: Academic Affairs
To conduct and coordinate the IICB PhD course work is the major focus of this Division which includes activities related to CSIR-IICB PhD Course Work program and academic-administrative guidance to the AcSIR activities in this institute.

The CSIR-IICB "Academic Affairs Committee (AAC)" acts as an Advisory Committee to the Academic Affairs Division/HRG in connection with CSIR-IICB PhD program and the AcSIR programme.'

Members of AAC are as follows:
Dr. Jayati Sengupta, Chairperson, AAC
Dr. K. Chattopadhyay, Member
Dr. Chinmay Chowdhury, Member
Dr. Subrata Adak, Member
Dr. Saikat Chakrabarti, Member
Dr. Rupasri Ain, Member
Dr. Indu Bhusan Deb, Member
Dr. Amitava Sengupta, Member
Dr. Sanjay Dutta, Member - Convener

CSIR-IICB PhD Course Work (CW): CSIR-IICB offers a mandatory PhD course work for the Research Fellows of the institute in their first year. The courses are taught by in-house faculty members as well as guest faculty from other Institutes/Universities. The framing of the course content & guidelines is designed in the line of AcSIR courses and as per UGC requirement. The curriculum of Course work plays a pivotal role for rejuvenating the creative nature in the scientific area of research.

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.

CSIR-IICB PhD Course Work comprises of Basic & Advanced level courses [total 18 credits taken by one student]:

A. Basic courses:

Research Methodology: Safety and Behavior at Workspace, Laboratory and Institutional Campus, Research Problem Identification and Research Design/Plan, Good Experimental, Observational and Data Analysis including Computer Applications, Intellectual Property, Patent Database Search and Patent Writing, Writing & Communication of Research Results and Inferences, Analytical Tools and Techniques in Research - A General Cross disciplinary Exposure.
Research and Publication Ethics: Philosophy and Ethics, Scientific Conduct, Publication Ethics, Open Access Publishing, Publication Misconduct, Databases and Research Metrics
Basic Biology & Basic Chemistry
Inter-disciplinary Learning: Cell and Tissue Engineering, Chemical Biology & Supramolecular chemistry and green chemistry

B. Advanced Courses:

Biology of Macromolecules, Cancer Biology, Cell Biology and Cell Signaling, Eukaryotic Gene Regulatory Mechanisms, Molecular and Cellular Immunology, Protein Science and Proteomics, Advanced Analytical Chemistry, Advanced Organic Chemistry, Natural Products and Drug Discovery & Total Synthesis

C. Societal program: Problem Understanding and Analysis

HRG functions as overall coordinating centre of CSIR-IICB PhD course work for PhD students. The PhD course work is co-ordinated with the advice of Chairperson & members of Academic Affairs Committee of the institute.

Total number of students of pursued Course work for 2023-24: 33 (Chemistry: 6, Biology: 27)

AcSIR Academy of Scientific & Innovative Research

Set up by an Act of Parliament, An Institute of National Importance

Academy of Scientific and Innovative Research (AcSIR) is established by an Act of Indian Parliament as an Institute of National Importance, provides opportunity to the CSIR students to work in areas of integrative and interdisciplinary areas of Science and Engineering.

AcSIR at IICB started enrolling students from 2012 session in the area of biological and chemical sciences. AcSIR ranked 12th in NIRF ranking of 2023.

Number of students enrolled in 2023-24: 49
Number of students awarded PhD degree during 2023-24: 12

AcSIR@IICB enrolls students twice in a year in January and August session. Students after enrolling with AcSIR had to take coursework in first two semesters. Also a Doctoral Advisory committee is formed for each research student to review their research progress and recommends thesis submission. The maximum duration of the PhD program for the AcSIR students in 6 years and minimum is 3 years which is followed in all CSIR institutes across India.

Human Resource: Dr. Sanjay Dutta, Senior Principal Scientist & Head; Ms. Debasree Das, Senior Technical Officer; Ms. Sutapa Ganguly, Md. Ayub Shah
AcSIR Co-ordinator: Dr. Jayati Sengupta, Senior Principal Scientist
Executive Assistant: Ms. Rohini Majumdar

Knowledge Resource Centre (KRC)
(Library & Documentation Division)

Group members of Knowledge Resource Centre

The Knowledge Resource Centre (Library and Documentation Division) of CSIR-IICB is one of the largest knowledge resource centres in biomedical sciences in the eastern zone of the country. With the establishment of the Indian Institute of Medical Research in January 01, 1935, the Library & Documentation Division started its journey as a prestigious department, and since then, it has been playing a pivotal role in the research & development programmes of the institute. The prime objective of this division is to organize various types of knowledge resources and disseminate those resources to its users. The library & Documentation division maintains print collection as well as electronic versions of knowledge resources, which includes books and journals. KOHA library management software is hosted at the IICB-KRC. Ten new computers were installed in the division for users to access e-resources.

The activities of Knowledge Resource Centre are monitored by library committee. The committee members provide valuable input regarding library activities during this period. The members of the Library Committee are,
Dr. Sucheta Tripathy, Chairperson
Dr. Partha Chakrabarti, Member
Dr. Ranjan Jana, Member
Dr. Shilpak Chatterjee, Member
Dr. Sujoy K Das, Member
Dr. Krishnananda Chattopadhyay, Convener

Collection strength (Hard Copy) (approx.):

- Books (including Hindi) - 14645
- Bound Volumes Journals – 33860

National Knowledge Resource Consortium (NKRC):

NKRC is a strong network of all CSIR & DST institutions for pooling and sharing of Knowledge Resources for catering best possible services to their users. The CSIR-NIScPR is the nodal agency for implementing and monitoring the activities of the NKRC and venturing the project successfully. Presently, more than 500 scholarly journals and databases are accessible in full-text through NKRC across the CSIR & DST Institutions.

CSIR-IICB gets access of the following e- resources from the NKRC

National Knowledge Resource Consortium (NKRC E-Resources/ Databases)	Different databases and More than 500 S & T journals from ScienceDirect, Wiley, Taylor & Francis, Royal Society of Chemistry, Emerald etc.	Standard Database	ASTM Standard (https://compass.astm.org/home/0)
		Writing Assistance Tool	Grammarly (https://www.grammarly.com/)
		Plagiarism Detection Tool	Ithenticate (https://www.ithenticate.com/)
		Chemical Abstract Database	SciFinder
		Citation Indexing Database	Web of Science (https://www.webofscience.com/wos/woscc/basic-search)
		E-Journals*	ACS Publications (https://pubs.acs.org/)
			Cell Press (https://www.cell.com/)
			Emerald (https://www.emerald.com/insight/)
			IEEE (https://ieeexplore.ieee.org/Xplore/home.jsp)
			Nature Publishing Group (https://www.nature.com/)
			PNAS (https://www.pnas.org/)
			RSC Journals (https://pubs.rsc.org/en/journals)
			Science|AAAS (https://www.science.org/)
			ScienceDirect Publications (https://www.sciencedirect.com/)
			Taylor & Francis (https://www.tandfonline.com/)
			Wiley (https://onlinelibrary.wiley.com/)

*List of E journals

I. American Chemical Society (ACS)			
01	Accounts of Chemical Research	18	ACS Chemical Neuroscience
02	Accounts of Materials Research	19	ACS Combinatorial Science [Journal of Combinatorial Chemistry (1999 - 2010)]
03	ACS Agricultural Science & Technology	20	ACS Earth and Space Chemistry
04	ACS Applied Bio Materials	21	ACS Energy Letters
05	ACS Applied Electronics Materials	22	ACS Engineering Au
06	ACS Applied Energy Materials	23	ACS Environmental Au
07	ACS Applied Engineering Materials	24	ACS ES & T Engineering
08	ACS Applied Materials & Interfaces	25	ACS ES & T Water
09	ACS Applied Nano Materials	26	ACS Food & Science Technology
10	ACS Applied Optical Materials	27	ACS Infectious Diseases
11	ACS Applied Polymer Materials	28	ACS Macro Letters
12	ACS Bio & Medchem Au	29	ACS Materials Au
13	ACS Biomaterials Science and Engineering	30	ACS Materials Letters
14	ACS Catalysis	31	ACS Measurement Science Au
15	ACS Central Science	32	ACS Medicinal Chemistry Letters
16	ACS Chemical Biology	33	ACS Nano
17	ACS Chemical Health & Safety	34	ACS Nano Science Au

35	ACS Omega	60	JACS Au
36	ACS Organic & Inorganic Au	61	Journal of Agricultural and Food Chemistry
37	ACS Pharmacology & Translation Science	62	Journal of Chemical & Engineering Data
38	ACS Photonics	63	Journal of Chemical Education
39	ACS Physical Chemistry Au	64	Journal of Chemical Information and Modeling
40	ACS Polymer Au	65	Journal of Chemical Theory and Computation
41	ACS Sensors	66	Journal of Medicinal Chemistry
42	ACS Sustainable Chemistry & Engineering	67	Journal of Natural Products
43	ACS Synthetic Biology	68	Journal of Proteome Research
44	Analytical Chemistry	69	Journal of the American Chemical Society
45	Biochemistry	70	Journal of the American Society for Mass Spectrometry
46	Bioconjugate Chemistry	71	Langmuir
47	Biomacromolecules	72	Macromolecules
48	C&EM Global Enterprise	73	Molecular Pharmaceutics
49	Chemical & Biomedical Imagine	74	Nano Letters
50	Chemical Research in Toxicology	75	Organic Letters
51	Chemical Reviews	76	Organic Process Research & Development
52	Chemistry of Materials	77	Organometallics
53	Crystal Growth & Design	78	Precision Chemistry
54	Energy & Fuels	79	The Journal of Organic Chemistry
55	Environment & Health	80	The Journal of Physical Chemistry A
56	Environmental Science & Technology	81	The Journal of Physical Chemistry B
57	Environmental Science & Technology Letters	82	The Journal of Physical Chemistry C
58	Industrial & Engineering Chemistry Research	83	The Journal of Physical Chemistry Letters
59	Inorganic Chemistry		
	II. Nature Publishing Group (NPG)		
84	Nature	95	Nature Neuroscience
85	British Journal of Cancer	96	Nature Protocols
86	Cell Death & Differentiation	97	Nature Reviews Cancer
87	Nature Biotechnology	98	Nature Reviews Drug Discovery
88	Nature Cell Biology	99	Nature Reviews Genetics
89	Nature Chemical Biology	100	Nature Reviews Immunology
90	Nature Chemistry	101	Nature Reviews Microbiology
91	Nature Genetics	102	Nature Reviews Molecular Cell Biology
92	Nature Immunology	103	Nature Reviews Neuroscience
93	Nature Medicine	104	Nature Structural & Molecular Biology
94	Nature Methods	105	Oncogene
	III. Cell Press / Science Direct		
106	Biophysical Journal	114	Immunity
107	Cancer Cell	115	Molecular Cell
108	Cell	116	Neuron
109	Cell Chemical Biology	117	Structure
110	Cell Host & Microbe	118	Blood
111	Cell Metabolism	119	Current opinion in Microbiology
112	Cell Stem Cell	120	Mitochodrion
113	Developmental Cell	121	The Lancet

IV. Other e-journals			
122	PNAS	124	Science Translation Medicine
123	Science		
V. Online Databases			
125	Grammerly	127	SciFinder
126	iThenticate	128	Web of Science
VI. Consortia e-resources			
129	ASTM Standards	133	Royal Society of Chemistry (RSC) - Regular
130	Emerald	134	Tailor & Francis
131	IEEE/IEL	135	Wiley
132	Oxford University Press		

Services

- The KRC serves as an important interface between users and the literature by ensuring uninterrupted access to the subscribed content besides regular services like circulation, reference, referral, document delivery and printouts services including the following others.
- The Online Public Access Catalogue (OPAC) is available at OPAC http://www.library.iicb.res.in/ which has been utilized as a very useful search interface for the library holdings.
- Resource sharing among CSIR & DST Libraries based on the demand placed by the users.
- Writing Assistance Tool Grammarly is introduced in the KRC. It reviews spelling, grammar, punctuation, clarity, engagement, and delivery mistakes in English texts.
- Similarity Index Report generation for the theses and research papers from IICB before submitting and communicating accordingly (as and when desired by the scholars and scientists). For reviewing the manuscripts, iThenticate – plagiarism detection database service is available in KRC.
- The KRC provides personalized information services using Science Citation Index Expanded. A 'Web of Science' service is also active at KRC.
- Approx. 68 user (membership) and IP based online user (all scietists, students, staffs)
- User Education & Orientation programme conducted by the KRC to maximize its utilization among the researchers.
- A collection of Hindi books 945 (approx.) has been classified and arranged in Hindi Section by KRC.

Human Resource: Dr. Krishnananda Chattopadhyay, Chief Scientist & Head; Dr. Sankar Kumar Moitra, Principal Technical office [Upto Feb 2024]; Mr. Manas Samanta, Sr. Technical Officer (1); Ms. Mahua Bhattacharjee, Senior Technician (2); Mr. Tapan Das, Senior Technician (2); Mr. Shyamal Nath, Lab. Assistant

Project Monitoring & Evaluation Group (PME)

Group members of Project Monitoring & Evaluation Group

The planning, monitoring and evaluation (PME) division manages the Institute's plan and CSIR Headquarters funded projects, grant-in aid projects (GAP), sponsored and collaborative R&D projects, consultancy and technical service projects. This division maintains liaison with Scientists and Technical officers who are Investigators of these projects and liaison with the Finance section and Purchase section and the funding agencies. PME provides proper logistic support for the management, monitoring and implementation of CSIR funded in house projects (Mission Mode, Major Lab Project, Fast Track Translational) and other externally funded projects that include those obtained from sponsored international agencies. PME's role is in an effective and successful implementation of the institute's commitments to all R&D endeavours. PME is also entrusted with appropriate dissemination of information regarding ongoing and completed projects to all statutory agencies like CSIR audit party, CAG audit etc. PME of CSIR-IICB, like other CSIR laboratories, is actively involved in the timely preparation and maintenance of databases for all intramural and extramural research projects, monitoring of project expenditure of projects, preparation of responses to Parliamentary queries in relation to the activities of the Institute, dissemination of information on all relevant National and International research program requests. PME from time to time provides information to scientists regarding terms and conditions of funding agencies, timely requirement of progress report and completion reports, respectively, of ongoing and completed projects. PME division participates in the preparation of the Institute's annual procurement plan and the budget, and maintains the expenditure data for the projects sanctioned, and maintains proper record keeping of all aspects of projects. It does regular interaction with finance division regarding the expenditure carried out against the projects. PME also processes all the relevant requirements for collaborative projects, approvals from competent authorities like Research Council, Management Council, and Director enabling smooth and quick submission of new projects to external funding agencies.

