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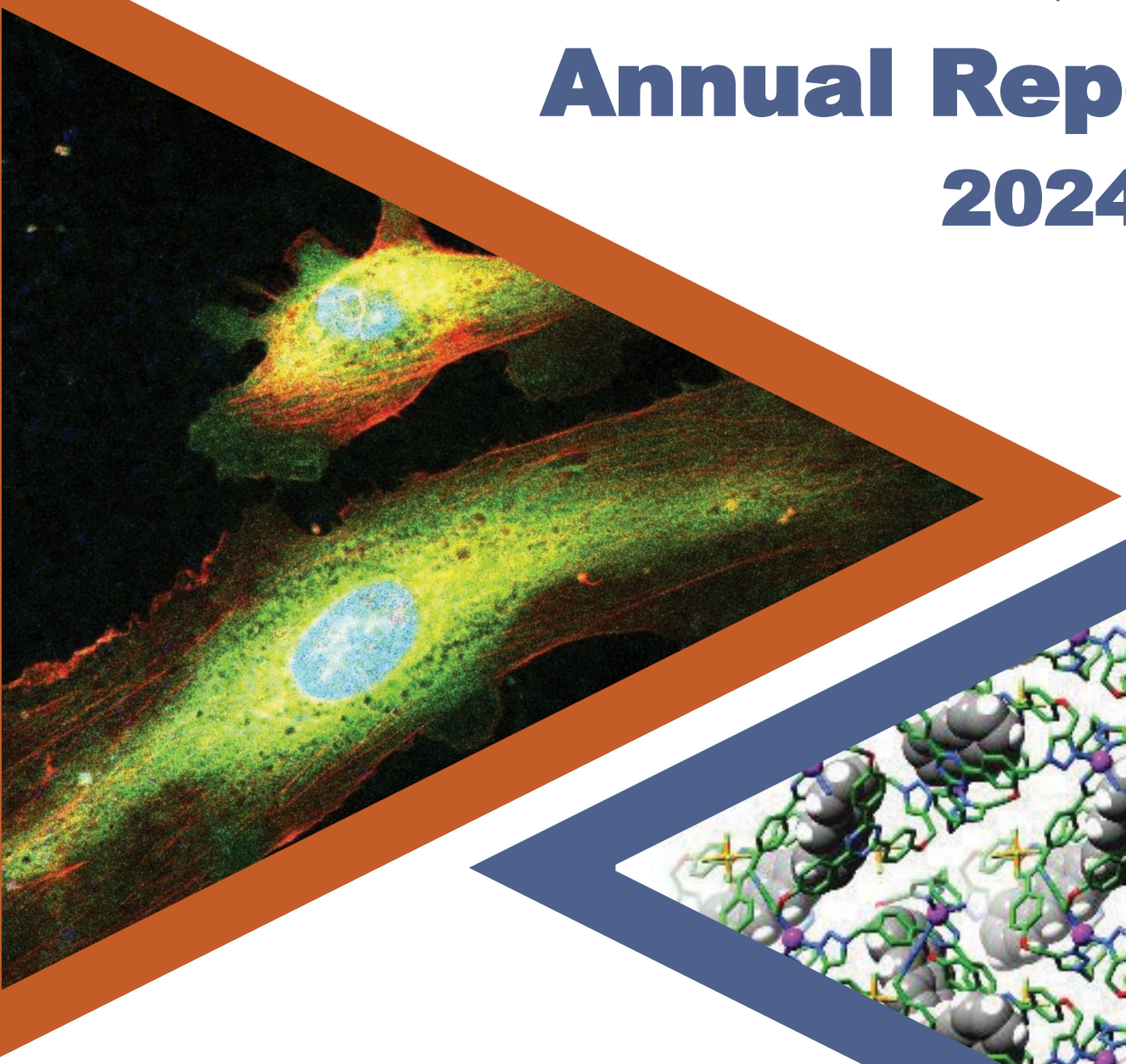
Annual Report
2024-25



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

CSIR-Indian Institute of Chemical Biology, Kolkata

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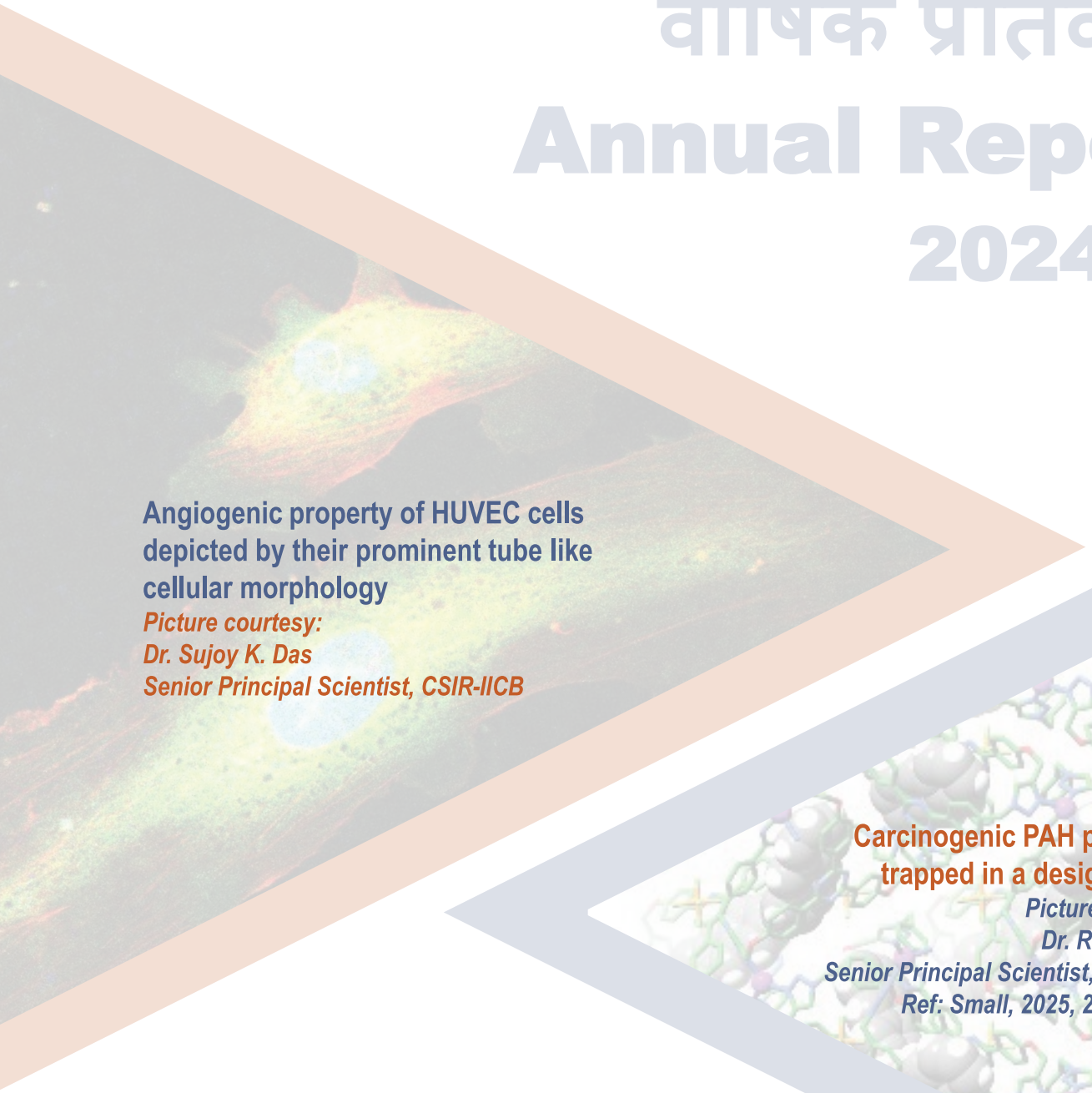

Angiogenic property of HUVEC cells depicted by their prominent tube like cellular morphology

Picture courtesy:
Dr. Sujoy K. Das
Senior Principal Scientist, CSIR-IICB

Carcinogenic PAH pollutants trapped in a designer MOF

Picture courtesy:
Dr. R. Natarajan
Senior Principal Scientist, CSIR-IICB
Ref: Small, 2025, 21, 2408482

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वार्षिक प्रतिवेदन

Annual Report

2024-25

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.