Human Resource: Dr. Subhas Chandra Biswas, Chief Scientist & Head, Dr. Ramalingam Natarajan, Senior Principal Scientist & Deputy Head; Mr. Shankar Bhakta, Private Secretary; Mr. Soumalya Sinha, Technician (2) and Mr. Samir Thami, Technician (2)

Publication and Information Division (P&I)

Group members of Publication and Information Division

The Publication and Information Division (P&I) handles a wide range of informational activities and the publication of many sorts of reports relevant to current science and technology. It is also in-charge of exhibiting the institute's operations to other laboratories and to the general public. Additionally, this section is actively planning and taking part in outreach programs like the CSIR JIGYASA program, which aims to popularize science among school children and participation in technology fairs (both locally and nationally). Such information is endeavored to be disseminated both in electronic and printed forms for extensive publicity of CSIR-IICB technologies, products and innovations. P&I's primary contributions are found in the yearly reports of the CSIR-IICB, which are published in both Hindi and English and assist scientists in outreach programs.

CSIR Jigyasa Programme

Students of Class XII of Jadavpur Vidyapith visited CSIR-IICB, Jadavpur Campus under CSIR Jigyasa Programme. The programme was conducted for three days on 16.6.2023, 19.6.2023 and 21.6.2023.


A Jigyasa Programme was organised at Khanrapara High School (H.S), South 24 Parganas on August 21, 2023. A lecture on 'Science behind the genetic management of the Society: DNA Fingerprinting' was delivered by Dr. Rupasri Ain, Chief Scientist, CSIR-IICB.

Climate Clock installed at Jadavpur Vidyapith to bring awareness on climate change among school children through the CSIR Jigyasa programme on August 23, 2023.


Two lectures on 'The story of human evolution: Where do we come from' and 'Artificial Cells: Life but not Alive' were delivered under CSIR Jigyasa Programme on 21st September, 2023, at Khanpur Nirmala Bala Sarkar Girls' High School. The lectures were delivered by Dr. Smrutisanjita Behera, Scientist, CSIR-IICB and Dr. Manish Debnath, Scientist, CSIR-IICB.


On the occasion of 82nd CSIR Foundation Day, an Open Day for school students was organized at CSIR-IICB Jadavpur Campus on September 22, 2023 under CSIR Jigyasa Programme. Total 199 students from eight schools participated in the event.


Two Jigyasa programmes were conducted on October 04, 2023 at at Zilla Public School, Tamluk, Purba Medinipur and Kelomal Santoshini High School, P. O-Kelomal, Dist.-Purba Medinipur. Dr. Ranjan Jana, Senior Principal Scientist, CSIR-IICB delivered the lecture on “Green Chemistry and Engineering from a Societal Perspective”.


As part of the celebration of '3rd Janjatiya Gaurav Divas', a one-day lab visit for school children, was organised at CSIR-IICB, Jadavpur Campus. Thirty students accompanied by three teachers from Krishnachandrapur High School (H.S.), Mathurapur visited CSIR-IICB on November 24, 2023.

CSIR-Indian institute of Chemical Biology, Kolkata organized an outreach activity for the 'India International Science Festival (IISF) 2023' on December 15, 2023.

CSIR has joined hands with the Energy Swaraj Foundation, Atal Innovation Mission and All India Council for Technical Education (AICTE) to bring awareness on climate change among school children through the CSIR Jigyasa programme. For this it was proposed that 100 Climate Clocks may be assembled by CSIR Scientists and school children under the Jigyasa programme. CSIR-IICB team demonstrated a climate clock to the students of Kendriya Vidyalaya, No. 2, Salt Lake on February 08, 2024. This was then handed over to the school authority.

A Jigyasa program was organized at Charigram Sri Ramkrishna Ashram Adarsha Balika Vidyalaya, Raghunathpur, Kolkata on 21st March 2024. Dr. Saikat Chakraborty, Senior Principal Scientist, CSIR-IICB delivered a lecture on 'AIDIAS: Artificial Intelligence-Based Diagnostic and Analytical Programme'. The session was incredibly interactive, shedding light on the recent advancements in AI technology and its applications in the field of diagnostics and analysis. Dr. Chakraborty's expertise enriched students' understanding of how AI is revolutionizing healthcare and scientific research.

Visit of college students

Students from the Department of Chemistry, Jogamaya Devi College, Kolkata and from Department of Microbiology (PG), Raja Narendra Lal Khan Women's College visited CSIR-IICB, Jadavpur campus on May 08, 2023.

Students from Shri Shikshayatan College, Kolkata (Botany Honours) and Adamas University, Kolkata (Department of Biotechnology), visited CSIR-IICB on January 15, 2024, for an Educational Tour.

M.Sc. 3rd semester students from the Department of Biotechnology, Gauhati University, Assam visited CSIR-IICB, Kolkata on January 24, 2024.

Human Resource: Dr. Sarita Ghosh, Principal Scientist & Head; Mr. Anirban Manna, Senor Technician (2)

Administrative Support Division

Administrative Division

Group Members of Director's Secretariat

Administrative Officer

Group Members of Recruitment Section

Group Members of General Section

Group Members of Bill & Cash Section

Group Members of Medical Cell

Group Members of Canteen

Security Officer

In today's complex and interconnected world, organizations rely heavily on administration to manage and maintain the smooth functioning of their operations. The administration ensures an organization's processes run efficiently and effectively.

It refers to the process of planning, organizing, staffing, directing, coordinating and controlling, and also acts as a function of managing people. It is also referred to as a body of knowledge, a practice and discipline.

In CSIR, the role of Administration is well defined. It ensures adherence and compliance with Govt. of India/CSIR guidelines issued from time to time. It provides necessary support system to run the Institute as per the mandate so identified by the Council. The backbone of the General Administration, herein at CSIR-IICB are the sections like Recruitment, Bill/DDO, Establishment, General, Medical, Legal, Vigilance.

However, at the apex of coordination is the Director's Secretariat managing Director's schedule, correspondence, and communications. They control access to the Director, maintaining due protocol and also ensures that all matters are handled efficiently and confidentially with proper record. Additionally, they coordinate meetings, prepare reports, and provide administrative support as needed by the Director. The basic essence of the Director's Secretariat is to maintain a liaison between the Competent Authority and the other members of the Institute.

Any Institution is built up by its employees and here a key role is played by the Recruitment Section, which is the fulcrum of every organisation, responsible for the entry of the right kind of workforce. At CSIR IICB, Recruitment also includes CR Cell and Legal and Vigilance Cells. On a whole, it deals with recruitments and appointments, conduct of examinations, posting on initial appointment, probation and confirmation-promotions of Scientific staffs in association with CSIR RAB and that of Administration, Technical and Support staffs in house, maintenance of manpower database, all the issues/queries received from CSIR-HQ/CSIR-RAB i.r.o administrative matters/ Parliaments Questions/ RTI. CR, Vigilance and Legal Cell being overseen by the Recruitment Section, evaluation and maintenance performance appraisal, action under CCS (CCA) Rules and Conduct Rules and legal assignments of the Institute are under the overarch of the Section.

The matters pertaining to the employees and their personal affairs related to their service records, like maintenance of service books, account of leave, issue of identity certificate for passport, issue of employment certificates, permissions for study leave, application for outside posts, permission to travel by air in respect of non-entitled officials, deputations within and outside CSIR, LTC, leave advance etc are taken care of by the Establishment Section.

Bill Section is an integrating force acting between Administration and Accounts. The section processes the monthly salary/stipend bills and arrear salary/stipend, TA/DA claims, gratuities, effecting recoveries from paybills, increments, admission to PRAN in the case of new recruits, forwarding monthly statement of contribution to NPS to PAO, provident funds, processing of various types of bills attaching bank account details of the individual for e payment, maintenance of cash book and allied records etc. Not confined to that only, the payments and deduction under IT / Prof tax etc. are being monitored by this Section. Upload of Income tax quarterly and yearly data for Form 16 generation. remittances of all payments through AMS Software. LTC advance and adjustments. reconcilement of GSLI, LIC, Professional Tax.

General Section takes care of all the time bound miscellaneous and odd jobs, which might not seem very attractive or alluring, but are crucial services, wherein failing any time frame could halt the system. The most important amongst the functions are the timely bill processing, tendering regarding hiring of cars/ manpower/ guest house /canteen & also monthly bills processing of the above-mentioned services. Booking of cars and also car procurement, air ticket booking and bills processing for payment of those air ticket/other services like electricity, telephone; booking of different Seminar halls and auditorium of the Institute, purchase of Swamy's handbook, observance of special days like 26th Jan, 15th Aug, Foundation day (Both IICB and also CSIR), Communal Harmony Day, Swachhata Pakhawada, Yoga Day etc., all come under the purview of this Section. It is also the duty of the General Section to ensure smooth functioning of the

canteen of the Institute. The Security Officer also reports to Section Officer, General Section.

Another crucial segment of Administration is the Medical Cell. It is the duty of this vital unit to maintain liaison with empaneled hospitals for treatment of staff members and pensioners and dependent family members, scrutinize medical bills for payment and ensure that medical facilities availed by staff and pensioners as per rules are smooth and hassle-free.

Human Resource:

Director Secretariat: Mrs. Pratima Banerjee, Private Secretary; Mr. Rabindranath Das, Private Secretary; Mr. Dinesh Mahali, Multi-Tasking Staff

Administrative Secretariat: Ms. Amrendra Kumar, Administrative Officer

Establishment Section: Mr. Mahesh Prasad, Section Officer (G); Mr. Tarun Kr. Sinha Roy, Assistant Section Officer (Gen); Mr. Sukhendu Biswas, Assistant Section Officer (Gen); Mr. Raju Kumar, Senior Secretariat Assistant (Gen); Mrs. Moumita Majumdar, Senior Stenographer

R&C Section: Mr. Kajal Saha Talukdar, Section Officer (G); Mr. Saugata Das, Assistant Section Officer (Gen); Mr. Ranjit Debnath, Assistant Section Officer (Gen); Mr. Pradipta Sarkar, Assistant Section Officer (Gen); Mr. Debtanu Pal, Senior Secretariat Assistant (Gen); Mr. Sumit Kumar Singh, Senior Secretariat Assistant (Gen); Mr. Rintu Bhattacharjee, Work Assistant

General Section: Mr. Manish Kr. Pandey, Section Officer (G); Mr. Tanumoy Sen, Senior Secretariat Assistant (Gen); Mr. Ram Kanai Mondal, Senior Secretariat Assistant (Gen)

Bill & Cash Section: Mr. Sudeep Sen, Section Officer (G); Mr. Sudhanshu Sekhar Roy, Section Officer (G); Mr. Alok Ray, Assistant Section Officer (Gen); Mrs. Mithu Kudu, Assistant Section Officer (Gen); Mr. Atanu Maitra, Senior Technician (2); Mr. Paresh Sarkar, Senior Technician (2); Mr. Asit Mitra, Multi-Tasking Staff

Medical Cell: Ms. Sanhita Ganguly, Section Officer (G); Mr. Anirudha Das, Assistant Section Officer (Gen)

Canteen: Mr. Ranjit Das, Senior Technician (2); Mr. Gopal Ch. Mandal, Multi-Tasking Staff

Security: Mr. Sabyasachi Karmarkar Security Officer

Finance & Accounts Division

Group Members of Finance & Accounts Division

CSIR-IICB Finance & Accounts Division is an indispensable management wing of the Organization dealing with Financial Management and Accounting of the Funds. IICB being a constituent Laboratory of CSIR, is mainly run with Government Grants received through CSIR and External Cash Flows received through Projects, Consultancy, Testing & Analysis and Technology Transfer Fees, etc.

The Finance & Accounts Division ensures optimum utilization of Public Money and Institutional Funds as per the canons of financial propriety. Reflection of the financial transactions and dealings automatically get reflected to CSIR Head Quarters through Accounting Managing Software. External monitoring of the Institute's financial aspects are also being handled by IICB Finance through coordination with the CAG & CSIR Internal Audit.

Overall, this wing advises and assists the Director in all financial matters, envisioning the road map for sustainable and self-supporting Financial Infrastructure for CSIR-IICB.

Key features include, Pre-Auditing of Proposals & Bills, releasing payments through PFMS & CNA-ZSBA, Book-Keeping of all financial transactions, Preparation of Annual Revised Estimates for the current financial year & Budget Estimates for the coming financial year. Assist PME Division for formulation of Annual Plans in Allocation of Funds for the Institute.

Human resource: Mr. Parag Patar, CoFA; Mr. Soumitra Chakraborty, SO(F&A); Ms. Chaitali Sarkar, SSA (F&A), Mr. Vishal Agarwal, ASO; Mr. Gautam Saha, Senior Stenographer

Store & Purchase Department

Group Members of Store & Purchase Department

The S&P division of the CSIR-IICB is dedicated in catering to the needs of the institute by procuring and distribution of the goods to its scientists and users. The main goal of the division is to achieve excellence in adequate and timely supply of goods by following due procedure which CSIR as well as GOI notify from time to time. The procurements are made by the following a uniform, systematic, efficient and cost effective procedure, ensuring fair and equitable treatment to its suppliers keeping itself within the ambit of statutory provisions, rules & regulations, vigilance and other GOI guidelines for public procurements.

Human Resources: Ms. Rubai Ray, CoSP, Mr. Bodhisatva Dhar, SPO; Mr. Rajib Ray, ASO (S&P); Mr. Bisweswar Das, ASO (S&P); Smt. Bula Pal, ASO (S&P); Mr. Ashoke Sardar, Technician; Mr. Prabir Das, Technician; Mr. S C Bose, SSA

Hindi activities

Member of Hindi Cell

Official Language in the Institute is being implemented with regular meetings, everyday Hindi words and phrases displayed in the electronic boards, Hindi workshops, observance of Hindi week etc.

The year 2023-24 saw many activities of the Official Language with workshop every quarter (three months).

Regular Hindi classes were arranged in the Institute (both campuses) wherein some employees passed Hindi Praveen/Pragya/Parangat examination conducted by the Home Ministry. Above 80% of the employees have passed Hindi examination and attained working knowledge / proficiency in the Official language of the government.

Official Language meetings are held with Director being the Chairman of all the OLIC meetings.

A quarterly Hindi workshop was organized on 28th June, 2023 (Wednesday) for the technical staffs., Mrs. Krishna Bhattacharjee, Senior Hindi Officer, CSIR-CGCRI, Kolkata was the speaker of this workshop. where the staff members were imparted training topic on “Difficulties in doing office work in Hindi and its solutions”.

Hindi pakhwada was celebrated from 14th to 29th September 2023. During this time many competitions were held in Hindi. The judges of these competitions were eminent professors, teachers and other noted personalities in Hindi language.

Hindi Recitation competition and Hindi Extempore Competition were organized on 19th September, 2023 (Tuesday). The program was inaugurated by the welcome speech by Amrendra Kumar, Administrative Officer of the Institute. Mr. Neeraj Chaddha, Scientific Officer (E) Computer and Information Science Group and Dr. Mamta Trivedi, Head, Hindi Department, Yogesh Chandra Chaudhary College were present as judges of Hindi Recitation competition and Hindi Extempore Competition.

On September 20, 2023, Hindi essay, noting & drafting competitions was organized in which participants of the institute participated in large numbers. Dr. Sunanda Roy Choudhary, Associate Professor, Hindi Department (East), Yogesh Chandra Choudhary College, Kolkata was the judge in these two competitions.

Hindi Debate Competition was organized on 21st September, 2023, the judges of which were Mr. Naveen Kumar Prajapati, Advisor, Central Translation Bureau (Official Language Department), and Mrs. Rita Bhattacharya, Former Chief Manager, Official Language UBI, Kolkata.

On September 22, 2023, a Hindi workshop was organized for administrative employees on the topic of 'Constitutional Provisions of Official Language' which was conducted by Mr. Priyankar Paliwal, Advisor, Bharatiya Vidya Mandir Kolkata. Everyone participated in this workshop.

Hindi Pakhwada Closing Ceremony and Prize Distribution Program was organized on 29th September, 2023. The Chief Guest of this program was Mrs. Parul Kush Jain, IPS, IGP, Traffic, West Bengal Police Directorate - Bhavani Bhawan, who was welcomed by the Director of our Institute, Dr. Arun Badyopadhyay. The participants who got first, second and third place in all the competitions organized from 14th to 29th September 2023 were awarded. Apart from this, the participants who participated in all the competitions were also honored with participation awards. The employees and research scholar present in the auditorium of the Institute were asked to write a word starting with 'त' in Hindi and they were awarded for writing the correct word. All the people present were very impressed by the lecture of Mrs. Parul Kush Jain. In the end, the program was successfully concluded with the national anthem and vote of thanks by the Hindi officer of the institute, Mrs. Ambalika Nag. The Hindi Officer Mrs. Ambalika Nag and team organised the programme.

A quarterly Hindi workshop was organized for technical staff on 18th March, 2024, Sri Anoop Kumar, Assistant Director, Hindi Teaching Scheme, Ministry of Home Affairs conducted the workshop on 'Word Processing on Computer'. The speaker of the workshop, Mr. Anup Kumar, trained everyone on the method of typing using Unicode Hindi Keyboard on the computer and he also told that for typing Hindi on the computer, voice typing can be done using earphones or mobile and all the employees participated enthusiastically in the workshop and everyone took a pledge to work in official language. The workshop was concluded with a vote of thanks by Mr. Mahesh Prasad, Section Officer (General), Establishment Department of the Institute.

Glimpses of Hindi Activities

Human Resource: Mrs. Ambalika Nag, Hindi Officer

Skill Development Programme

Skill Development Programme

CSIR Integrated Skill Initiative: Empowering the Future

Core members of Skill Development Programme

Overview

In alignment with the Government Policy of the National Skill Mission, CSIR launched a significant program, the "CSIR Integrated Skill Initiative," during its Platinum Jubilee Year in 2016. This initiative, inaugurated on September 23, 2016, aims to unify all CSIR skill and training programs under one comprehensive framework. The program is designed to serve a diverse cross-section of people, addressing various domains within the industrial and service sectors. By leveraging its technical expertise, CSIR is committed to extending its benefits to society through extensive skill development and training opportunities.

CSIR-IICB's Contribution

CSIR-IICB has actively participated in the CSIR Integrated Skill Initiative with a focus on fostering research aptitude among students and providing substantial practical exposure to the latest technologies aligned with industry and academic needs. This approach is expected to significantly contribute to employment generation. During the 2023-2024 period, CSIR-IICB offered 49 certificate courses as part of its Skill Development Programme. These courses provided youth with hands-on training, scientific knowledge, analytical skills, and technical proficiency in understanding advanced technologies used in research.

The trainees participated in two-week intensive programs that combined lectures and practical sessions across various advanced areas of CSIR-IICB's expertise.

Skill Development Sessions 2023-2024

Throughout the 2023-2024 period, CSIR-IICB conducted multiple skilling courses under the CSIR Integrated Skill Initiative. The sessions were structured as follows:

First Session (April 2023)
12 skill courses conducted in parallel (held during April 2023).

Second Session (July-August 2023)
14 skill courses conducted in parallel (held during July-Aug 2023).

Third Session (November-December 2023)
11 skill courses conducted in parallel (held during Nov-Dec 2023).

Fourth Session (February-March 2024)
12 skill courses conducted in parallel (held during Feb-March 2024).

These sessions collectively enhanced the practical and theoretical knowledge of participants, preparing them for various industrial and academic challenges.

Impact and Future Prospects

The CSIR Integrated Skill Initiative has successfully created a platform for knowledge dissemination and skill enhancement. By offering diverse courses and practical exposure, CSIR-IICB has contributed to building a skilled workforce ready to meet the demands of modern industries and research institutions. Moving forward, CSIR-IICB aims to expand this initiative further, continually adapting to emerging technological trends and societal needs.

The Courses conducted and Number of Candidates trained during the 2023-24 are tabulated below-

Course	Session-I	Session-II	Session-III	Session-IV	Grand Total
Cryo EM:Sample optimization and 3D structure reconstruction	06	08	05	06	25
High end equipments for clinical applications -Flow cytometry	05	10	07	10	32
Liquid Chromatography-Mass Spectrometry	06	07	05	07	36
Clinical Biochemistry,Microbiology and Pathology techniques for biomedical applications	09	10	07	10	36
Nuclear Magnetic Resonance Spectroscopy	03	04	-	04	11
High end equipments for clinical applications-Optical Microscopy	-	03	-	08	11
Real time PCR (Duration:1 week)	13	09	09	10	41
Protein X-ray crystallography	08	05	05	-	18
X-Ray crystallography (Small molecules)	-	04	-	-	04

Gas Chromatography Mass Spectrometry	04	03	04	04	15
Molecular Cloning,Protein expression and structural characterization	09	09	08	12	38
Separation Techniques for organic molecules	04	11	03	04	22
Advanced Bioinformatics	11	14	10	15	50
High Performance Liquid Chromatography	08	10	09	09	36
Total	86	107	72	99	364

Glimpses of CSIR-IICB Skill Development Programme

Practical sessions during Skill Development Programme

Training Program on Course-Protein X-ray crystallography

Training program on Course-Cryo EM:Sample optimization and 3D structure reconstruction

Training Program on Course-Real time PCR

Training Program on Course-High Performance Liquid Chromatography

Training program on Course-Liquid Chromatography-Mass Spectrometry

Training program on Course-Molecular Cloning,Protein expression and structural characterization

Training program on Course-Separation Techniques for organic molecules

Training program on Course-Nuclear Magnetic Resonance Spectroscopy

Training program on Advanced Bioinformatics

Training Program on Course-Gas Chromatography Mass Spectrometry

Training Program on Course-High end equipments for clinical applications-Optical Microscopy

Training Program on Course-Clinical Biochemistry,Microbiology and Pathology techniques for biomedical applications

Skill Development Programme Valedictory Day

Training session conducted from 17th April to 28th April 2023

Training session conducted from 31st July- 11th Aug 2023

Training session conducted from 28th Nov to 11th Dec 2023

Training session conducted from 19th Feb- 01st March 2024

Glimpses of course completion certificate received by trainees

CSIR-IICB Skill Development Management Team

Dr.Parasuraman Jaisankar, Chief Scientist & Head, Organic & Medicinal Chemistry Division Nodal Officer,Skill Development Programme,CSIR-IICB
Dr.Ramalingam Natarajan, Senior Principal Scientist, Co-Nodal Officer
Mrs Arti Grover, Senior Technical Officer (2), Convener
Md Ayub Shah,Sr. Technician (2)

CSIR-IICB Skill Development Faculty Team

SDP Course	Faculty Team Member
Cryo EM:Sample optimization and 3D structure reconstruction	Dr .Jayati Sengupta As Course Coordinator with other Faculty Team Member
High end equipments for clinical applications -Flow cytometry	Dr. Shilpak Chatterjee As Course Coordinator with other Faculty Team Member
Liquid Chromatography-Mass Spectrometry	Dr. Ranjan Jana As Course Coordinator with other Faculty Team Member
Clinical Biochemistry,Microbiology and Pathology techniques for biomedical applications	Dr. Partha Chakrabarti As Course Coordinator with other Faculty Team Member
Nuclear Magnetic Resonance Spectroscopy	Dr. Indu Bhusan Deb As Course Coordinator with other Faculty Team Member
High end equipments for clinical applications-Optical Microscopy	Dr. S.C.Biswas As Course Coordinator with other Faculty Team Member
Real time PCR	Dr. Debabrata Biswas As Course Coordinator with other Faculty Team Member
Protein X-ray crystallography	Dr. Saumen Dutta As Course Coordinator with other Faculty Team Member
X-Ray crystallography (Small molecules)	Dr. R.Natarajan As Course Coordinator with other Faculty Team Member
Gas Chromatography Mass Spectrometry	Dr. Indu Bhusan Deb As Course Coordinator with other Faculty Team Member
Molecular Cloning,Protein expression and structural characterization	Dr. Sib Sankar Roy As Course Coordinator with other Faculty Team Member
Separation Techniques for organic molecules	Dr. Biswadip Banerji As Course Coordinator with other Faculty Team Member
Advanced Bioinformatics	Dr. Sucheta Tripathy As Course Coordinator with other Faculty Team Member
High Performance Liquid Chromatography	Dr. Deepak Kumar As Course Coordinator with other Faculty Team Member

Visit of Dignitaries and Other Events

A popular lecture on Diabetes was arranged at the J.C. Ray Auditorium of CSIR-IICB on the sixth day of the 'One Week One Lab' Campaign.

Foundation Day celebration of CSIR-IICB on April 02, 2023.

सीएसआईआर-भारतीय रासायनिक जीवविज्ञान संस्थान में दिनांक 21.3.2023 को आयोजित हिंदी कार्यशाला

Dr. K. Nagaya, Chief Scientist & Head, Centre for Natural Products & Traditional Knowledge, CSIR-IICT, Hyderabad, delivered a lecture on the 'Natural Products & Traditional Knowledge' on April 25, 2023

Carla Rothlin, PhD, Dorys McConnell Duberg Professor of Immunobiology and Professor of Pharmacology; Co-Leader, Cancer Immunology, Yale Cancer Center delivered a talk on 'Principles of resolving and non-resolving inflammation' on May 2, 2023 at CSIR-Indian Institute of Chemical Biology, Kolkata.

A special cleanliness drive of entire outdoor and common spaces was organised at CSIR-IICB, Kolkata on May 04, 2023, as one of the activities during the 'Swachhta Pakhwada' programme 2023.

Plantation of trees and delivery of 'Swachhta Message' on May 11, 2023.

CSIR-IICB celebrated the National Technology Day 2023 on May 17, 2023. Professor Suman Chakraborty, IIT Kharagpur, delivered a lecture on 'Engineering Human Blood Vessels – Fact or Fiction?'

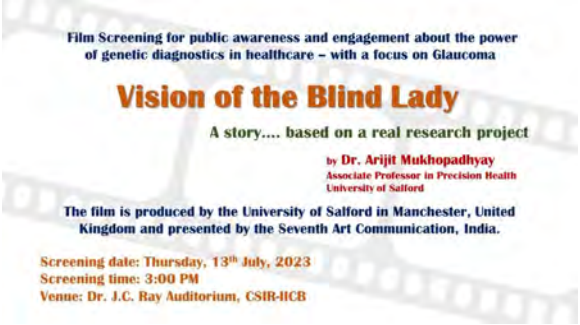
9th International Yoga Day was observed at CSIR-IICB on June 21, 2023. Mrs. Lili Gouda, Yoga Teacher, was present as a special invitee of the programme.

CSIR-IICB organized a 2-day meeting on 'Review of IP Filing Activities', in association with CSIR-URDIP and CSIR-IPU on 26th and 27th June 2023.

दिनांक 28 जून, 2023 को भारतीय रासायनिक जीवविज्ञान संस्थान में संस्थान के तकनीकी कर्मचारियों के लिए हिन्दी कार्यशाला

Dr. Satish Kumar Devarapu (PhD), Director of Preclinical Research, PreviPharma, Germany delivered a brief talk regarding PreviPharma Company's profile along with the opportunities for collaboration at CSIR-IICB TRUE campus.

National Intellectual Property Festival was celebrated at CSIR-IICB on July 24, 2023.



Lecture on Vision of the Blind Lady by Dr. Arijit Mukhopadhyay at CSIR-IICB, Kolkata

Dr. Arnob Dutta, from University of Rhode Island, delivered a lecture on "Switching usage of the SWI/SNF chromatin remodeller complex" on July 14, 2023

A seminar was organized jointly by NeuroUpdate Kolkata and CSIR-IICB on neurological disorders on July 12, 2023 at CSIR-IICB, Jadavpur campus.

Prof. Amal Mitra, Director of SPH Global Health Initiatives for the Southeast Asia and Western Pacific Regions, Jackson State University, USA delivered a lecture on "Psychological Impact of Covid-19 among Adolescents in West Bengal, India" on 10.08.2023.