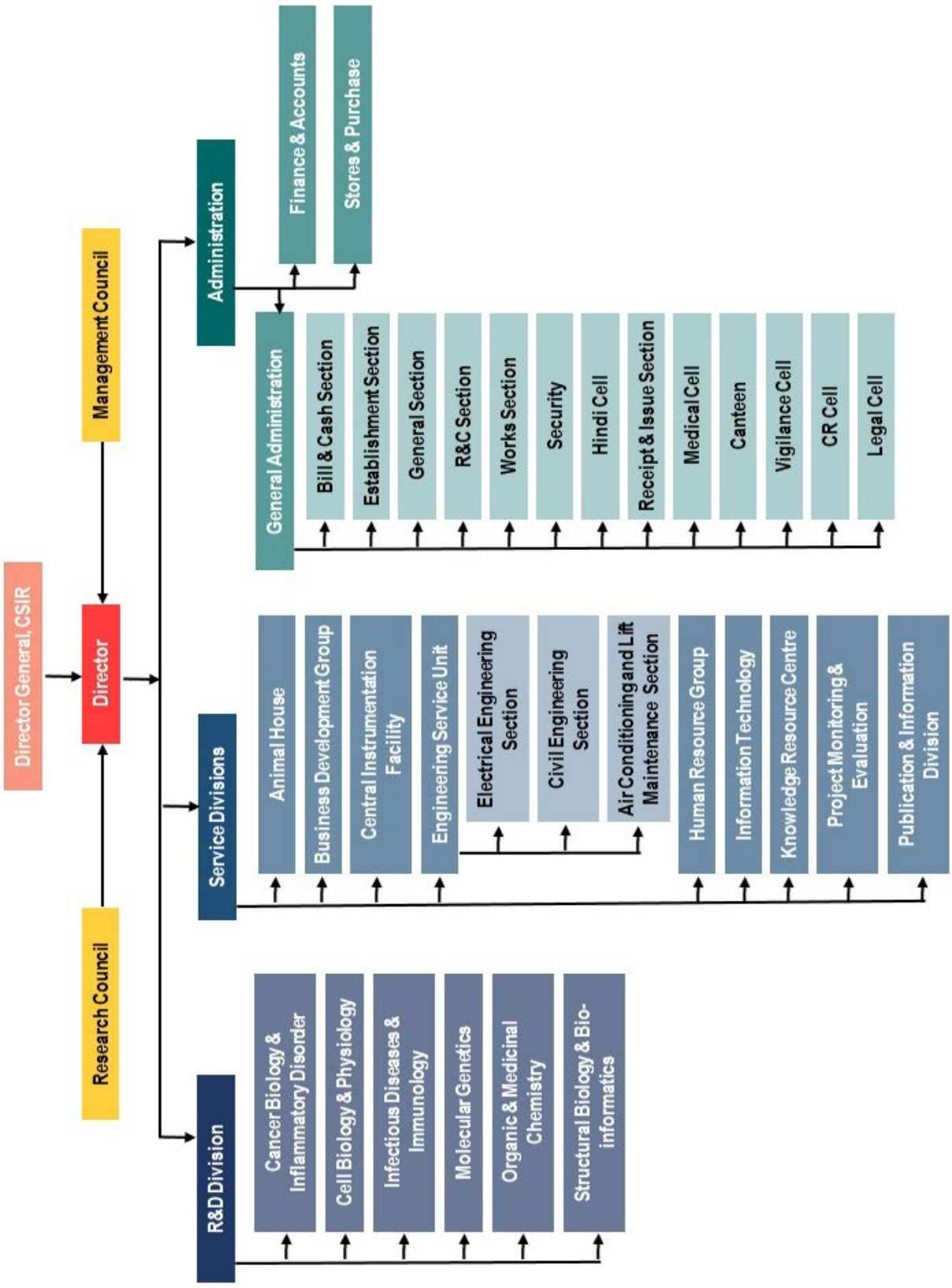
Mandate

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 CSIR-IICB Annual Report for the financial year 2024-25. The CSIR-Indian Institute of Chemical Biology (CSIR-IICB), located in Kolkata, stands as a witness to India's enduring commitment to biomedical research and chemical biology. Established in 1935 as the Indian Institute of Medical Research and later integrated into the Council of Scientific and Industrial Research (CSIR) in 1956, CSIR-IICB has been making sustained contributions to national and global health priorities. This Annual report summarizes in all aspects, the achievements and progress of the Institute during the past financial year.

CSIR-IICB operates through six synergistic research divisions: Cancer Biology & Inflammatory Disorders, Cell Biology & Physiology, Infectious Diseases & Immunology, Molecular Genetics, Organic & Medicinal Chemistry and Structural Biology & Bioinformatics. These divisions bring together expertise in molecular biology, synthetic and natural product chemistry, structural biology and pharmacology to address some of the most pressing biomedical challenges. In the past year, CSIR-IICB scientists have been recognized for their groundbreaking work. Our scientists are actively working on CAR-T cell therapy, antimicrobial resistance, which poses a major global health threat. We are also working on phytopharmaceuticals, deep ocean mission, Alzheimer's Disease (AD) detection system using brain MRI processing and Deep Learning algorithms, advanced drug designing. We are also strengthening our collaborations with hospitals, industries for translational research to bridge the gap between laboratory discoveries and clinical applications.

Our research runs smoothly and efficiently because of our strong support divisions and facilities at CSIR-IICB. The institute hosts state-of-the-art infrastructure, including a 600 MHz NMR spectrometer, confocal and super resolution microscopes, LC-MS/MS platforms, X-ray crystallography facilities and modern animal testing units. A state-of-the-art GLP-compliant translational research campus was set up in Salt Lake (TRUE) to accelerate technology transfer.

We are proud to report our major achievements of the institute as a team. Our success is measured by the tangible results that are reflected in our 159 publications in peer reviewed journal including Journal of the American Chemical Society, Nature Communications, Small, Journal of Biomedical Science, Materials Horizons, PNAS. 1 patent granted in India and 1 in Kenya. 8 new Indian Patent applications filed, and 38 new applications filed in foreign countries (12 Patent families).

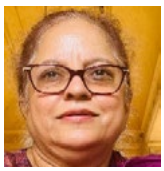
CSIR-IICB is running Skill Development Programme under CSIR Integrated Skill Initiative as well as CSIR Jigyasa 2.0. Both the programmes offer training to undergraduate student, graduate students and school students regularly. In the last one year, around 1,455 school students participated in various activities under the CSIR Jigyasa programme and nearly 288 students were trained through skill development initiatives, equipping them with job-oriented knowledge and practical skills that can enhance their future career opportunities.

I would like to appreciate the efforts of our scientists, staffs, students and stakeholders for their dedication to achieve our goals. I also take this opportunity to convey my heartfelt thanks to the DG, CSIR and our Mentor for their invaluable guidance. My sincere gratitude is also extended to the members of the Research Council and Management Council for their unwavering support.

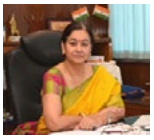
As we look ahead, CSIR-IICB envisions becoming a global leader in chemical biology, personalized healthcare and sustainable innovation.

Vibha Tandon
Director, CSIR-IICB, Kolkata

सीएसआईआर-आईआईसीबी अनुसंधान परिषद / CSIR-IICB Research Council

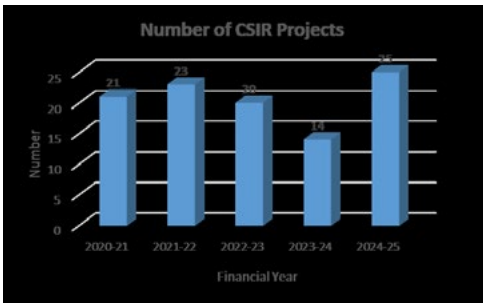
	**डॉ. तापस कुंडू / Dr. Tapas Kundu** पूर्व निदेशक, सीएसआईआर-सीडीआरआई; प्रोफेसर, जेएनसीएएसआर, जक्कुर, बेंगलुरु / Former Director, CSIR-CDRI; Professor, JNCASR, Jakkur, Bengaluru	अध्यक्ष / Chairman
	**डॉ. टी. राजमन्नार / Dr. T. Rajamannar** कार्यकारी उपाध्यक्ष और एमडी के सलाहकार, प्रमुख, उच्च प्रभाव नवाचार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

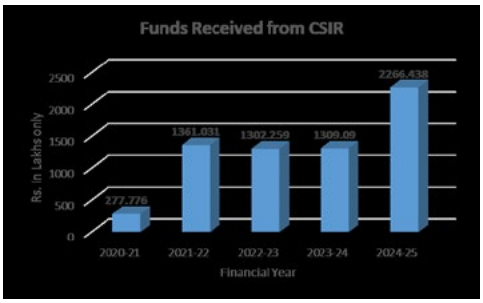
सीएसआईआर-आईआईसीबी प्रबंधन परिषद / CSIR-IICB Management Council

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

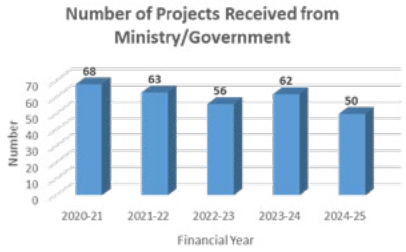
सीएसआईआर-आईआईसीबी पर एक नजर / CSIR-IICB at a Glance