Prof. Aditya Prasad Dash, Vice Chancellor, AIPH University visited CSIR-IICB Kolkata and interacted with the scientists and research scholars of CSIR-IICB, during August 01-03, 2023.

Visit of DG, CSIR at CSIR-IICB, Kolkata.

An International Conference on Metabolic Diseases 2023 was organised at CSIR-IICB on August 19, 2023.

Climate Clock installed at CSIR-IICB on August 24, 2023. The clock was inaugurated by Dr. Ramanuj Narayan, Director, CSIR-IMMT in presence of Dr. Arun Bandyopadhyay, Director, CSIR-IICB.

CSIR-IICB celebrated National Sports Day on August 29, 2023.

'Phenome India' project awareness program was organised for all the CSIR-IICB employees on September 15, 2023 at CSIR-IICB, Jadavpur Campus.

82nd CSIR Foundation Day lecture by Prof. Arun K. Shukla

CSIR-IICB participated in the Mega Exhibition at Bharat Mandapam, New Delhi organized on 82nd CSIR Foundation Day.

संस्थान में हिंदी पखवाड़ा समारोह दिनांक 14.9.2023 से 29.9.2023

CSIR-IICB, Kolkata celebrated 8th Ayurveda day under the theme “Ayurveda for one health” on 18/10/2023 with CARI, Kolkata -CCRAS, Ministry of Ayush, at CSIR-IICB, TRUE campus.

"Fit India Swachhata Freedom Run, 4.0", organized by CSIR-IICB on 27.10.2023, 30.10.2023 and 31.10.2023 at CSIR-IICB, Jadavpur Campus.

Neuroupdate 2023 meeting was held during November 25-26, 2023 at CSIR-IICB, Jadavpur.

CSIR-IICB at the CSIR exhibition stall in the Global Bio-India Technology-related exhibition at Bharat Mandapam, Pragati Maidan, New Delhi, during December 4-6, 2023.

Dr. Didier Raboisson, the Attaché for Scientific Cooperation at the Embassy of France in India, and Mr. Aymeric Voquang, Project Manager for Scientific and University Cooperation, visited CSIR-IICB on December 5, 2023 to explore potential research collaborations between India and France.

Madhumita Jajodia, the former principal of Durgapur Womens' College, delivered a talk on the occasion of the sensitization workshop on 'Sexual Harassment at Workplace Prevention Week' was organized at CSIR-IICB on December 08, 2023. Prof..

Dr. Sankhya Chattopadhyay, Ex-GM BRIT, Kolkata addressed the gathering on the occasion of "Radiation Awareness and GIC-I usage safety Program 2023"

CSIR-IICB at the CSIR pavilion of IISF Expo 2023 at Faridabad, Haryana, during January 17-20, 2024.

CSIR-IICB Annual Research Conclave 2024 was organized on January 25, 2024.

Prof. T. P. Singh, SERB, Distinguished Scientist & President, Chemical Biology Society (India) delivering lecture on the occasion of CSIR-IICB Annual Research Conclave 2024 was organized on January 25, 2024

Prof. Akhilesh K. Verma, a senior professor of the Department of Chemistry, Delhi University, delivered a research colloquium, "A Journey from Benzotriazole to Alkynes,". This event was held on February 15, 2024 at

On February 16, 2024, CSIR-IICB celebrated the 'International Day of Women and Girls in Science' with a captivating lecture by Prof. Chandrima Shaha, J.C. Bose Chair Distinguished Professor, CSIR-IICB,

Hands-on-workshop on" Genome Informatics and Annotation workshop/Jamboree" sponsored by DBT, was organized for 14 days during 29th Jan to 9th Feb 2024 at CSIR- IICB

A Workshop on Gender Sensitization and Provisions of POSH Act was held at CSIR-IICB during February 22-23, 2024.

CSIR-IICB celebrated national Science Day on February 28, 2024. An insightful lecture was delivered by Dr. Kapil Maithal, President-Vaccines & Diagnostics, Zydus Lifesciences Limited

DFG delegates, visited CSIR-IICB on February 28, 2024 and shared insights into their programs and opportunities, which are available for Indo-German collaborations.

Prof. Jyotirmayee Dash, Senior Professor, IACS, Kolkata delivering lecture on the occasion of "International Women's Day" on March 8, 2024.

71st Research Council Meeting of CSIR-IICB on March 13-14, 2024

सीएसआईआर-आईआईसीबी के तकनीकी कर्मचारी सदस्यों के लिए 18 मार्च, 2024 (सोमवार) को अपराह्न 3.30 बजे से "कंप्यूटर पर शब्द संसाधन" विषय पर हिंदी कार्यशाला

Prof. Manas K. Ghorai from the Department of Chemistry, IIT Kanpur delivered a research colloquium talk on the Synthesis of Biologically Significant Complex N/O-Heterocycles via Ring-Opening Transformations of Small Ring Aza Heterocycles on March 20, 2024 at Dr. J. C. Ray Auditorium, CSIR-IICB.

CSIR-IICB organized a hands-on training on 'Laboratory Animals: Care & Experimentation' from 20.03.2024 to 21.03.2024. Dr. Dinesh Yadav, Senior Veterinary Officer at CLAR, JNU, New Delhi, and Dr. Vijay Pal Singh, Veterinary Officer and Animal Facility In-Charge at CSIR-IGIB, New Delhi, conducted interactive sessions and demonstrations.

Key Performance Indices

Awards/Honours

Prof. Vibha Tandon, Director

Fellow of the National Academy of Sciences, India (NASI)

Dr. Dipyaman Ganguly, Senior Scientist

- Fellow, Indian Academy of Sciences, Bangalore
- Fellow of the Royal Society of Biology, UK

Dr. Krishnananda Chattopadhyay, Chief Scientist

- Fellow of the National Academy of Sciences, India (NASI)
- Fellow of the Indian Academy of Sciences, Bangalore
- Received Dr. Bishnu Pada Mukerjee Memorial Award Lecture from Indian Photobiology Society, Jul 15, 2023

Dr. Debabrata Biswas, Senior Principal Scientist

Fellow of the National Academy of Sciences, India (NASI)

Dr. Amitava Sengupta, Senior Principal Scientist

S Ramachandran National Bioscience Award for Career Development, Dept. of Biotechnology, Govt. of India

Dr. Nakul Chandra Maity, Senior Principal Scientist

Fellow of the West Bengal Academy of Science and Technolodgy (FAcST) in January 2024

Dr. Sucheta Tripathy, Senior Principal Scientist

Fellow for West Bengal Academy of Science and Technology in January 24

Dr. Subhas C. Biswas, Chief Scientist

Fellow of Indian Academy of Neurosciences

Dr. Rupasri Ain, Chief Scientist

Received Prof. N.R. Moudgal Memorial Oration Award (2024), from Indian Society for the Study of Reproduction and Fertility

Dr. Upasana Roy, Senior Scientist

Appointed as a Royal Society of Biology (RSB) Ambassador

Mr. Subham Kumar Bandyopadhyay, DBT-SRF

- American Society of Hematology Abstract Achievement Award, San Diego, USA &
- SERB International Travel Grant, Dept. of Science & Technology, Govt. of India

Mr. Kajal Mandal, SRF

- Shimamoto Travel award from International Society of Plant Microbe Interaction (IS-MPMI) to attend IS-MPMI congress in, Rhode Island, USA
- SERB International Travel support to attend and present his work in the same conference. Date: 16th July 2023 - 20th July 2023

Dr. Bornita Das, Women Scientist

Travel award to attend Gordon research conference to be held between 10-15th March 24. The travel award she won was Carl Storm International diversity award and CSIR foreign travel grant to present her work.

Dr. Himadri Sekhar Sarkar, Research Associate-III

Went to US with a travel Grant from SERB and CSIR and got BEST POSTER AWARD from ACS Chemical Biology.

List of MoU Signed and agreements

Sl. No.	Name of the Party/Company with Address	Type of Agreement	Date of Signature
01	CSIR-IICB and Central Ayurveda Research Institute, Central Council for Research in Ayurvedic Sciences	Memorandum of Understanding for Collaborative Research	12.04.2023
02	National Institute of Pharmaceutical Education and Research, Kolkata	Memorandum of Understanding for Collaborative Research	13.04.2023
03	University of Calcutta	Memorandum of Understanding for Collaborative Research	01.05.2023
04	Kolkata Gynecological Oncology Trials and Translational Research Group (KolGO-Trg)	Memorandum of Understanding for Collaborative Research	05.06.2023
05	Depart of Biotechnology (DBT)	Memorandum of Agreement for Research Support (Grant-In-Aid)	18.07.2023
06	IMP-Research Institute of Molecular Pathology, Vienna Biocenter, Austria (IMP)	Material Transfer Agreement	03.08.2023
07	Institute of Neurosciences, Kolkata	Memorandum of Understanding for Collaborative Research	09.08.2023
08	Cellogen Therapeutic Pvt. Ltd. Delhi	Memorandum of Agreement for Sponsored Research	23.08.2023
09	GCC Biotech (India) Pvt. Ltd.	Memorandum of Understanding for Sponsored Research	26.08.2023
10	K Patel Chemopharma Pvt. Ltd.	Non-Disclosure Agreement (NDA)	23.02.2024
11	Zydus Life Sciences Limited	Non-Disclosure Agreement (NDA)	01.03.2024
12	Central Council for Research in Ayurvedic Sciences (CCRAS), Ministry of AYUSH, No. 61-65, JLNBCAHAB, Institutional Area, Opposite D Block, Janakpuri, New Delhi – 110 058 & Central Ayurveda Research Institute, 4-CN Block, Sector – V, Bidhannagar, Kolkata	Memorandum of Understanding for Collaborative Research	21.03.2024

Patents Filed/Granted 2023-24

Granted in India

Sl. No.	Title	Inventors	Prov. Filing Date	Comp. Filing Date	Application No.	Grant Date	Patent No.
1	Bicycle topoisomerase I inhibiting compounds, process for preparation and use thereof	Talukdar Arindam, Das Benu Brata, Kundu Biswajit, Sarkar Dipayan, Pal Sourav, Bhattacharya Debomita, Mukherjee Ayan, Roy Subhajit, Paul Chowdhuri Srijita, Das Subhendu K	--	29.05.2018	201811020003	09.01.2024	496455

Granted Abroad

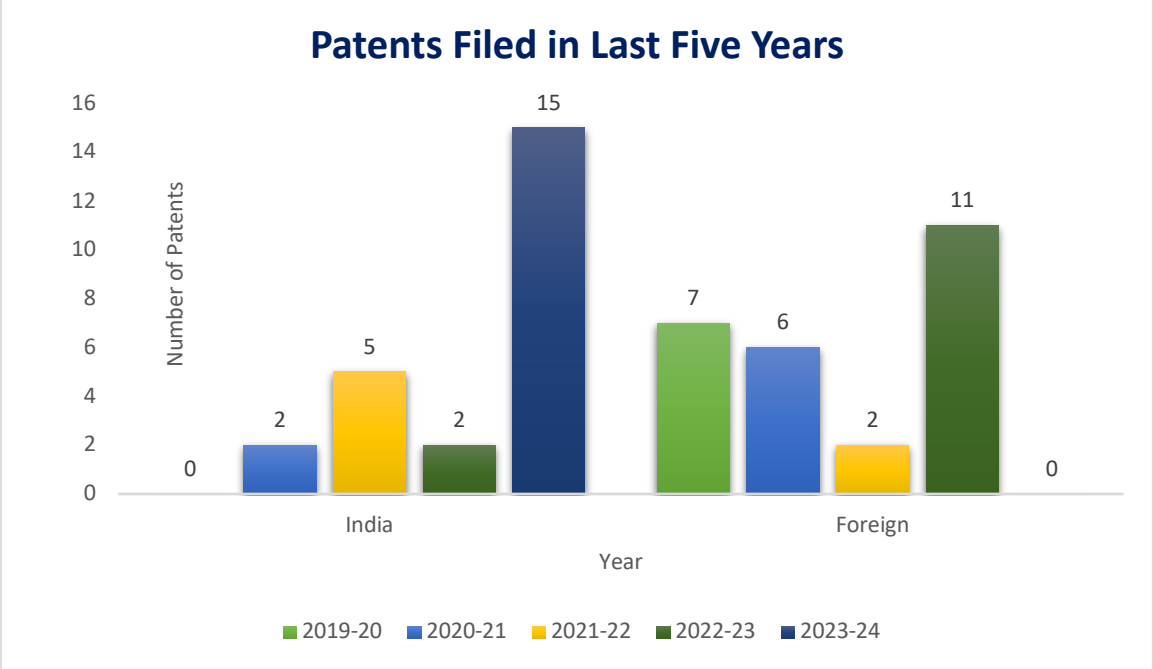
Sl. No.	Country	Title	Inventors	Grant Date	Patent No.
1	South Africa	An easy-to-use diagnostic system for rapid dengue virus detection using fluorescence-based molecular probes	Biswas Subhajit, Ghosh Surajit, Sukla Soumi, Mondal Prasenjit	26-04-2023	2022/09493

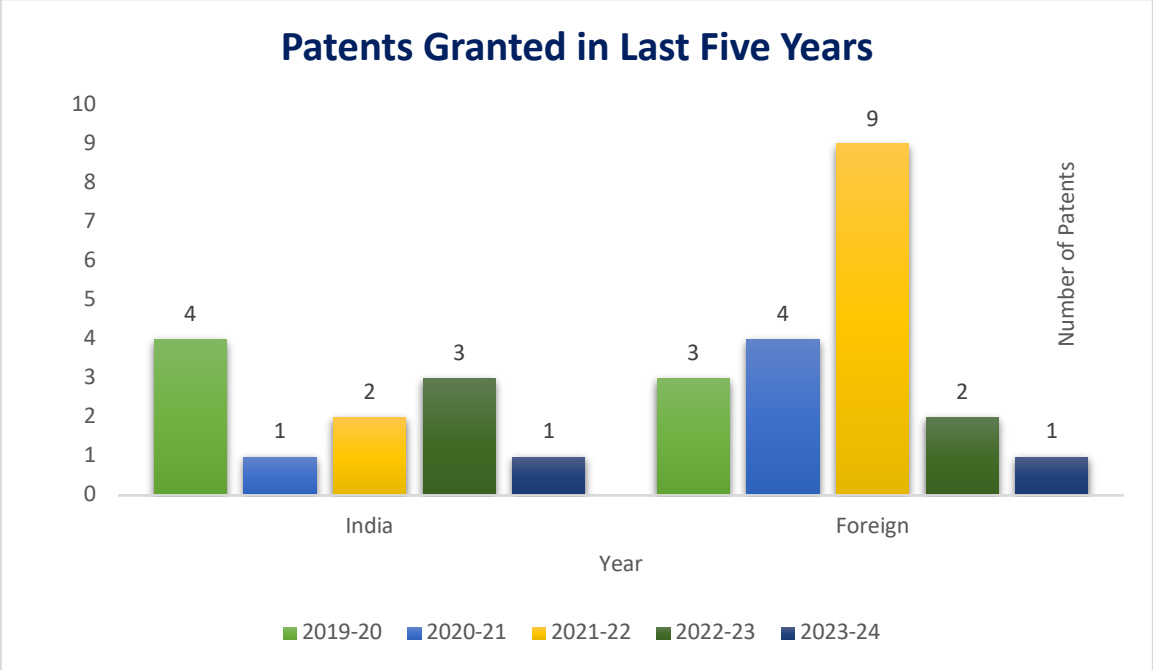
Filed in India

Sl. No.	Title	Inventors	Prov. Filing Date	Comp. Filing Date	Application No.
1	Liposomal formulation for treatment of visceral leishmaniasis	Nahid Ali, Nicky Didwania, Mohd Kamran, Abdus Sabur, Sarfaraz Ahmad Ejazi	---	20.04.2023	202311028946
2	Small molecules for adoptive t-cell therapy (act) through activation of the mtor signalling pathway, process for prepartion thereof	Arindam Talukdar, Shilpak Chatterjee, Sunny Goon, Dipika Sarkar, Puspendu Ghosh, Uddipta Ghosh Dastidar, Trisha Ghosh	---	18.05.2023	202311034981
3	Protacs for ASK1 protein degradation: preparation and use thereof	Arindam Talukdar, Himadri Sekhar Sarkar, Partha Chakrabarti, Israful Hoque, Abhishek Sen, Uddipta Ghosh Dastidar, Anindita Dey	---	18.05.2023	202311034982
4	Detection system for Alzheimer's disease using magnetic resonance image processing and machine learning techniques	Saikat Chakrabarti, Subhrangshu Das, Priyanka Panigrahi	09.06.2023	---	202311039559
5	3,3-BIINDOLE BASED FLORESCENCE DYE PROBE AND APPLICATION THEREOF	Parasuraman Jaisankar, Sreya Gupta, Velayutham Ravichandiran, Arun Bandyopadhyay, Aakriti Garg	---	09.06.2023	202311039884
6	A process for the synthesis of 2-(4-chlorophenyl)-2-hydroxy-N-(3-methoxy-4-(prop-2-yn-1-yloxy)phenethyl)acetamide, a key intermediate of Mandipropamid	Indubhusan Deb, Imtiaj Mondal, Koushik Naskar, Shantonu Roy	---	29.11.2023	202311081168
7	Purine based small molecule modulators for PPARy in ameliorating non-alcoholic fatty liver disease: Preparation and application thereof	Arindam Talukdar, Partha Chakrabarti, Sunny Goon, Dipayan Sarkar, Sujay Krishna Maity, Avinil Das Sharma, Debomita Bhattacharya, Soupayan Pal, Himadri Sekhar Sarkar	---	05.12.2023	202311083005
8	rRNA selective fluorescent bio-probe for tracking viscoelastic nature of intracellular nucleolus	Aakriti Garg, Parasuraman Jaisankar, Sreya Gupta, Velayutham Ravichandiran, Arun Bandyopadhyay	---	13.12.2023	202311085302

Sl. No.	Title	Inventors	Prov. Filing Date	Comp. Filing Date	Application No.
9	Indole based fluorescent bio-probe for the super-resolution wash-free live cell imaging of endoplasmic reticulum	Aakriti Garg, Parasuraman Jaisankar, Sreya Gupta, Velayutham Ravichandiran, Arun Bandyopadhyay	---	13.12.2023	202311085301
10	Agonism-antagonism in endosomal tlrs by modulating chemical features in 8-oxopurine: process for preparation and application thereof	Arindam Talukdar, Dipyaman Ganguly, Dipika Sarkar, Shrestha Pattanayak, Uddipta Ghosh Dastidar, Purbita Bandopadhyay, Bishnu Prasad Sinha, Shreya Roy, Jafar Sarif, Ranit D. Rozario, Trisha Ghosh, Rimica Das	07.03.2024	---	202411016656
11	Dihydrobenzo[b,e]pyrroloazepines hybrids and a process for the preparation thereof	Indubhusan Deb, Shantonu Roy, Koushik Naskar, Imtiaj Mondal	07.03.2024	---	202411016683
12	Quinoline compounds for the treatment of fatty liver disease and process for preparation thereof	Subhadeep Palit, Tanusree Das, Bhim Majhi, Partha Chakrabarti, Sanjay Dutta	---	07.03.2024	202411017222
13	Indole based small molecule antivirals against SARS-COV-2	Arindam Talukdar, Israful Hoque, Binita Patra, Nirmal Das, Krishan Gopal Thakur, Rajesh Ringe, Nittu Singh, Akshay Joshi, Ravneet Singh Chawla	---	26.03.2024	202411023758
14	Encapsulated dihydrofolate formulation for dietary supplementation as effective nutraceutical supplement and method of preparation thereof	Bijesh Puthusseri, Vikas Singh Chauhan, Ajana Pathikkal, Ulaganathan Mabalirajan, Sunita Das, Atmaja Karmakar, Divya Peethambaran	26.03.2024	---	202411023759
15	A non-invasive system and method for automatic identification of haemorrhagic stroke regions	Saikat Chakrabarti, Subhrangshu Das, Priyanka Panigrahi	---	27.03.2024	202411024504

Patents at a Glance





List of research fellow to receive their doctorate degree at CSIR-IICB

Sl. No.	Recipient's Name	University	Award Date	Supervisor's Name	Thesis title
1	Dr. Anirban Manna	University of Calcutta	14.07.2023	Dr. Santu Bandyopadyay (Retd.) & joint supervisor Dr. Snehasikta Swarnakar	Targeting the Stress Response to Reactive Oxygen/Nitrogen Species by Natural Molecules for Anti-Cancer Activity
2	Dr. Ankita Sarkar	AcSIR	06.12.2023	Dr. Partha Chakrabarti	Impact of gut microbiota derived metabolites in metaflammation
3	Dr. Anuradha Pandit	University of Calcutta	12.07.2023	Dr. Snehasikta Swarnakar	Studies on the Role of Matrix Metalloproteinase 13 (MMP 13) In the Risk and Progression of Endometriosis
4	Dr. Arkaprabha Choudhury	AcSIR	10.05.2023	Dr. Saumen Datta	Structural and biophysical characterization of proteins pertaining to pantothenate biosynthesis pathway and type three secretion system of gram-negative bacteria
5	Dr. Arup Bhowmik	Jadavpur University	15.12.2023	Dr. Indu Bhusan Deb	Development of C-C Bond Forming Reactions Through C(sp^3)-H Bond Functionalization: Approach for the Construction of Novel (Spiro) heterocycles
6	Dr. Ashish Jaiswal	AcSIR	25.07.2023	Dr. U. Mabalirajan	Elucidating the novel mediators, Rad50 and sPLA2, in lung fibrosis
7	Dr. Bidisha Das	AcSIR	05.10.2023	Dr. Krishnananda Chattopadhyaya	Role of metal ion co-factors in the aggregation of SOD1
8	Dr. Chittran Roy	Jadavpur University	08.05.2023	Dr. Saumen Datta	Insight into the structural and functional characterization of T3SS's
9	Dr. Debomita Bhattacharya	University of Calcutta	29.12.2023	Dr. Arindam Talukdar	Design, Synthesis and Evaluation of Small Molecule Inhibitors for Protein Arginine Methyltransferase
10	Dr. Deepesh Kumar Padhan	University of Calcutta	29.05.2023	Dr. Malini Sen	Elucidating the Role of Wnt Induced Secreted Protein 3 (WISP3) In Mitochondrial Function
11	Dr. Dipak Kar	University of Calcutta	30.05.2023	Dr. Arun Bandyopadhyaya	Implications of Mitochondrial Dysfunction in the Pathogenesis of Heart Disease
12	Dr. Dipayan Sarkar	AcSIR	04.03.2024	Dr. Arindam Talukdar	Design, synthesis and biological validation of small molecules as metabolic modifiers
13	Dr. Diptankar Bandyopadhyay	University of Calcutta	14.08.2023	Dr. Suvendra Nath Bhattacharyya	Role of Lipids in Controlling Abundance and Activities of Micro RNA Machineries
14	Dr. Eshani Karmakar	University of Calcutta	03.07.2023	Dr. Sib Sankar Roy	Understanding The Mechanism of Insulin Resistance and Its Downstream Complications
15	Dr. Gouranga Saha	University of Calcutta	09.11.2023	Dr. Mrinal Kanti Ghosh	The Regulation of Deubiquitinase USP7 Through Various Signaling Network and Its Role in Oncogenesis

Sl. No.	Recipient's Name	University	Award Date	Supervisor's Name	Thesis title
16	Dr. Kasarla Varalaxmi	NIPER-Kolkata	17.07.2023	Dr. Ranjan Jana	Development of Divergent Prenylation Reactions and Synthesis of Carbazole Alkaloids
17	Dr. Krishna Kumar	University of Calcutta	07.06.2023	Dr. Saikat Chakrabarti	Analysis of the Bio-Molecular Interactions and Pathways Inter-Connectivity In Cervical Cancer Using Network Biology Approaches
18	Dr. Moumita Saha	University of Calcutta	11.04.2023	Dr. Krishna Das Saha	Role of Melatonin in Obesity and Its Associated Inflammation
19	Dr. Nirmal Das	AcSIR	12.03.2024	Dr. Arindam Talukdar	Design and synthesis of potential small molecules as plausible treatment for leishmaniasis, auto-immune disease and COVID-19
20	Dr. Pallabi Bhattacharyya	Jadavpur University	30.05.2023	Dr. Subhas C. Biswas	miRNA mediated regulation of neurodeneration in parminson's disease models
21	Dr. Priyanka Boro	University of Calcutta	09.11.2023	Dr. Sharmila Chattopadhyay	Elucidation of the Relationship Between Glutathione and Plant Defense in *Arabidopsis thaliana*
22	Dr. Quoelee Biswas	University of Calcutta	29.05.2023	Dr. Rupak Kr. Bhadra	Molecular Studies on Virulence Genes and Regulators Of *Vibrio cholerae* non-O1/non-O139
23	Dr. Rajeev Kumar	Jadavpur University	16.10.2023	Dr. Saumen Datta	Structural and Functional Study of Type Three Secretion System Proteins from *Yersinia enterocolitica*
24	Dr. Raju Biswas	AcSIR	29.12.2023	Dr. Ramalingam Natarajan	Novel synthetic receptors from *N,N'*-dimethyl urea for the recognition of ions
25	Dr. Ritesh Pal	AcSIR	24.04.2023	Dr. Sanjay Dutta	Mechanistic investigation of biologically relevant quinoxaline compounds targeting DNA: Exploiting antibacterial and antiproliferative activities
26	Dr. Ruchi Supekar	AcSIR	26.06.2023	Dr. Subhajit Biswas	Molecular characterization of occult hepatitis B virus infection (OBI) in India
27	Dr. Saheli Roy	Jadavpur University	22.03.2023	Dr. Krishna Das Saha	Study on potential of Chrysin and its nano formulations in ameliorating pulmonary inflammatory disorders
28	Dr. Sandipan Ghorai	AcSIR	26.12.2023	Dr. Ramalingam Natarajan	Chiral self-sorting in metal-organic cages and helicates
29	Dr. Saswati Ghosh	Jadavpur University	04.08.2023	Dr. Biswadip Banerji	Synthesis and Morphological Elucidation of Cysteine Based Short Peptide Nanostructures and Their Efficacy Studies
30	Dr. Satadeepa Kal	University of Calcutta	26.07.2023	Dr. Mrinal Kanti Ghosh	New Insights of Chaperone Associated E3 Ubiquitin Ligase CHIP In Cancer
31	Dr. Shantanu Nandi	Jadavpur University	13.04.2023	Dr. Ranjan Jana	Development of Novel Carboxylation Reactions and Chemoselective Transformation Carboxylic Acids
32	Dr. Shiladitya Nag	University of Calcutta	03.07.2023	Dr. Uday Bandyopadhyay	Studies on Nucleic Acid Interacting Activity of ALBA Family Protein from *Plasmodium falciparum*

Sl. No.	Recipient's Name	University	Award Date	Supervisor's Name	Thesis title
33	Dr. Shrabastee Chakraborty	AcSIR	18.03.2024	Dr. Mrinal Kanti Ghosh	Insights into post-translational modifications of PTEN with respect to its nuclear import and its implications in cancer
34	Dr. Shreyasi Maity	University of Calcutta	04.10.2023	Dr. Malini Sen	Wnt Signalling Regulates *Leishmania donovani* Infection
35	Dr. Subhajit Ghosh	University of Calcutta	31.07.2023	Dr. Surajit Ghosh	Bioinspired Scaffold and Platform for Advancement of Therapeutic Potential of Microtubule Targeted Drug And Monitoring Microtubule Dynamics
36	Dr. Subhashis Debsharma	Jadavpur University	11.12.2023	Dr. Uday Bandyopadhyay	Identification and validation of Sirtuin 3 as a new common target of non-steroidal anti-inflammatory drugs (NSAIDs) to induce gastric mucosal injury and gastric adenocarcinoma cell death
37	Dr. Sujay Pal	AcSIR	05.07.2023	Dr. Debabrata Biswas	Mechanistic understanding of eukaryotic transcriptional regulation by elongation factor ELL during genetoxic stress
38	Dr. Sukanya De	Jadavpur University	16.06.2023	Dr. Chinmay Chowdhury	Synthesis of Heterocycles of Biological Interests via Metal Catalyzed Cyclizations of Acetylenic Compounds
39	Dr. Sumit Das	Jadavpur University	17.04.2023	Dr. Subrata Adak	Biochemical Characterization of the ChaC family of ϒ-glutamyl cyclotransferases from *Leishmania major*
40	Dr. Tresa Rani Sarraf	University of Calcutta	15.01.2024	Dr. Malini Sen	Role of Wnt5A Signaling in Antigen Processing and Presentation
41	Dr. Trishita Basak	University of Calcutta	02.06.2023	Dr. Rupasri Ain	Hippo Signalling pathway and the cell polarity modulator Angiomotin in placental development and trophoblast differentiation