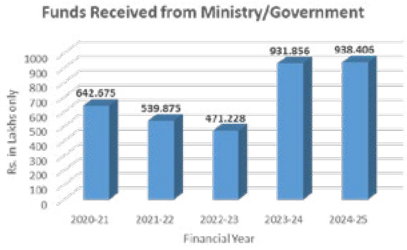
CSIR Funded Projects at CSIR-IICB

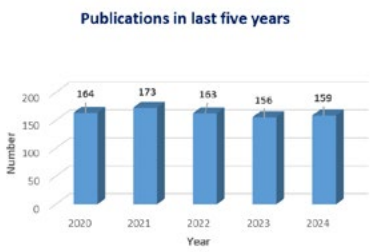


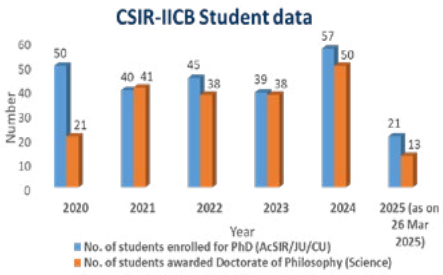


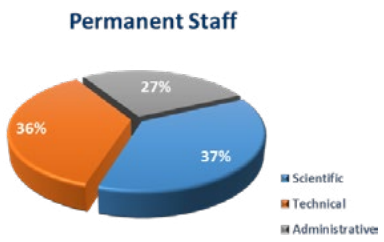
Externally Funded Projects at CSIR-IICB

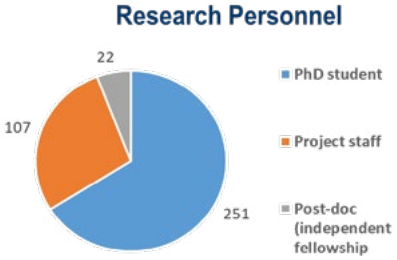


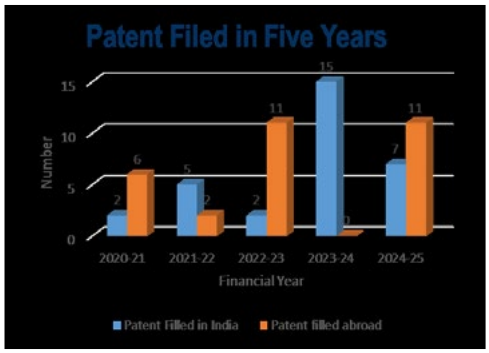


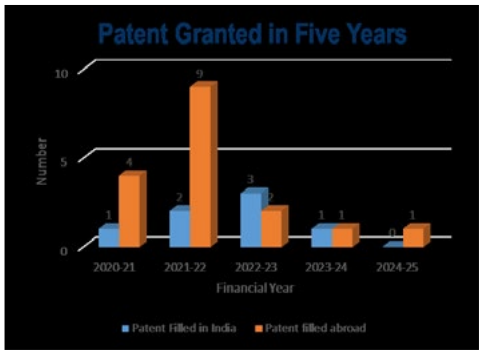












RESEARCH & DEVELOPMENT @CSIR-IICB

CANCER BIOLOGY & INFLAMMATORY DISORDER DIVISION

The Cancer Biology & Inflammatory Disorder Division is investigating basic and translational aspects of cancer research, which includes mechanistic understanding of translesion DNA synthesis in promoting chemoresistance in ovarian cancer; epigenetic regulation of inflammatory signaling and immunomodulation in acute myeloid leukemia; interrogating cell death mechanisms in pancreatic cancer pathogenesis; harnessing nanotheraputics for targeting glioblastoma; metabolic reprogramming of T lymphocyte subsets within tumor microenvironment and developing next generation engineered T cells for cancer immunotherapy. Briefly, Dr. Srivastava has recently identified that the EXO1/Polη/Polι is targeted by miR-3163, resulting in the inhibition of cell growth and induction of apoptosis in NSCLC cancer stem-like cells (Bose, Br J Pharmacol 2025). Ongoing research from Dr. Sengupta's laboratory informs critical immunomodulatory function of KDM6 family of histone lysine demethylases, through epigenetic reprogramming in acute myeloid leukemia (Bandyopadhyay, manuscript). Dr. Nayak's lab is studying the role of concentrative nucleoside transporter 3 (CNT3) in epithelial-mesenchymal transition in pancreatic cancer. They have identified that interferon-inducer Tilorone hydrochloride can reprogram tumor-immune microenvironment. Dr. Ghosh's lab has revealed p68 mediated gene regulation in colon cancer and its implication in temozolomide chemoresistance (Shaw, BBA Gene Regul Mech 2023). In addition, in the tumor microenvironment, Tregs adapt to nutrient stress via CD38-mediated NAD^+ depletion, shifting metabolism away from the TCA cycle. In this regard, Dr. Chatterjee's group has illustrated that targeting CD38 selectively destabilizes intratumoral Tregs, enhancing anti-tumor immunity by disrupting their metabolic fitness (Sarkar, Sci Adv 2025). Finally, Dr. Sarkar's lab is developing chimeric antigen receptor-T/NK cells targeting neo-antigens or cancer surface, which can induce cancer cell killing independent of MHC expression in solid tumor models (Sarkar, J Ovarian Res 2024).

Dr. Amit Kumar Srivastava and his group members

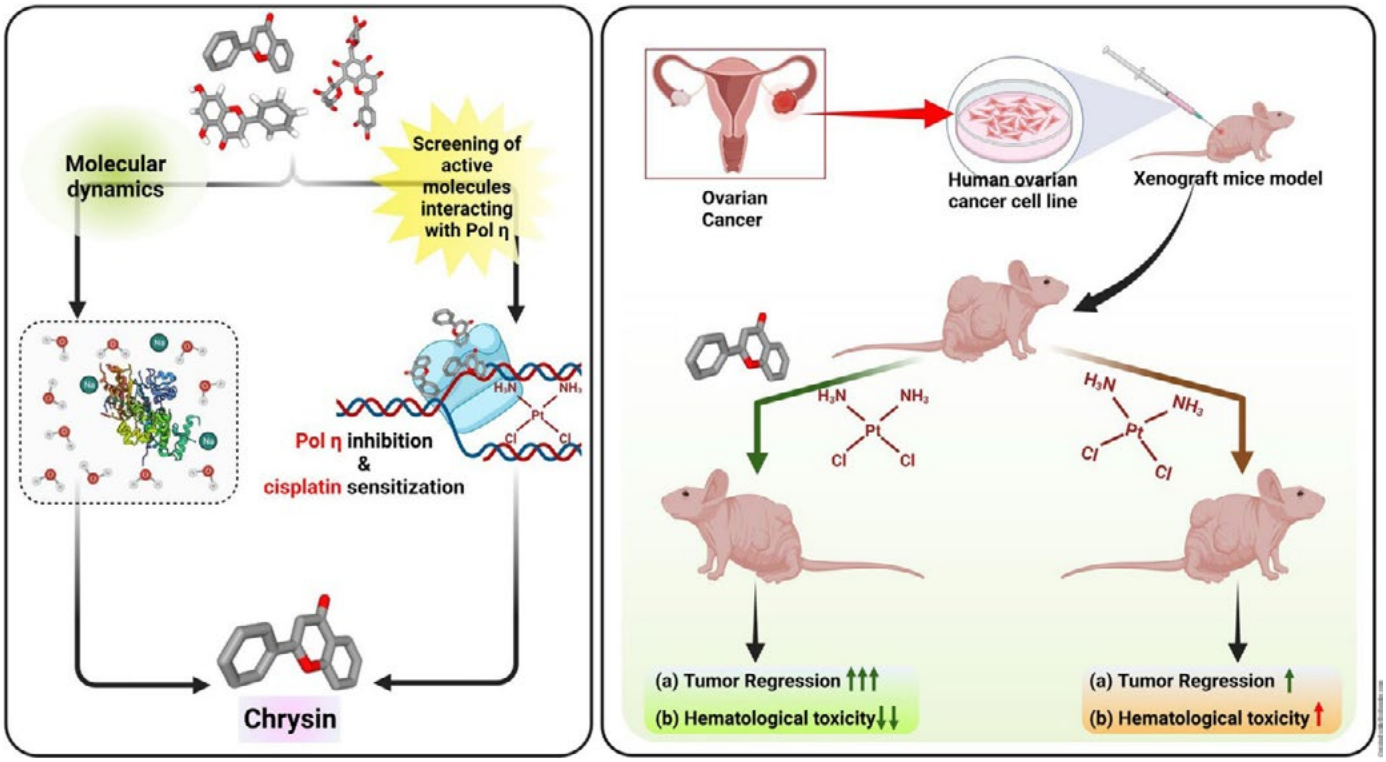
Understanding and targeting chemoresistance mechanisms in cancer

Research Activities

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

Development of chemoresistance and tumor relapse are 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 lesionsites. 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 (Figure 2).

The EXO1/Polη/Polι axis as a promising target for miR-3163-mediated attenuation of cancer stem-like cells in non-small cell lung carcinoma

Cancer stem-like cells (CSLCs) drive tumour progression and chemoresistance. The concerted efforts of EXO1 and TLS polymerases safeguard DNA integrity against chemotherapeutic drugs. In absence of potential drug targets, non-small cell lung carcinoma (NSCLC) patients have few therapeutic options. In current scenario, microRNAs offer a potential avenue for eradicating CSLCs. EXO1 downregulation in NSCLC CSLCs induces DNA lesions, triggering apoptosis and enhances cisplatin sensitivity. It collaborates

with Polη and Polι in DNA repair, contributing to cisplatin resistance in CSLCs. Absence of Polη and Polι impairs repair and reduces cisplatin-induced mutagenesis. Co-downregulation of Polη and Polι in xenografts reduces tumour proliferation significantly. MiR-3163 overexpression sensitises CSLCs to cisplatin via targeting EXO1/Polη/Polι axis, as shown in mechanistic studies. This study unveils a novel regulatory pathway involving EXO1/Polη/Polι axis and miR-3163, providing insights into CSLCs regulation in NSCLC. EXO1/Polη/Polι axis targeted by miR-3163, resulting in the inhibition of cell growth and induction of apoptosis in NSCLC CSLCs.

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. Moreover, as a part of mission mode project, we are developing TAG72 based CART cell therapy for the treatment of ovarian cancer.