Completed Extramural/Sponsored/Consultancy Projects (2023-2024)

Sl. No.	Name of the project	Project code	Name of PI	Total Project Cost received (Rs. In Lakhs)	Funding Agency	Start Date	Completion Date
1	Hippo Dynamics is a critical regulator of trophoblast self-renewed and differentiation	GAP-430	Dr. Rupasri Ain	14.13	ICMR, Govt. of India	21.11.2020	20.11.2023
2	Cooperative Metal-Catalysed Carboboration/Carbosilyation of Alkles/Alkenes via C-H activation	GAP-431	Dr. Indu Bhusan Deb	41.72	SERB	17.12.2020	16.12.2023
3	The steroid sensitizing role of RXR-Gamma, a nuclear receptor, in the pathogenesis of emphysema	GAP-432	Dr. U. Mabalirajan	28.29	SERB	05.02.2021	04.02.2024
4	Exploring the role of DNAse1L3in obesity – associated metaflammation and type2 diabetes	GAP-433	Dr. Dipyaman Ganguly	26.41	CEFIPRA	01.03.2021	29.02.2024
5	Adipose tissue-Beta cell axis in the pathophysiology of Non-obese Type 2 Diabetes: Role of Adipokines	GAP-434	Dr. Partha Chakrabarti	24.56	ICMR, Govt. of India	29.03.2021	28.03.2024
6	Understanding the role of translesion DNA synthesis in chemoresistance of lung adenocarcinoma	GAP-435	Dr. Amit Kumar Srivastava	20.30	ICMR, Govt. of India	16.03.2021	05.03.2024
7	SERB-POWER Fellowship	GAP-436	Dr. Upasana Ray	38.10	SERB, Govt. of India	30.03.2021	29.03.2024
8	Evaluation of cytotoxicity, pharmacokinectics, anti-cancer activity, detailed molecular mechanisms of Bhallatakadi Modaka	GAP-438	Dr. Amit Kumar Srivastava	23.92	CCRAS, Govt. of India	12.11.2021	11.11.2023

Sanctioned and Implemented Extramural/ Sponsored/Consultancy Projects (2023-2024)

Sl. No.	Name of the project	Project code	Name of PI	Total Sanctioned Project Cost (Rs. In Lakhs)	Funding Agency	Start Date	Completion Date
1	Mechanistic understanding of functional role of human TRIM28 and ELL in eukaryotic transcriptional regulation involving NELF complex	GAP-463	Dr. Debabrata Biswas	61.77	SERB, Govt. of India	18.07.2023	17.07.2026
2	Mechanistic understanding of dynamic regulations of SEC functions during genotoxic stress-dependant global transcriptional inhibiton and subsequent recovery for efficient DNA repair and cell survival	GAP-464	Dr. Debabrata Biswas	443.24	DBT Wellcome Trust	01.09.2023	31.08.2028
3	Elucidating the structural and functional role of TONSL, a novel histone chaperone and chromatin dependent DNA damage response protein in SPONASTRIME Dysplasia, a rare skeletal dysplasia in human	GAP-465	Dr. Siddhartha Roy	50.26	SERB, Govt. of India	11.09.2023	10.09.2026
4	Impact of Voltage-dependant anion-selective channel 1(VDAC1) protein mitochondrial shaping and dynamics	GAP-466	Dr. Joy Chakraborty	47.98	ICMR, Govt. of India	04.10.2023	03.10.2026
5	Developing leishmanial kinetoplastid membrane protein-11 as a possible target to block host invasion b Leishmania donovani	GAP-467	Dr. Krishnananda Chattopadhyay	79.56	ICMR, Govt of India	29.09.2023	28.09.2026
6	Structural characterization of zinc finger MYND domain containing protein with GATAD2A subunit of NuRD complex implicated in Neural Differentiation	GAP-468	Dr. Siddhartha Roy	74.33	DBT, Govt of India	21.09.2023	20.09.2026
7	Development of clinical data repository and analysis platform for disease detection and prognosis	GAP-469	Dr. Sucheta Tripathy	16.97	DBT, Govt of India	06.11.2023	05.11.2028

Sl. No.	Name of the project	Project code	Name of PI	Total Sanctioned Project Cost (Rs. In Lakhs)	Funding Agency	Start Date	Completion Date
8	Exploring the role of Plasmacytoid dendritic cells in Parkinson's Disease	GAP-470	Dr. Dipyaman Ganguly	15.00	IGNITE Life Science Foundation	28.12.2023	27.06.2024
9	Targeting FOLR1 for treating progressive inflammatory lung disorders such as COPD	GAP-471	Dr. Bijesh P	30.57	SERB, Govt. Of India	27.12.2023	26.12.2025
10	National Network Component	GAP-472	Dr. Sucheta Tripathy	169.87	DBT, Govt of India	06.11.2023	05.11.2028
11	Study of infection dynamics of Leishmania donovani in the presence of Lepsy NLV1 virus : Role of the virus	GAP-473	Dr. Subhajit Biswas	113.46	ICMR Govt of India	06.02.2024	05.02.2027
12	Development of antimicrobial peptide tagged nanoformulation for targeted combination therapy against Pseudomonas aeruginosa	GAP-474	Dr. Sujoy Kumar Das	28.13	DBT Govt of West Bengal	09.02.2024	08.02.2027
13	Mutation aggregation profiling of Amytrophic lateral sclerosis (ALS) patients in West Bengal	GAP-475	Dr. Krishnananda Chattopadhyay	65.79	DBT Govt of West Bengal	18.01.2024	17.01.2027
14	Development of chemically modified aptamers for targeting neuronal exosomes	GAP-476	Dr. Manish Debnath	27.761	SERB	19.02.2024	18.02.2026
15	Role of Mother-Neonate Dyad Interaction in Resolving Pediatric Viral Infection	GAP-477	Dr Sourish Ghosh	354.896	DBT Wellcome India Alliance	01.03.2024	28.02.2029
16	Chemo preventive effects of Opuntia elatior fruits against Chemotherapy-Induced toxicity in Ovarian Cancer Pre clinical models	GAP-478	Dr. Amit Kumar Srivastava	37.65	CCRAS	22.03.2024	21.03.2026
17	Evaluation of neuroprotective potential of Bhrami Ghrita, Panchgavya Ghrita and Ayush 56 in Epilepsy model, its functional significance and mechanism	GAP-479	Dr. Prem Prakash Tripath	42.27	CCRAS	22.03.2024	21.03.2026
18	Harnessing epigenetic dependencies for immunomodulation in acute myeloid leukemia	GAP-480	Dr. Amitava Sengupta	100.00	Lady Tata Memorial Trust	28.03.2024	27.03.2027

Ongoing In-House Projects (2023-2024)

Sl. No.	Name of the project	Project code	Name of PI	Total Sanctioned Project Cost (Rs. In Lakhs)	Start Date	Completion Date
1	CSIR Integrated Skill Initiative Program	NWP-100 (Phase II)	Dr. P. Jaisankar	343.000	16.10.2020	31.03.2025
2	PAN CSIR Cancer Research Program making Cancer care affordable empowering women's health: Focusing on breast and gynaelogical cancers of Indian Relevance	HCP-40	Dr. Sib Sankar Roy	1008.100	29.06.2021	28.06.2026
3	Discovery & Pre-clinical Development of Antivirals for COVID-19 & other Diseases.	HCP-41	Dr. Arindam Talukdar	247.000	08.11.2021	31.03.2023
4	Indian Breast Cancer Genome Atlas	HCP-43	Dr. Shilpak Chatterjee	22.750	02.11.2021	31.03.2026
5	Phenome India-CSIR Health Cohort Knowledgebase	HCP-47	Dr. Partha Chakrabarti	1044.360	31.08.2022	31.03.2027
6	CSIR JIGYASA 2 Virtual Laboratory Integration Project	HCP-101	Dr. Sarita Ghosh	12.500	27.07.2022	31.03.2026
7	Innovative processes and technologies for Crop Protection Chemicals (Agromission 2)	HCP-49	Dr. Indrajit Das	199.890	11.04.2023	31.03.2026
8	Active Pharmaceutical Ingredients for Affordable Health Care (API-AHC)	HCP-50	Dr. Indu Bhusan Deb	168.000	03.07.2023	02.07.2025
9	Deriving a pan-omics diagnostic pipeline for systems level immune health and therapeutic targeting in systemic autoimmunity	MLP-135	Dr. Dipyaman Ganguly	370.000	03.03.2021	31.03.2025
10	Leishmaniasis: Target specific approaches to affect host-pathogen interaction and disease process	MLP-136	Dr. Subrata Adak	300.000	03.03.2021	31.03.2025
11	Modern innovative solutions for Environmental/ Occupational Lung Health challenges using clinical and pre-clinical strategies	MLP-137	Dr. U. Mabalirajan	406.000	03.03.2021	31.03.2025
12	Non-alcoholic Fatty Liver Disease (NAFLD): Novel Pathogenetic mechanism and therapeutic development	MLP-138	Dr. Partha Chakrabarti	499.490	03.03.2021	31.03.2025
13	Targeting RNA driven processes: Novel Chemical Biology Apporaches to Identify New Classes of RNA Modulators	MLP-139	Dr. Suvendra N Bhattacharya/ Dr. Sanjay Dutta	410.000	03.03.2021	31.03.2025
14	CSIR Multi-centric long term T cell immune monitoring for COVID-19 (PoV-CoV)	MLP-2105	Dr. Dipyaman Ganguly	132.480	01.04.2021	31.03.2024

Publications in Peer Reviewed Journal (Jan'23 – Dec'23)

1	Sarkar, P; Banerjee, S; Chakrabarti, S; Chakrabarti, P; Bandyopadhyay, A; Mitra, AG; Saha, S; Roy, A; Sarkar, S (2023) Genome characterization, phylogenomic assessment and spatio-temporal dynamics study of highly mutated BA variants from India. *Indian Journal of Medical Microbiology*, 43, 66-72
2	Karmakar, E; Das, P; Yatham, P; Kumar, D; Mukhopadhyay, S; Roy, SS (2023) Seedpod extracts of *Wrightia tinctoria* shows significant anti-inflammatory effects *in* HepG2 and RAW-264.7cell lines. *Natural Product Research*, 37, 3158-3162
3	Choudhury, A; Saha, S; Maiti, NC; Datta, S (2023) Exploring structural features and potential lipid interactions of *Pseudomonas aeruginosa* type three secretion effector PemB by spectroscopic and calorimetric experiments. *Protein Science*, 32, e4627
4	Sarkar, P; Banerjee, S; Saha, SA; Mitra, P; Sarkar, S (2023) Genome surveillance of SARS-CoV-2 variants and their role in pathogenesis focusing on second wave of COVID-19 in India. *Scientific Reports*, 13, 4692
5	Ramalingam, B; Das, SK (2023) Biofabricated graphene-magnetite nanobioaerogel with antibiofilm property: Response surface methodology based optimization for effective removal of heavy metal ions and killing of bacterial pathogens. *Chemical Engineering Journal*, 475, 145976
6	Rudra, DS; Chatterjee, S; Pal, U; Mandal, M; Chaudhuri, SR; Bhunia, M; Maiti, NC; Besra, SE; Jaisankar, P; Swarnakar, S (2023) Newly Synthesized 3-Indolyl Furanoi d Inhibits Matrix Metalloproteinase-9 Activity and Prevents Nonsteroidal Anti-inflammatory Drug-Induced Gastric Ulceration. *Journal of Medicinal Chemistry*, 66, 8917-8928
7	Pramanik, SK; Sanphui, P; Das, AK; Banerji, B; Biswas, SC (2023) Small-Molecule Cdc25A Inhibitors Protect Neuronal Cells from Death Evoked by NGF Deprivation and 6-Hydroxydopamine. *ACS Chemical Neuroscience Journal,* 14, 1226-1237
8	Choudhary, P; Ramalingam, B; Das, SK (2023) Rational design of antimicrobial peptide conjugated graphene-silver nanoparticle loaded chitosan wound dressing. *International Journal of Biological Macromolecules*, 246, 125347
9	Pandit, E; Das, L; Das, AK; Dolui, S; Saha, S; Pal, U; Mondal, A; Chowdhury, J; Biswas, SC; Maiti, NC (2023) Single point mutations at the S129 residue of α-synuclein and their effect on structure, aggregation, and neurotoxicity. *Frontiers in Chemistry*, 11, 1145877
10	Mondal, R; Banerjee, C; Nandy, S; Roy, M; Chakraborty, J (2023) Calcineurin inhibition protects against dopamine toxicity and attenuates behavioral decline in a Parkinson's disease model. *Cell & Bioscience*, 13, 140
11	Sinha, BP; Mehta, P; Hoque, MA; Bandopadhyay, P; Nandi, A; Saha, I; Mitra, AN; Mondal, A; Bhattacharjee, B; Chamilos, G; Pandey, R; Basu, K; Ganguly, D (2023) Deficient Phagocytosis in Circulating Monocytes from Patients with COVID-19-Associated Mucormycosis. *mBio*, 14, e0059023
12	Ghosh, AR; Bandopadhyay, P; Sarkar, J; Khanna, S; Chaudhuri, T; Tantia, O; Chakrabarti, P; Ganguly, D (2023) Mitochondrial sourcing of interferogenic ligands and an autoantigen in human obesity-associated metaflammation. *Obesity*, 31, 2229-2234
13	Mondal, I; Roy, S; Naskar, K; Karmakar, S; Chowdhury, M; Deb, I (2023) [3+2] Cascade Ring-Closing/Ring-Opening Strategy: Access to *N*-Indene-Tethered Amino Alcohols. *Organic Letters*, 25, 8199-8204
14	De, S; Chowdhury, C (2023) Iron(III)-Catalyzed Carboannulations of Homopropargylic Alcohols: A One-Pot General Synthesis of 4-(2,2-Diarylvinyl)quinolines and 4-(2,2-Diarylvinyl)-2 *H*-chromenes. *Journal of Organic Chemistry*, 88, 7539-7550
15	Saha, M; Das, S; Manna, K; Das Saha, K (2023) Melatonin targets ferroptosis through bimodal alteration of redox environment and cellular pathways in NAFLD model. *Bioscience Reports*, 43, BSR20230128
16	Basak, D; Mondal, S; Srivastava, SK; Sarkar, D; Sarkar, I; Basu, S; Bhoumik, A; Chowdhury, S; Pal, DK; Chatterjee, S (2023) Intratumoral $PD1^{+}CD38^{+}$ $Tim3^{+}$ $CD8^{+}$ T Cells in Pre-BCG Tumor Tissues Are Associated with Poor Responsiveness to BCG Immunotherapy in Patients with Non-Muscle Invasive Bladder Cancer. *Cells*, 12, 1939
17	Boila, LD; Sengupta, A (2023) Unifying targeted therapy for leukemia in the era of PARP inhibition. *Experimental Hematology,* 124, 1-14
18	Das, N; Bhattacharya, D; Bandopadhyay, P; Dastidar, UG; Paul, B; Rahaman, O; Hoque, I; Patra, B; Ganguly, D; Talukdar, A (2023) Mitigating hERG Liability of Toll-Like Receptor 9 and 7 Antagonists through Structure-Based Design. *ChemMedChem*, 18, e202300069