Extramural / CSIR Funding

1. Evaluation of anti-cancerous potential: in silico phrenological analysis and molecular mechanism of Kanchanar guggulu in ovarian cancer µTumor spheroids, and in in vivo models. Funding Agency: CCRAS, Ministry of Ayush, India, 2 years, 2023, 44.64 lakhs (Principal Investigator). GAP-457
2. Anti-cancer potential and molecular mechanism of Rasa Sindhoor on ovarian cancer cells. Funding Agency: CCRAS, Ministry of Ayush, India, 2 years, 2023 40.64 lakhs (Principal Investigator). GAP-455
3. Chemopreventive Effects of Opuntia elatior Fruits Against Chemotherapy-Induced Toxicity in Ovarian Cancer Pre-Clinical Models. Funding Agency: CCRAS, Ministry of Ayush, India, 2 years, 2024, 37.65 lakhs (Principal Investigator). GAP-478
4. Utilizing the Principles of Coordination Chemistry to Develop Combination Prodrugs and Nanotherapeutics with a Synthetic Lethality-Like Concept. Funding agency: Science and Engineering Research Board-Department of Science and Technology, 3 years, 2023, 8.37 lakhs (Principal Investigator). GAP-462.
5. Towards discovery and development of novel drugs and pharmaceuticals. Deep Ocean Mission, Ministry of Erath Sciences, 2 years, 01/03/2025 to 28/02/2027 Budget: 9.76 Crore (Co-Nodal). GAP-490
6. Evaluation of Neuroprotective Potential of Brahmi Ghrita and Ayush 56 in epilepsy model, its functional significance and mechanism. Funding Agency: CCRAS, Ministry of Ayush, India, 2 years, 2024, 40 lakhs (Co-Principal Investigator). GAP-479
7. Development of Genetically Engineered “off the Shelf” Inducible CAR-T Cells for the Cancer Therapeutics. Funding agency: Department of Biotechnology, 3 years, 2022, 2.99 crore (Co-Principal Investigator). GAP-448
8. Advancing Cellular Therapies for Cancers and Inflammatory Disorders: A Comprehensive Indian Initiative (ACT-CID). Funding agency: CSIR, 3 years, 2025-2028, (Co- Principal Investigator).
9. Pan-CSIR Cancer Research Program “Making Cancer Care Affordable” Empowering Women’s Health: Focusing on Breast and Gynaecological Cancers of Indian Relevance. Funding agency: CSIR, 5 years, 2021) (Co-Principal Investigator). HCP-40.

Publications

1. Bose S, Saha P, Alam MT, Chatterjee B, Sarkar M, Dixit A, Kumar D, Tripathi P, Srivastava AK*. Inhibition of DNA polymerase eta mediated translesion DNA synthesis with small molecule sensitizes ovarian cancer stem-like cells to chemotherapy. British Journal of Pharmacology, 2025, (*Corresponding author): DOI: 10.1111/bph.70037. IF-6.8
2. Shukla D, Mandal T, Mishra S, Charan M, Dixit AK, Ganju R, Srivastava AK*. MicroRNA-379-5p Attenuates Cancer Stem Cells and Reduces Cisplatin Resistance in Ovarian Cancer by Regulating RAD18/POLH axis. Cell Death & Disease, 2025, 16(1):140. DOI: 10.1038/s41419-025-07430-5. (*Corresponding author). IF-9.2
3. Mandal T, Shukla D, Alam M, Senthil Kumar G, Srivastava AK*. The EXO1/POLH/POLI axis, a potential target for miR-3163 mediated attenuation of Cancer stem like-cell in non-small cell lung carcinoma. British Journal of Cancer, 2024, 131(10):1668-1682. (*Corresponding author): DOI: 10.1038/s41416-024- 02840-2. IF-6.4
4. Shakir M, Ansari MS, Divya, Faizan MI, Chauhan V, Singh A, Iqbal Azmi RA, Sharma S, Pracha M, Insha Mohi uddin, Bashir U, Shahin SN, Chaudhuri R, Albogami S, Ganguly R, Sagar S, Singh VP, Kharya G, Srivastava AK, Mabalirajan U, Ahmad T. Bioengineering the metabolic network of CAR T-cells with GLP-1 and Urolithin A increases persistence and long-term anti-tumor activity. Cell Reports Medicine, 2025, 6(3):102021. DOI: 10.1016/j.xcrm.2025.102021. IF-11.7

5. Chatterjee B, Bose S, Singh R, Dixit AK, Puia L, Srivastava AK*. MiRNA-3163 limits ovarian cancer stem-like cells via targeting SOX-2 transcription factor. Non- coding RNA Research, 2024, 9(4):1308-1314. doi: 10.1016/j.ncrna.2024.06.012. (*Corresponding author). IF-5.9
6. Begum Y, Pandit A, Shukla S, Gupta R, Mahapatra PD, Srivastava AK, Swarnakar S. Suppression of endometriosis by miRNA-34a via inhibition of matrix metalloproteinase-2: An alternative pathway to impede invasion. Non-coding RNA Research, 2025, 12:92-101. doi: 10.1016/j.ncrna.2025.02.001. IF-5.9
7. Das S, Mallik MH, Chattopadyay P, Mallick S, Karmakar D, Ghora S, Begum F, Chatterjee B, Srivastava AK, Dluya Thagriki, and Ray U. Dengue virus NS1 leads to Downregulation of HNF4 alpha in liver cells resulting in a decrease in coagulation factors I, V, X and XIII, contributing to coagulopathy. Journal of Virology, 2024, 98(12):e0141824, doi: 10.1128/jvi.01418-24. Epub 2024 Nov 8. IF-4
8. Gope TK, Pal D, Srivastava AK, Chatterjee B, Bose S, Ain R. ARID3A inhibits colorectal cancer cell stemness and drug-resistance by targeting a multitude of stemness-associated genes. Life Sciences, 2025, (Accepted Article). IF-5.2
9. Shukla D, Mandal T, Srivastava AK*. Neil1 Deficiency Facilitates Chemoresistance through Upregulation of RAD18 Expression in Ovarian Cancer Stem Cells. Biochemical and Biophysical Research Communications, 2024, (in press). doi: https://doi.org/10.1016/j.bbrc.2024.149907 (*Corresponding author). IF-2.5

Patents

Composition for treating ovarian cancer and a preparation method thereof. Kumar D, Srivastava AK, Roy SS, Sarma SS, Bose S. Year: 2024. Application no. 202411045945 (Indian Patent)

Conferences Attended

Chaired a session at 2nd Annual Conference of Society for Pediatric Cellular Therapy and Transplant held at New Delhi, from 01/03/2025 to 02/03/2025.

Member of Society

Member, AACR since 2016

Dr. Amit Kumar Srivastava, Senior Scientist

Group Members: Dr. Mrinmoy Sarkar, DBT-RA; Devendra Shukla, CSIR-SRF, Tanima Mandal, CSIR-SRF; Bilash Chatterjee, UGC-SRF; Subhankar Bose, CSIR-SRF; Momi Paul, DST inspire-JRF; Debanjan Ghosh, Project-JRF; Sangita Mishra, Project-JRF; Nitisha Shrivastava, Project Associate

Collaborators: Prof. Ramesh Ganhu, Department of Pathology, The Ohio State University, USA; Prof. Qi-En Wang, Department of Radiology, The Ohio State University, USA; Dr. Rakesh Pathak, Department of Chemistry, IISER, Berhumpur

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; one form of blood cancer) initially respond to chemotherapy, many of them subsequently relapse, and the mechanistic basis for AML persistence following chemotherapy remains poorly understood. In our laboratory we are testing the hypothesis that epigenetic derangements within hematopoietic compartment contributes to AML pathogenesis. We are interested in investigating the cell-autonomous regulation of hematopoietic stem/progenitor cell transformation in AML, and leveraging unique epigenetic and transcriptional dependencies for immunomodulation.

Identifying tumor cell-epigenetic regulation of immune activation in acute myeloid leukemia (AML) would be instrumental in developing next-generation of targeted therapy. AML cells have low mutational burden; inefficient 'cross-presentation' through conventional dendritic cells (DC) and immune activation are the major challenges for AML immunomodulation. 'Immunogenic cell death' (ICD) represents changes in the composition of the tumor cell surface as well as the release of 'damage associated molecular patterns' (DAMPs) in the tumor microenvironment that stimulates the dysfunctional immune system. DAMPs in turn operate on a series of receptors expressed by DCs and natural killer (NK) cells and contribute to long-lasting, protective anti-tumor immunity. KDM6A is a histone 3 lysine 27 demethylase that plays tumor suppressor function in AML (Gozdecka, Nat Genet 2018; Sera, Blood 2021). KDM6A escapes X-chromosome inactivation and loss-of-function deletion or point mutations associate with resistance to '3+7' chemotherapy (Stief, Leukemia 2020). We have identified that in comparison to control AML cells, deficiency of KDM6A or its pharmacolog inhibition associated with daunorubicin/etoposide-induced ICD, which was manifested by significant increase in cell surface calreticulin with extracellular release of HMGB1 and ATP (Figure 1). Gene set enrichment analysis revealed a significant enrichment of upregulated type I interferon signatures in $Kdm6a^{-/-}$ primary leukemia cells. Re-analysis of ChIP-seq results indicated 1647 Kdm6a occupied genes, which were upregulated upon Kdm6a loss. Gene ontology (GO) analysis of the 1647 genes further suggested an enrichment of type I interferon-responsive GO terms, indicating Kdm6a role in interferon signaling.

Additionally, AML blasts-healthy immune cells ex vivo co-culture experiments (Figure 1) revealed that increase in ICD in KDM6A deficient AML was associated with activation of DCs. Earlier we reported that loss of KDM6A bestows 'BRCAness' (Boila, Leukemia

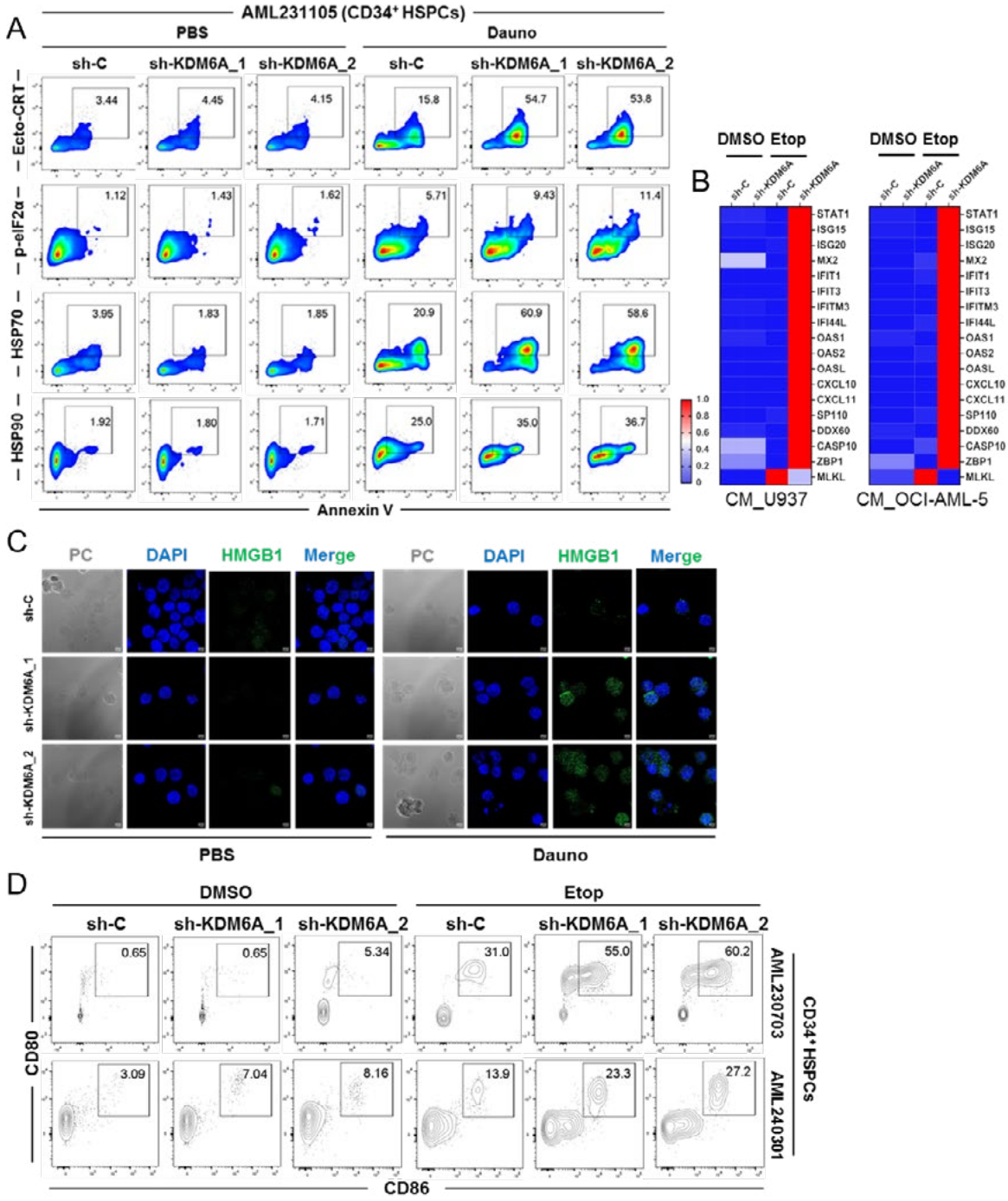


Figure 1. KDM6A restrains immunogenic cell death (ICD) program in AML. (A) Cell surface expression of 'eat-me' signals in primary AML HSPCs in response to ICD. (B) Expression analysis in conditioned media (CM) derived from AML cells. (C) Immunofluorescence analysis in AML. (D) Activation of healthy, primary NK cells co-cultured with ICD-exposed versus ICD-naïve AML HSPCs.

2023), and PARP inhibition itself can cause ICD and augment tumor immunity. We observed that there was a significant induction in ICD and expression of NKG2D ligands in KDM6A deficient AML cells treated with olaparib. In addition, olaparib and GSK-J4 treatment showed additive effects in ICD and immune activation using primary AML patient derived CD34⁺ hematopoietic stem/progenitor cells. Together, we illustrate that KDM6A regulates ICD through epigenetic mechanisms, while KDM6A deficient AML subtypes could be sensitized with immunomodulatory targeted therapy (Bandyopadhyay, manuscript in preparation).

Future Research Plans

Age-related chronic inflammation emerges to be a driver in tumorigenesis, and growing single-cell multimodal studies have suggested that AML bone marrow 'inflammation score' correlates with leukemia evolution and therapy response. However molecular regulation of tumor cell-intrinsic sterile inflammatory cues driving clonal fitness and evolution in AML development in vivo is poorly understood. Employing relevant cellular and cutting edge physiological models of AML that includes analysis of primary diagnosis & relapsed AML patient derived hematopoietic stem/progenitor cells, CRISPR/Cas9 editing, syngenic models, transplantation assays, tumor vaccination studies into immunocompetent mice, cell line/AML patient derived xenografts into immunodeficient mice models and epigenomic analyses, we aim to dissect molecular, cellular and physiological regulation of sterile inflammation and innate immune sensing pathways in the context of pre/leukemic hematopoiesis and evolution of AML immune microenvironment ecosystem. In addition, we are interested in developing enginerred NK cells for adoptive therapy in AML.

Extramural / CSIR Funding

1. Harnessing epigenetic dependencies for immunomodulation in acute myeloid leukemia. Lady Tata Memorial Trust, 2024-27, 100 Lakhs (IRPG).
2. Understanding nucleosome remodeler plasticity in human AML pathogenesis. S Ramachandran National Bioscience Award for Career Development, Department of Biotechnology (DBT), 2024-27, 15 Lakhs, (102/IFD/SAN/2749/2023-2024).
3. Epigenetic regulation of AML pathogenesis & targeted therapy. CSIR, 2024-25, 10 Lakhs (OLP-121).
4. Adoptive natural killer cell therapy for homologous recombination-deficient adult acute myeloid leukemia. CSIR, 2024-25, 6 Lakhs, (RDSF00003).

Publications

1. Bandyopadhyay S, K., Bose, A., Chattopadhyay, A., Ghosh, S., Bhowmik, S., Samanta, S. K., Bhattacharyya, M., Sengupta, A. (2023) Histone lysine demethylase modulate anti-tumor immune response in human acute myeloid leukemia. Blood. 142, 2753. 65th American Society of Hematology (ASH) Annual Meeting, San Diego, CA, USA.

Invited Lectures

Harnessing epigenetics for immunomodulation in acute myeloid leukemia. Tata Translational Cancer Research Centre, Tata Medical Centre, Kolkata. EMBO Workshop on Molecular Basis and Mechanisms of Therapy Personalisation in Paediatric Leukaemia, 5-8 February 2025.

Conferences Attended

Gordon Research Conference: Cell Death, Newry, ME, USA, 28 July-2 August 2024.

Dr. Amitava Sengupta, Senior Principal Scientist

Group Members: Subham K. Bandyopadhyay, DBT-SRF; Subhadeep Ghosh, CSIR-SRF; Anwesha Bose, CSIR-SRF; Satyaki Bhowmik, CSIR-SRF; Ipsita Banerjee, CSIR-JRF; Sudip Dey, UGC-JRF

Collaborators: Maitreyee Bhattacharyya, DM, Inst. of Hematology & Transfusion Medicine, Medical College & Hospital, Kolkata; Arnab Chattopadhyay, MD, Medical College & Hospital, Kolkata; Sambit K. Samanta, DM, Medical College & Hospital, Kolkata; Prakas K. Mandal, MD, NRS Medical College & Hospital, Kolkata

Dr. Debasis Nayak and his group members

Understanding and Targeting the Mechanisms of Chemoresistance in Pancreatic Cancer

Research Activities

Pancreatic cancer, the most common type called pancreatic ductal adenocarcinoma (PDAC), is a lethal malignancy often characterized by its rapid rate of metastasis and extremely low patient survival rate. Cytotoxic drugs such as gemcitabine and 5-fluorouracil are the cornerstones of chemotherapy currently in clinical use for the treatment of PDAC. However, therapeutic resistance emerges due to critical factors such as an immunosuppressive tumor microenvironment (TME), epithelial-mesenchymal transition (EMT), and metastasis, which together contribute to cancer progression.

My research group is currently working on understanding the role of a membrane protein SLC28A3 (solute carrier family 28, member 3), also called concentrative nucleoside transporter 3 (CNT3), in pancreatic cancer. CNT3 is known to transport endogenous nucleosides and nucleoside analog anticancer drugs such as gemcitabine. Therefore, CNT3 expression determines the therapeutic efficacy of these drugs in pancreatic cancer. Our investigations on CNT3 expression in pancreatic cancer patient tissues demonstrate that this protein is downregulated in poorly differentiated/metastatic pancreatic cancer patient tissues compared to the well-differentiated and adjacent normal tissues. Loss of expression of this protein is also observed in subsets of PDAC cell lines compared to the normal pancreatic ductal epithelial cells. However, a comprehensive understanding of the role of CNT3 in cancer progression and chemoresistance remains elusive.