19	Bhattacharyya, P; Biswas, A; Biswas, SC (2023) Brain-enriched miR-128: Reduced in exosomes from Parkinson's patient plasma, improves synaptic integrity, and prevents 6-OHDA mediated neuronal apoptosis. *Frontiers in Cellular Neuroscience*, 16, 1037903
20	Kamran, M; Bhattacharjee, R; Das, S; Mukherjee, S; Ali, N (2023) The paradigm of intracellular parasite survival and drug resistance in leishmanial parasite through genome plasticity and epigenetics: Perception and future perspective. *Frontiers in Cellular and Infection Microbiology*, 13, 1001973
21	Begum, F; Srivastava, AK; Tripathi, PP; Ray, U (2023) A substrate for a cell free in vitro assay system to screen drugs targeting trypsin like protease-based cleavage of SARS-CoV-2 spike glycoprotein and viral entry. *Journal of Medical Virology*, 95, e28796
22	Adhikary, S; Banerji, B (2023) Iodine Mediated One-Pot Synthesis of Polyarylated-Oxazoles from Internal Alkynes. *ChemistrySelect,* 8, e202300076
23	Ramalingam, B; Das, SK (2023) Biomimetic strategy for fabrication of bifunctional graphene oxide-biomaterial aerogel as highly porous antifouling material for oil/water separation. *Chemical Engineering Journal*, 475, 145906
24	D'Rozario, R; Raychaudhuri, D; Bandopadhyay, P; Sarif, J; Mehta, P; Liu, CSC; Sinha, BP; Roy, J; Bhaduri, R; Das, M; Bandyopadhyay, S; Paul, SR; Chatterjee, S; Pandey, R; Ray, Y; Ganguly, D (2023) Circulating Interleukin-8 Dynamics Parallels Disease Course and Is Linked to Clinical Outcomes in Severe COVID-19. *Viruses-Basel*, 15, 549
25	Chatterjee, P; Bhowmik, D; Roy, SS (2023) A systemic analysis of monocarboxylate transporters in ovarian cancer and possible therapeutic interventions. *Channels*, 17, 2273008
26	Maity, S; Sengupta, S; Sen, M (2023) Therapeutic potential of rWnt5A in curbing *Leishmania donovani* infection. *Infection and Immunity*, 91, e0026723
27	Bandopadhyay, S; Kamal, IM; Padmanaban, E; Ghosh, DD; Chakrabarti, S; Roy, SS (2023) Oncogene-mediated nuclear accumulation of lactate promotes epigenetic alterations to induce cancer cell proliferation. *Journal of Cellular Biochemistry*, 124, 495-519
28	Sarkar, A; Mitra, P; Lahiri, A; Das, T; Sarkar, J; Paul, S; Chakrabarti, P (2023) Butyrate limits inflammatory macrophage niche in NASH. *Cell Death & Disease*, 14, 332
29	Biswas, R; Ghorai, S; Paul, B; Maji, S; Natarajan, R (2023) Cleft Receptor for the Recognition and Extraction of Tetrahedral Oxyanions. *Crystal Growth & Design*, 23, 4384-4394
30	Biswas, R; Samanta, K; Ghorai, S; Maji, S; Natarajan, R (2023) Conformationally Flexible Cleft Receptor for Chloride Anion Transport. *ACS Omega*, 8, 19625-19631
31	Talukdar, D; Bandopadhyay, P; Ray, Y; Paul, SR; Sarif, J; D'Rozario, R; Lahiri, A; Das, S; Bhowmick, D; Chatterjee, S; Das, B; Ganguly, D (2023) Association of gut microbial dysbiosis with disease severity, response to therapy and disease outcomes in Indian patients with COVID-19. *Gut Pathogens*, 15, 22
32	Singh, S; Dutta, J; Ray, A; Karmakar, A; Mabalirajan, U (2023) Airway Epithelium: A Neglected but Crucial Cell Type in Asthma Pathobiology. *Diagnostics*, 13, 808
33	Kamal, IM; Chakrabarti, S (2023) MetaDOCK: A Combinatorial Molecular Docking Approach. *ACS Omega*, 8, 5850-5860
34	Das, B; Roychowdhury, S; Mohanty, P; Rizuan, A; Chakraborty, J; Mittal, J; Chattopadhyay, K (2023) A Zn-dependent structural transition of SOD1 modulates its ability to undergo phase separation. *The EMBO Journal*, 42, e111185
35	Chakravarty, R; Banerjee, PC (2023) Survival of a Novel Bacterium *Acidiphilium symbioticum* H8 under *Thermal Stress. Microbiology*, 92, 534-544
36	Bera, B; Mondal, S; Mandal, S; Saha, KD; Mondal, TK (2023) New palladium (II) and platinum (II) complexes with coumarin based O,N,N pincer: Synthesis, structure elucidation, BSA protein binding studies, and anticancer activity. *Applied Organometallic Chemistry*, 37, e7185
37	Ghosh, D; Pakhira, S; Das Ghosh, D; Roychoudhury, S; Roy, SS (2023) Ets1 facilitates EMT/invasion through Drp1-mediated mitochondrial fragmentation in ovarian cancer. *iScience*, 26, 107537
38	Sarkar, D; Chowdhury, S; Goon, S; Sen, A; Dastidar, UG; Mondal, MA; Chakrabarti, P; Talukdar, A (2023) Discovery and Development of Quinazolinones and Quinazolinediones for Ameliorating Nonalcoholic Fatty Liver Disease (NAFLD) by Modulating COP1-ATGL Axis. *Journal of Medicinal Chemistry*, 66, 16728-16761
39	Roychowdhury, S; Chattopadhyay, K (2023) A tale of (disordered) tail. *Communications Biology*, 6, 411
40	Basu, S; Nandy, A; Ghosh, A; Mall, DP; Biswas, D (2023) Degradation of CDK9 by Ubiquitin E3 Ligase STUB1 Regulates P-TEFb Level and Its Functions for Global Target Gene Expression within Mammalian Cells. *Molecular and Cellular Biology*, 43, 451-471

41	Das, A; Saha, M; Mandal, S; Das, S; Das Saha, K; Mondal, TK (2023) New palladium(ii) and platinum(ii) complexes with an ONS donor azo-thioether pincer ligand: synthesis, characterization, protein binding study and *in vitro* cytotoxicity. *New Journal of Chemistry*, 47, 4931-4943
42	Banerjee, J; Ranjan, RP; Alam, MT; Deshmukh, S; Tripathi, PP; Gandhi, S; Banerjee, S (2023) Virus-associated neuroendocrine cancers: Pathogenesis and current therapeutics. *Pathology - Research and Practice*, 248, 154720
43	Ganguly, A; Padhan, DK; Sengupta, A; Chakraborty, P; Sen, M (2023) CCN6 influences transcription and controls mitochondrial mass and muscle organization. *The FASEB Journal*, 37, e22815
44	Adhya, S; Banik, M (2023) Many OX PHOS and replication factor mRNAs target mitochondria through specific binding to the organelle surface, independent of co-translational protein import. *Journal of Genetics*, 102, 20
45	Garg, A; Goel, N; Abhinav, N; Varma, T; Achari, A; Bhattacharjee, P; Kamal, IM; Chakrabarti, S; Ravichandiran, V; Reddy, AM; Gupta, S; Jaisankar, P (2023) Virtual screening of natural products inspired in-house library to discover potential lead molecules against the SARS-CoV-2 main protease. *Journal of Biomolecular Structure & Dynamics*, 41, 2033-2045
46	Mani, S; Kaur, A; Jakhar, K; Kumari, G; Sonar, S; Kumar, A; Das, S; Kumar, S; Kumar, V; Kundu, R; Pandey, AK; Singh, UP; Majumdar, T (2023) Targeting DPP4-RBD interactions by sitagliptin and linagliptin delivers a potential host-directed therapy against pan-SARS-CoV-2 infections. *International Journal of Biological Macromolecules*, 245, 125444
47	Misra, R; Maity, A; Kundu, S; Bhunia, M; Nanda, B; Maiti, NC; Pal, U (2023) Loop Dynamics and Conformational Flexibility in Dengue Serine Protease Activity: Noninvasive Perturbation by Solvent Exchange. *Journal of Chemical Information and Modeling*, 63, 2122-2132
48	Roy, S; Karmakar, S; Mondal, I; Naskar, K; Sarkar, W; Deb, I (2023) Electrochemical C(sp^3)-C(sp^3) cross-dehydrogenative coupling: enabling access to 9-substituted fluorescent acridanes. *Chemical Communications*, 59, 9074-9077
49	Roy, S; Gupta, AK; Banerjee, M; Das, PK; Ukil, A (2023) PD-1 negatively tunes macrophage immune activation by turning off JNK and STAT1 signaling: Exploited by Leishmania for its intra-macrophage survival. *Cellular Immunology*, 391, 104758
50	Bhowmik, A; Naskar, K; Roy, S; Karmakar, S; Sarkar, W; Mondal, I; Sana, A; Deb, I (2023) A condition-tuned unorthodox approach to indole-3-carboxylic acids and anthranilic acids via carbon atom translocation. *Chemical Communications*, 59, 13899-13902
51	De, SKY; Chowdhury, C (2023) Substrate-Controlled Product Divergence in Iron(III)-Catalyzed Reactions of Propargylic Alcohols: Easy Access to Spiro-indenyl 1,4-Benzoxazines and 2-(2,2-Diarylvinyl)quinoxalines. *Chemistry - A European Journal*, 29, e202203993
52	Sen, H; Choudhury, GB; Pawar, G; Sharma, Y; Bhalerao, SE; Chaudhari, VD; Datta, S; Raychaudhuri, S (2023) Diversity in the ligand binding pocket of HapR attributes to its uniqueness towards several inhibitors with respect to other homologues-A structural and molecular perspective. *International Journal of Biological Macromolecules*, 233, 123495
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2	Sarkar, J., and Chakrabarti, P. (2023) Metabolic Syndrome: From Mechanisms to Interventions, 1st Ed, Elsevier, New York.
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4	Das, A., Ali, N. Emerging Concepts in *Leishmania* Vaccine Adjuvants in Challenges and Solutions in Visceral Leishmaniasis by A. Selvapandiyan, R. Singh, N. Puri, N. K. Ganguly, Springer Nature Singapore Pvt Ltd.ISBN 978-981-99-6999-9.
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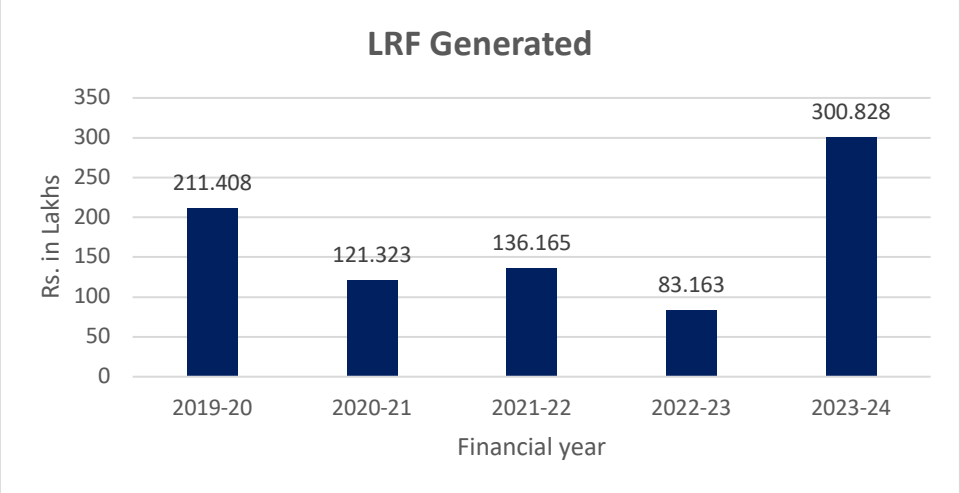
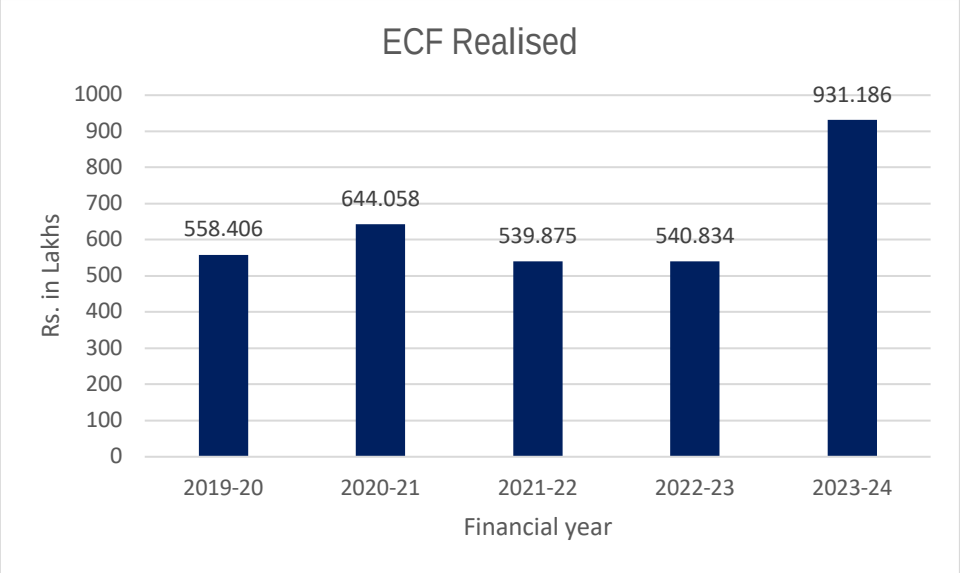
Financial data