Another aspect on which my group is currently working is exploring the role of TME in chemoresistance of pancreatic and breast cancers. Chemotherapy drugs increase the number of senescent cancer cells in the TME, which secrete senescence-associated secretory phenotypes (SASPs) that later cause tumor recurrence and metastasis. Our group is involved in understanding the crosstalk between senescent cancer cells and cancer-associated fibroblasts in chemotherapy-treated conditions and assessing their impact on the tumor immune environment. Pharmacological interventions that can cause immunogenic cell death and

regulate such immunosuppressive TME may hold promise in controlling tumor growth, metastasis, and chemoresistance properties of cancer cells.

Immunohistochemistry (IHC) analysis of CNT3 expression in tissue icroarray from human pancreatic cancer patients revealed loss of CNT3 expression in moderately differentiated and poorly differentiated patient tissues compared to normal adjacent and well-differentiated tumor tissues (Fig. 1A). Overexpression of CNT3 in human pancreatic cancer MiaPaca-2 cells through lentiviral transduction showed loss of cell proliferation and epithelial phenotypes (Fig. 1B, C). Immunocytochemistry analysis of Vimentin (a marker of cell proliferation and EMT) showed loss of vimentin expression in CNT3-overexpressing (OE) clones (Fig. 1D). CNT3-knockdown clones were generated in PANC-1 human pancreatic cancer cells and are being characterized by Western blotting (Fig. 1E).

Bioinformatic analysis reveals transcription factors (TFs): zinc finger E-box binding homeobox 1 (ZEB1) and SRY-box transcription factor 10 (SOX10), having maximum relative score (1.0) and binding site frequency (59 sites) to the CNT3 promoter. We have

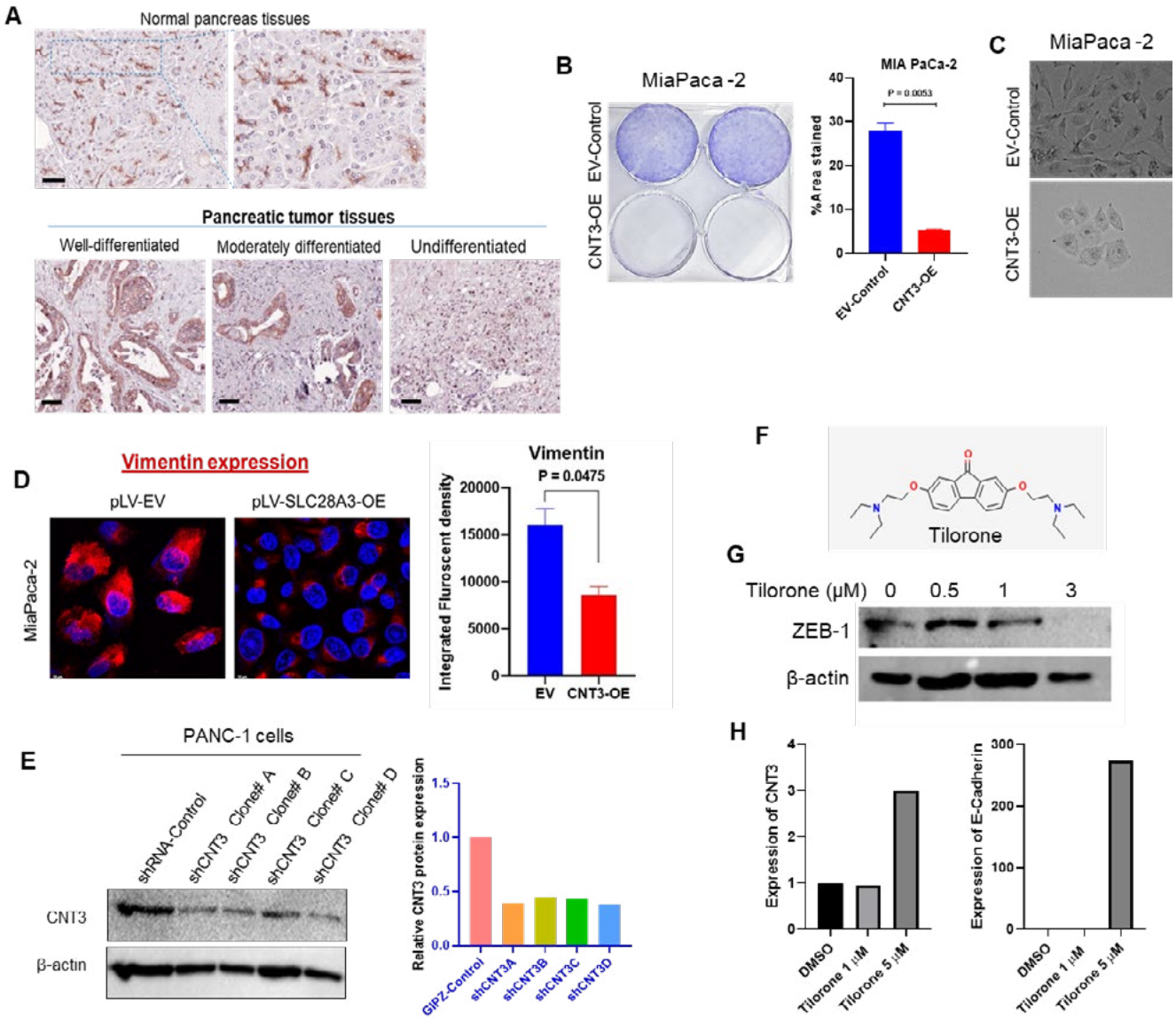


Figure 1: (A) Immunohistochemistry (IHC) images showing CNT3 expression in human pancreatic tumor tissues and adjacent normal tissues in a tissue microarray. (B) Colony-forming abilities of CNT3-overexpressing (OE) clones. (C) Morphological analysis of the CNT3-OE clones through bright field microscopy. (D) Immunocytochemistry analysis of the Vimentin expression in CNT3-OE clones. (E) Western blotting analysis of CNT3 expression in CNT3-knockdown clones of PANC-1 cells. (F) Structure of Tilorone. (G) Western blotting analysis of ZEB-1 expression in Tilorone-treated MiaPaca-2 cells. (H) mRNA expression of CNT3 and E-cadherin in tilorone-treated MiaPaca-2 cells.

identified tilorone dihydrochloride (TLH-1), a known interferon inducer antiviral drug that can inhibit ZEB-1 expression and restore CNT3 expression in MiaPaca-2 cells. TLH-1 can also induce E-cadherin expression (epithelial cell marker) in MiaPaca-2 cells (Fig. 1F-H), which suggests this compound can regulate EMT properties of invasive PDAC cells.

Future Research Plans

- Understanding the mechanism of loss of CNT3 in pancreatic cancer.
- Exploring small molecules that can restore CNT3 expression in invasive cancer cells.
- Elucidating the mechanism of cell death by Tilorone hydrochloride in PDAC and breast cancers.
- Development of CAR T cells targeting solid tumors (ovarian).
- Identification of bioactive small molecules from deep ocean sources targeting mitochondrial dysfunction in cancer cells.

Extramural / CSIR Funding

1. Restoring CNT3 expression for boosting antitumor immunity and suppressing pancreatic cancer progression, Prime Minister's Early Career Research Grant (PM-ECRG), Anusandhan National Research Foundation (ANRF) 2025-2028. 60 lakhs. (ANRF/ECRG/2024/005685/LS).
2. Screening for the identification of mitophagy inhibitors to use as anti-cancer agents against metastatic breast and colorectal cancer. Deep Ocean Mission: Discovery and development of novel drugs and pharmaceuticals, Ministry of Earth Sciences, Government of India (2025-2027).
3. Exploring the role of solute carrier SLC22A15 in colorectal cancer stemness and chemoresistance, and the effect of its pharmacological modulation. Other Lab Project (OLP), CSIR-IICB (2025-26).

Conferences Attended

Adjudicated poster presentation competition for Research Fellows on the occasion of "44th Annual Meeting of The Indian Association for Cancer Research (IACR)" and International Conference on "Convergence of Fundamental and Translational Approaches in Cancer Theranostics," organized by Chittaranjan National Cancer Institute (CNCI), Kolkata, in collaboration with the IACR West Bengal Chapter during 16th to 18th January 2025 at Kolkata.

Dr. Debasis Nayak, Scientist

Group Members: Ritwik Mandal, DBT-JRF; Tanaya Mondal, UGC-JRF; Bappaditya Mitra, UGC-JRF; Subhrajit Mukherjee, Research Intern; Sohni Ghosh, Research Intern

Dr. Mrinal Kanti Ghosh and his group members

Using Nanoparticles to Deliver DIM and Temozolomide Together for Better Treatment of Brain Cancer

Research Activities

Grade IV astrocytes, also known as glioblastoma multiforme (GBM), are among the most aggressive brain tumours. The prognosis for those who have it is restricted to 12 to 15 months, and there are very few options for medication. GBMs primarily affect the frontal and temporal lobes of the brain, but they can also develop from lower-grade astrocytoma's or start from scratch. Glioma patients, especially those with GBM, still have a poor chance of improving their survival despite receiving therapies including intensive surgery, chemotherapy, and radiation therapy. The presence of the blood-brain barrier (BBB), chemoresistance, the existence of glial stem cells, acquired radio resistance, and tumour heterogeneity are among of the issues that lead to decreased chemotherapy and radiotherapy efficacy and higher recurrence rates.

Since the approval of TMZ in 2005, to treat newly diagnosed GBM, it has established itself as a common chemotherapeutic. One major obstacle to glioma therapy with TMZ is the emergence of resistance. Epigenetic regulation, autophagy activation, and increased MGMT expression are some of the processes that contribute to the development of resistance to TMZ-based glioma treatment. Higher TMZ concentrations might be necessary to overcome resistance, however there is a chance of adverse consequences. Examining logical combination therapy becomes essential when beneficial remedies are recognised. By jointly targeting pathways, anticancer medication combinations may increase efficacy and perhaps lower cost. DIM is a possible low-toxicity chemotherapeutic drug that is generated from indole 2 carbinol found in cruciferous vegetables. Preclinical evidence of anti-tumor properties of DIM shows that it targets the advancement of cancer in models through EGFR-JAK2-STAT3 signalling modulation, checkpoint activation, caspase activation, ER stress production, autophagy, and anoikis. DIM reduces toxicity and drug resistance, especially when used with drugs by increasing the sensitivity of cancer cells to common chemotherapeutic agents. Hence, DIM is frequently utilised in combination therapy, minimises concurrent medication toxicity while promoting chemo sensitization.

With the use of BBB-penetrating polymeric nanoparticles like PLGA, nanotechnology offers a viable cancer treatment platform with precise drug delivery to tumour locations. This strategy guarantees effective and safe drug release in GBM cells, resulting in notable therapeutic improvements. To sum up, PLGA nanoparticles offer a popular and extremely successful method of treating cancer. Therefore, in this project DIM along with TMZ (both individually and in combination) are nano encapsulated using PLGA to target GBM cells.

Aims and objectives

- To prepare individual nano formulations of DIM, TMZ and also dual loaded DIM and TMZ nanoparticles.
- To study the characterisation of the nano formulations of DIM and TMZ both individually and in combination using AFM, FTIR etc.
- To apply targeted drug delivery systems using nanoparticles in delivering drugs individually or in combination both in in-vitro and in-vivo conditions.

Work achieved

Orchestration of PLGA nanoparticles loaded with dual drugs to treat GBM

To assess the chemotherapeutic potential of the drugs selected for this investigation, performed several in vitro tests on GBM cells were performed. Initially, the IC50 values were calculated using MTT assay. The synergistic effect of the two drugs were calculated using Chou-Talay's method. The lowest Combination Index (CI) was then selected for the subsequent experimentation. Using in-vitro tests, the synergistic potential of the two medications, DIM and TMZ, was ascertained. Reactive oxygen species (ROS) generation was tracked and IC50 values were established. The study revealed that when the drugs were administered in combination, there was a notable rise in ROS generation and a fall in MMP or matrix metalloproteinase levels. These findings thus confirm that the synergistic dosing of medications enhances apoptosis and cell death mechanisms. To highlight the lethal effect of the synergistic dual concentration in comparison with individual IC50 concentration, evaluation of the apoptotic cell populations of cells were performed using Annexin V/PI-FACS analysis. It shows increased apoptosis and consequent reduction of the necrotic effect on C6 cells with the synergistic doses of DIM and TMZ. Therefore, leading to the notable

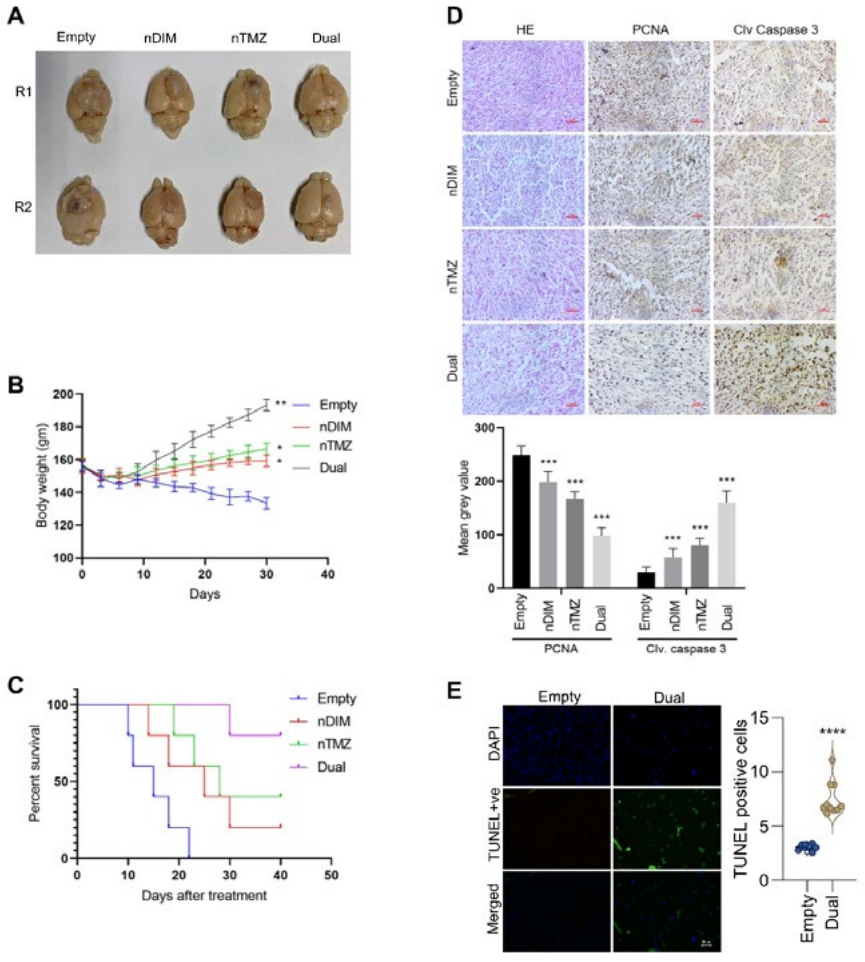


Figure 1: *In* vivo efficacy of dual-loaded nanoparticles in orthotropic/intracranial tumors. A. Representative images of dual-loaded nanoformulation or empty vehicle treated rat brain tumors (Orthotopic models). B) Comparison of body weight of same dual-loaded nanoformulation or empty vehicle treated tumor bearing rats (n=4). Data is represented as mean ±SE. C) Represents Survival curve. D. H&E staining and IHC image analysis of PCNA and cleaved Caspase 3 in vehicle treated and dual-loaded nanoformulation treated tumor tissue sections. Scattered plot represents normalized mean intensities. E. TUNNEL-positive cells in empty vehicle and dual-loaded nanoformulation treated groups.

emergence of early and late apoptotic populations. Other in-vitro experiments conducted like scratch assay, colony assay, western blots also lead to similar conclusion. Combination therapy may be a more successful treatment for C6 rat glioma cells than either treatment alone, but further research is needed to thoroughly examine the underlying processes of this synergistic impact.

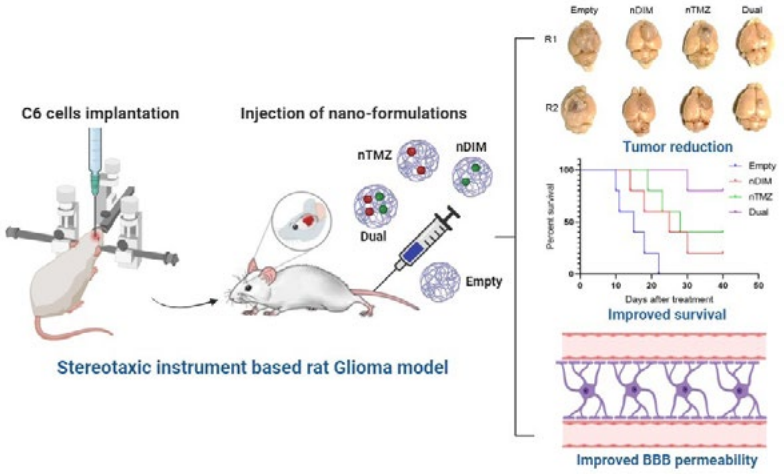


Figure 2: Model shows how dual-loaded nanoformulation delivered and works in glioma therapy. Validated effectivity of dual-loaded nanoformulations in-vivo in orthotopic glioma model. Delivery of the combination drug treatment would have a better clinical outcome.

Target specificity, efficient drug release, and improved solubility are all aided by the innovative drug delivery method that uses PLGA nano formulation. A dual-loaded nano formulation was evaluated in SD rats using an orthotopic cerebral glioma model. For 40 days following tumour development, the rats were given the individual and dual drug loaded nano formulation (2.5 mg/kg body weight) every other day, which significantly inhibited their growth. On the other hand, rats in the control group that received identical injections of empty nanoparticles revealed tumours that did not shrink. While the control group displayed early indications of rapid tumour growth during the treatment period, rats treated with dual-loaded nano formulation did not exhibit any notable changes in tumour size. Additionally, compared to rats treated with individually packed molecules and the control groups, animals treated with dual-loaded nano formulation had significantly smaller tumour weights and volumes. The tumours were collected and processed for Immunohistology (IHC), TUNEL assay, Haematoxylin and eosin (H&E) experiments. IHC showed that due to the production of enhanced apoptosis, the rats treated with the combinatorial drug encapsulated nano formulation had decreased tumour development and decreased PCNA staining. In comparison to those treated with separate drugs, TUNEL assay also demonstrated improved survivorship after treatment. Thus, tailored drug delivery of nanoparticles to the tumour site may offer a viable therapy strategy for patients with brain cancer.

Future Research Plans

- To decipher the role of USP7 in oxidative stress focusing on colorectal carcinoma.
- To understand the gene regulation of USP7.
- To establish mechanism of cyto-nuclear distribution of CHIP.

Extramural / CSIR Funding

1. Study the mechanism of Inflammation and Cancer Chemoresistance: Targeted therapy in cancer, CSIR-IICB (OLP-121). **(Ongoing)**

2. **PI/Mentor:** Women Scientist Scheme, WIDUSHI, WISE KIRAN, DST, GoI (2025 – 2029). A combinatorial approach of targeting XIAP and MDM2 in TNBC therapy.