Statement of Expenditure upto 31-03-2024

	31.03.2024 को व्यय विवरण/Expenditure Statement as on 31.03.2024										
Financial Year: 2023-24 Budget Heads (Rs. in lakh)	प्रोजेक्ट्स		%	गैर-प्रोजेक्ट्स		%	कुल		%	Lab Reserve	
	आवंटन	व्यय	व्यय	आवंटन	व्यय	व्यय	आवंटन	व्यय	व्यय		
1. National Laboratory	Projects		%	Non-Projects		%	Total		%	Projects	Non-Projects
	Allocation	Exp.	Exp.	Allocation	Exp.	Exp.	Allocation	Exp.	Exp.	Exp.	Exp.
A. Grants-in-Aid -Salaries											
1. Sal. & Sal. Linked Allow.				3238.838	3238.838	100	3238.838	3238.838	100		
2. Other Allowances											
(i) Medical Reimbursement				99.733	99.733	100	99.733	99.733	100		
(ii) Overtime Allowance/Honorarium				0.645	0.645	100	0.645	0.645	100		
(iii) Leave Travel Concession				28.462	28.462	100	28.462	28.462	100		
(iv) T.A. (India)	15.620	15.620	100	19.996	19.996	100	35.616	35.616	100		
(v) T.A. (Foreign)							0.000	0.000			
(vi) Professional Update Allowance							0.000	0.000			
Total Other Allowances (i to vi)	15.620	15.620	100	148.836	148.836	100	164.456	164.456	100	0.000	0.000
A. Total Salaries (1+2)	15.620	15.620	100	3387.674	3387.674	100	3403.294	3403.294	100	0.000	0.000
B. Grants-in-Aid -General											
3. P-04 Contingencies	22.819	22.819	100	419.978	419.978	100	442.797	442.797	100		
5. P-05 H.R.D.							0.000	0.000			
5. P-06 Lab. Maintenance				600.283	600.283	100	600.283	600.283	100		
5. P-701 Staff Qrs. Maintenance							0.000	0.000			
6. P57 Chem/Con&ORE	971.186	971.186	100	1460.500	1460.500	100	2431.686	2431.686	100		
7. P-584 Pension & Other retirement benefits				3473.934	3473.934	100	3473.934	3473.934	100		
8. P906 - Advance											
(i) Conveyance/Computer Advance							0.000	0.000			
(ii) House Building Advance							0.000	0.000			
9. Other Heads (for CSIR Hqrs only)											
10. P-801 and P-42 /ISTADE							0.000	0.000			
11. P-803 /PPD/TMBD							0.000	0.000			
12. P-805 /HRD							0.000	0.000			
13. P-60506 /RAB							0.000	0.000			
14. P-807 Publicity & Exhibition							0.000	0.000			
15. P6060 CSIR Guest House (Science Centre)							0.000	0.000			
16. P6060 Celebrations							0.000	0.000			
17. P-16 IPTM							0.000	0.000			
18. P-61 NMITLI (Recurring)											
B. Total GIA-General (3 to 18)	994.005	994.005	100	5954.695	5954.695	100	6948.700	6948.700	100	0.000	0.000
C. Grants for Creation of Capital Assets											
1. P-50 Land Cost											
2. P-50 Works & Services/Electrical Installations (Lumpsum)				240.422	240.422	100	240.422	240.422	100		6.325
3. P-50 Works & Services/Electrical Installations (other)				102.173	102.173	100	102.173	102.173	100		
4. P-50 App. & Eqp./Computer Eqp.	287.323	287.323	100	546.671	546.671	100	833.994	833.994	100		
5. P-50 Workshop Machinery							0.000	0.000			
6. P-50 Office Equipments							0.000	0.000			
7. P-50 Furniture & Fittings							0.000	0.000			0.221
8. P-50 Library							0.000	0.000			
i) Books							0.000	0.000			
ii) Journals							0.000	0.000			
iii) e-Journal							0.000	0.000			
9. P-50 Model & Exhibits							0.000	0.000			
10. P-50 Vehicles							0.000	0.000			
11. P-50 Tools & Plants							0.000	0.000			
12. P-50 Software development/procurement/LAN/WAN							0.000	0.000			
13. P-26 (ACT)							0.000	0.000			
14. P-702 Staff Qrs. (Const./Lumpsum)				14.423	14.423	100	14.423	14.423	100		
15. P-702 Staff Qrs. (Construction) (Other)							0.000	0.000			
16. P-61 NMITLI (Capital)											
C. Total Capital (1 to 16)	287.323	287.323	100	903.689	903.689	100	1191.012	1191.012	100	0.000	6.546
Total National Labs (A+B+C)	1296.948	1296.948	100	10246.058	10246.058	100	11543.006	11543.006	100	0.000	6.546

Section Officer Finance & Accounts
CSIR-INDIAN INSTITUTE OF CHEMICAL BIOLOGY
Kolkata - 700 032

वित्त एवं लेखा नियंत्रक/Controller of Finance & Accounts
CSIR-INDIAN INSTITUTE OF CHEMICAL BIOLOGY
कोलकाता/Kolkata - 700 032

(₹ in lakhs)

Statement of Expenditure for Non-CSIR funding agencies & LRF				
Year	ECF		LRF	
	Realised	Expenditure	Generated	Utilised
2023-24	931.186	753.610	300.828	6.546

वित्त एवं लेखा नियंत्रक/Controller of Finance & Accounts
सी.एस.आई.आर-भारतीय रासायनिक जीवविज्ञान संस्थान
CSIR-INDIAN INSTITUTE OF CHEMICAL BIOLOGY
कोलकाता/Kolkata - 700 032

Human Resource

Human Resource as on March 31, 2024 / 31 मार्च, 2023 को मानव संसाधन

Prof. Vibha Tandon / प्रो. विभा टंडन Director, CSIR-IICB / निदेशक, सीएसआईआर-आईआईसीबी	
Scientific & Technical Staff / **वैज्ञानिक एवं तकनीकी कर्मचारी**	
Dr. P. Jaisankar / डॉ. पी. जयशंकर	Chief Scientist / मुख्य वैज्ञानिक
Dr. Aditya Konar / डॉ. आदित्य कोणार	Chief Scientist / मुख्य वैज्ञानिक
Dr. K.N. Chattopadhyay / डॉ. के.एन. चट्टोपाध्याय	Chief Scientist / मुख्य वैज्ञानिक
Dr. Mrinal Kanti Ghosh / डॉ. मृणाल कांति घोष	Chief Scientist / मुख्य वैज्ञानिक
Dr. Sib Sankar Roy / डॉ. सिब शंकर रॉय	Chief Scientist / मुख्य वैज्ञानिक
Dr. S. N. Bhattacharya / डॉ. एस.एन. भट्टाचार्य	Chief Scientist / मुख्य वैज्ञानिक
Dr. Saumen Datta / डॉ. सौमेन दत्त	Chief Scientist / मुख्य वैज्ञानिक
Dr. Chinmay Chowdhury / डॉ. चिन्मय चौधरी	Chief Scientist / मुख्य वैज्ञानिक
Dr. Subrata Adak / डॉ. सुब्रत आदक	Chief Scientist / मुख्य वैज्ञानिक
Dr. Rupasri Ain / डॉ. रुपाश्री ऐन	Chief Scientist / मुख्य वैज्ञानिक
Dr. Subhas Ch. Biswas / डॉ. सुभाष चंद्र विश्वास	Chief Scientist / मुख्य वैज्ञानिक
Dr. Biswadip Banerji / डॉ. बिस्वदीप बनर्जी	Chief Scientist / मुख्य वैज्ञानिक
Dr. Jayati Sengupta / डॉ. जयति सेनगुप्ता	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Sucheta Tripathy / डॉ. सुचेता त्रिपाठी	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Saikat Chakrabarti / डॉ. सैकत चक्रवर्ती	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Debabrata Biswas / डॉ. देबब्रत विश्वास	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
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Dr. Nakul Ch. Maiti / डॉ. नकुल च. मैती	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Ranjan Jana / डॉ. रंजन जाना	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Arindam Talukdar / डॉ. अरिन्दम तालुकदार	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Sanjoy Dutta / डॉ. संजय दत्त	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Siddhartha Roy / डॉ. सिद्धार्थ रॉय	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Ramalingam Natarajan / डॉ. रामलिंगम नटराजन	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Sarita Ghosh / डॉ. सरिता घोष	Senior Principal Scientist / वरिष्ठ प्रधान वैज्ञानिक
Dr. Umesh Prasad Singh / डॉ. उमेश प्रसाद सिंह	Principal Scientist / प्रधान वैज्ञानिक
Dr. Indu Bhusan Deb / डॉ. इंदु भूषण देब	Principal Scientist / प्रधान वैज्ञानिक
Dr. Dipyaman Ganguly / डॉ. दीपयामन गांगुली	Principal Scientist / प्रधान वैज्ञानिक
Dr. Amitava Sengupta / डॉ. अमिताव सेनगुप्ता	Principal Scientist / प्रधान वैज्ञानिक
Dr. Subhajit Biswas / डॉ. सुभजीत विश्वास	Principal Scientist / प्रधान वैज्ञानिक
Dr. Sujoy Kr. Das / डॉ. सुजॉय कुमार दास	Principal Scientist / प्रधान वैज्ञानिक
Dr. Indrajit Das / डॉ. इंद्रजीत दास	Principal Scientist / प्रधान वैज्ञानिक
Dr. Susanta Kar / डॉ. सुशांत कर	Principal Scientist / प्रधान वैज्ञानिक
Dr. U. Mabalirajan / डॉ. यू. मबलीराजन	Principal Scientist / प्रधान वैज्ञानिक
Dr. Upasana Ray / डॉ. उपासना रे	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. Shilpak Chatterjee / डॉ. शिल्पक चटर्जी	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. G. Senthil Kumar / डॉ. जी सेंथिल कुमार	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. Sourish Ghosh / डॉ. सौरीश घोष	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. Dhabaleswar Patra / डॉ. धबलेश्वर पात्रा	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. Prem Prakash Tripathi / डॉ. प्रेम प्रकाश त्रिपाठी	Senior Scientist / वरिष्ठ वैज्ञानिक

Dr. Siddik Sarkar / डॉ. सिद्दीक सरकार	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. Saikat Majumder/ डॉ. सैकत मजूमदार	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. Ashim Paul/ डॉ. असीम पॉल	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. Tanaya Bose/ डॉ. तनया बोस	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. Vijay Suresh Akhade/ डॉ. विजय सुरेश अखाड़े	Senior Scientist / वरिष्ठ वैज्ञानिक
Dr. Saraswati Garai / डॉ. सरस्वती गराई	Scientist / वैज्ञानिक
Dr. Amit Kr. Srivastava / डॉ. अमित कुमार श्रीवास्तव	Scientist / वैज्ञानिक
Dr. Deepak Kumar / डॉ. दीपक कुमार	Scientist / वैज्ञानिक
Dr. Joy Chakraborty / डॉ. जॉय चक्रवर्ती	Scientist / वैज्ञानिक
Mr. Sandeep Aggarwal / श्री संदीप अग्रवाल	Scientist / वैज्ञानिक
Dr. Smrutisanjita Behera / डॉ. स्मृतिसंजिता बेहरा	Scientist / वैज्ञानिक
Dr. Md. Jahangir Alam / डॉ. एमडी जहांगीर आलम	Scientist / वैज्ञानिक
Dr. Manish Debnath / डॉ. मनीष देबनाथ	Scientist / वैज्ञानिक
Dr. Bijesh P. / डॉ. बिजेश पी.	Scientist / वैज्ञानिक
Dr. Rashmi Gaur / डॉ. रश्मि गौर	Scientist / वैज्ञानिक
Dr. Debasis Nayak / डॉ. देबासीस नायक	Scientist / वैज्ञानिक
Dr. Ratanti Sarkhel/ डॉ. रतनति सरखेल	Scientist / वैज्ञानिक
Dr. Bhatiya Shirishkumar Ishwarbhai/ डॉ. भाटिया शिरीषकुमार ईश्वरभाई	Scientist / वैज्ञानिक
Mr. Sandip Saha / श्री संदीप साहा	Senior Superintending Engineer (Civil) / वरिष्ठ अधीक्षण अभियंता (सिविल)
Mr. Binayak Pal / श्री बिनायक पाल	Principal Technical Officer / प्रधान तकनीकी अधिकारी
Dr. Aparna Laskar / डॉ. अपर्णा लश्कर	Principal Technical Officer / प्रधान तकनीकी अधिकारी
Dr. Ardhendu Kr. Mandal / डॉ. अर्धेन्दु कुमार मंडल	Principal Technical Officer / प्रधान तकनीकी अधिकारी
Mr. P. Gangopadhyay / श्री पी. गंगोपाध्याय	Senior Superintending Engineer (Air Cond.) / वरिष्ठ अधीक्षण अभियंता (एआईआर कंड.)
Dr. E. Padmanaban / डॉ. ई. पद्मनाबन	Principal Technical Officer / प्रधान तकनीकी अधिकारी
Mr. Susanta Ray / श्री सुसांता रे	Senior Superintending Engineer (Civil) / वरिष्ठ अधीक्षण अभियंता (सिविल)
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