   Rs. 80.0 Lakhs (WIDUSHI, DST: Awarded to Dr. Sibani Sarkar). **(Ongoing)**

3. **PI/Mentor:** Women Scientist Scheme, WISE-PhD, DST, GoI (2025 – 2030). Targeting USP7 along with p53-MDM2 interface peptide in Glioma: A combinatorial nanotherapeutic approach.

   Rs.36.3600 Lakhs (PhD, WISE KIRAN, DST: Awarded to Ms. Sabana Begam). **(Ongoing).**

4. **PI/Mentor:** Women Scientist Scheme, DHR, GoI (2024 – 2027). Targeting deubiquitinase USP7 along with EGFR for successful TNBC therapy - A combinatorial nanotherapeutic approach successful TNBC therapy - A combinatorial nanotherapeutic approach.

   Rs. 60.9628 Lakhs (WoS, Awarded to Dr. Nilanjana Das). **(Ongoing)**

5. **PI/Mentor:** Women Scientist Scheme, DHR, GoI (2023 – 2026). Combinatorial application of nanoformulated p68si/sh-RNA and EGFR inhibitor DIM for successful Glioma therapy.

Publications

1. Saha G[#] and Ghosh MK[#,*] (2025). The key vulnerabilities and therapeutic opportunities in the USP7-p53/MDM2 axis in cancer. *BBA - Molecular Cell Research* 1872, 119908. *{IF=5.1; Ci=1} In press*
2. Karmakar S, Chatterjee M, Basu M and Ghosh MK* (2025). CK2: the master regulator in tumor immune-microenvironment - a crucial target in oncotherapy. *European Journal of Pharmacology* 994,177376. *{IF=4.2; Ci=0}. In press*
3. Sarkar S[#], Kumar S[#], Saha G, Basu M and Ghosh MK* (2024). Glioma nanotherapy: Unleashing the synergy of dual-loaded DIM and TMZ. *Int. J. Pharmaceutics* 665, 124697. *{IF=5.3; Ci=1}*
4. Kumar S[#], Ansari A[#], Basu M[#], Ghosh S[#], Begam S[#] and Ghosh MK[#,*] (2024). Carbon Nanotubes in Cancer Diagnosis and Treatment: Current Trends and Future Perspectives. *Advanced Therapeutics* 8, 2400283. *{IF=4.6; Ci=1} In press*
5. Kumar S, Basu M and Ghosh MK* (2024). E3 ubiquitin ligases and deubiquitinases in colorectal cancer: Emerging molecular insights and therapeutic opportunities. *BBA - Molecular Cell Research* 1871, 119827 *{IF=5.1; Ci=0} In press*
6. Ghosh MK*, Kumar S, Begam S, Ghosh S and Basu M (2024). Glioma Immunotherapy: Exploring Molecular and Clinical Frontiers. *Life Sciences 356, 123018 {IF=5.2; Ci=3} In press*
7. Kumar S, Basu M*, Chakraborty D, Ghosh P and Ghosh MK* (2024). Unraveling COVID-19 diagnostics: A roadmap for future pandemic. *Nature Cell & Science* 2(3):151–184.

Book Chapters

1. Ghosh MK*, Kumar S and Basu M (2024). Ubiquitin Specific Protease 7 (USP7) – Role in Human Pathologies and Potential Targeting Opportunities in Cancer. *Handbook of Proteases in Cancer: Cellular and Molecular Aspects.* Published by Tayler & Francis. In press
2. Ghosh MK*, Roy S, Chatterjee M, Begam S and Basu M (2024). The Dichotomous Role of CHIP in Cancer. *Handbook of Proteases in Cancer: Cellular and Molecular Aspects. Published by Tayler & Francis. In press*

Invited Lectures

1. *Cancer in the 21st Century: Integrating Biology and Emerging Technology - A Holistic Approach. Microbiologists Society of India. Nov 07, 2024.*
2. *Modern Cancer Research.* Vigyan Prasange Organized by Doordarshan Channel (DD Bangla)-PRASAR BHARATI, October 18, 2024. https://www.youtube.com/live/nXOmMI02VwU?si=sT08Ii2xklac31D2

Awards

Senior Scientist Award, Microbiologists Society, India (2025)

Dr. Mrinal Kanti Ghosh, Chief Scientist

Group Members: Sunny Kumar, SRF (CSIR); Subhajit Karmakar, SRF (CSIR); Srija Roy, SRF (CSIR); Sayani Ghosh, SRF (ICMR); Mouli Chatterjee, JRF (INSPIRE, DST); Sabana Begam, JRF, DST-WISE; Dr. Meeta Gera (Women Scientist, ICMR-DHR); Dr. Nilanjana Das (Women Scientist, ICMR-DHR); Dr. Sibani Sarkar (Women Scientist, WIDUSHI, DST)

Collaborators: Dr. Suresh Bajoria, RTIICS (Narayan Health), Kolkata; Dr. Uttara Chatterjee, IPGMER & Park Clinic, Kolkata

Dr. Shilpak Chatterjee and his group members

Deciphering metabolic-epigenetic crosstalk in determining the stability and function of regulatory T cells (Tregs) in the tumor microenvironment

Research Activities

Intratumoral Tregs express CD38. To elucidate the functional relevance of CD38 in intratumoral Tregs, we first examined their abundance at the tumor site. Analysis of tumor tissues and paired peripheral blood samples from patients with breast and muscle-invasive bladder cancer (MIBC) revealed that Tregs infiltration, marked by $CD4^+$ and $FoxP3^+$ expression, was significantly higher in tumor tissue than in peripheral blood (Fig. 1A and 1C), as reported. However, interestingly, upon analysis of $CD4^+FoxP3^+$ cells, we noted that the expression of CD38 was more frequent on intratumoral Tregs compared to Tregs from peripheral blood (Fig. 1B and 1D).

To confirm this observation, we employed various preclinical models in which mice were subcutaneously implanted with B16-F10 melanoma, YUMM1.7 melanoma, or EL-4 thymoma. As anticipated, the abundance of Tregs was markedly higher at tumor sites compared to the spleen and draining lymph nodes (DLN) (Fig. 1E-1G). Notably, across all tumor types assessed, CD38-expressing Tregs were significantly enriched at tumor sites compared to the spleen and DLN (Fig. 1H-1J). Furthermore, $CD38^+$ Tregs were scarce in non-lymphoid tissues such as the skin and liver (Fig. 1H-1J). When evaluating CD38 expression levels, we found that intratumoral Tregs exhibited markedly higher CD38 expression than their lymphoid and non-lymphoid counterparts (Fig. 1K-1M). Together, these findings suggest that intratumoral Tregs have a strong propensity to express CD38, in stark contrast to Tregs residing in peripheral tissues, where CD38 expression is markedly lower.

$CD38^{Hi}$ Tregs exhibit superior suppressive activity. We first checked if *in vitro* differentiated Tregs (iTregs) also expressed CD38. We observed that naïve $CD4^+$ T cells differentiated to effector T cells (Teff) barely express CD38, while the frequency of $CD38^+$ cells was significantly higher in iTregs, comprising approximately 70-75% of the iTregs population (Fig. 2A and 2B).

Given the expression of CD38 on iTregs, we examined if the CD38-expressing iTregs subset also harbours the suppressive gene signature as observed in intratumoral $CD38^+$ Tregs. We sorted iTregs based on the CD38 expression and analyzed immunosuppressive gene expression in $CD38^{Hi}$ and $CD38^{Lo}$ subsets. We found that the expression of *Ctla4, Icos, IL2ra, Ikzf2, Nrp1, Entpd1* (gene

encodes CD39), and *Lag3* genes associated with the immunosuppressive potential of Tregs, were markedly upregulated in CD38^{Hi} iTregs compared to CD38^{Lo} iTregs (Fig. 2C). Next, we subjected the sorted CD38^{Hi} and CD38^{Lo} iTregs to the suppression assay with naïve T cells purified from wild type B6 mice. We observed that CD38^{Hi} iTregs were superior to CD38^{Lo} iTregs in suppressing the proliferation and effector cytokine production of T cells at all the tested ratios (Fig. 2D and 2E). Notably, this differential suppressive capacity was not due to differences in viability, as both subsets remained equally viable after the assay (Fif. 2F). Together, these findings suggest that CD38 expression on iTregs is pivotal for their immunosuppressive potential and aids in maintaining FoxP3 expression, highlighting its critical role in Treg stability and function.

CD38^{Hi}-NAD^{Lo} axis redirects lactate metabolism for the generation of PEP in Tregs. Uptake and metabolism of lactate is a hallmark of intratumoral Tregs. The metabolic fate of lactate is usually determined by two enzymes- pyruvate dehydrogenase (PDH) and pyruvate carboxylase (PC). To assess the contribution of these enzymes in lactate metabolism in CD38^{Hi} and CD38^{Lo} iTregs, we first traced the metabolic fate of lactate by incubating the cells with uniformly labeled ^{13}C3 L-lactate for 18 hours in glucose-free medium. We tracked ^{13}C incorporation into acetyl CoA and PEP, reflecting lactate's commitment to entering the TCA cycle or gluconeogenesis, respectively. Notably, CD38^{Hi} iTregs exhibited significantly higher allocation of ^{13}C to PEP (m+3), while CD38^{Lo} iTregs showed an increase, albeit non-significant, in ^{13}C labeling in acetyl-CoA (m+2) (Fig. 3A, 3B, and 3C).

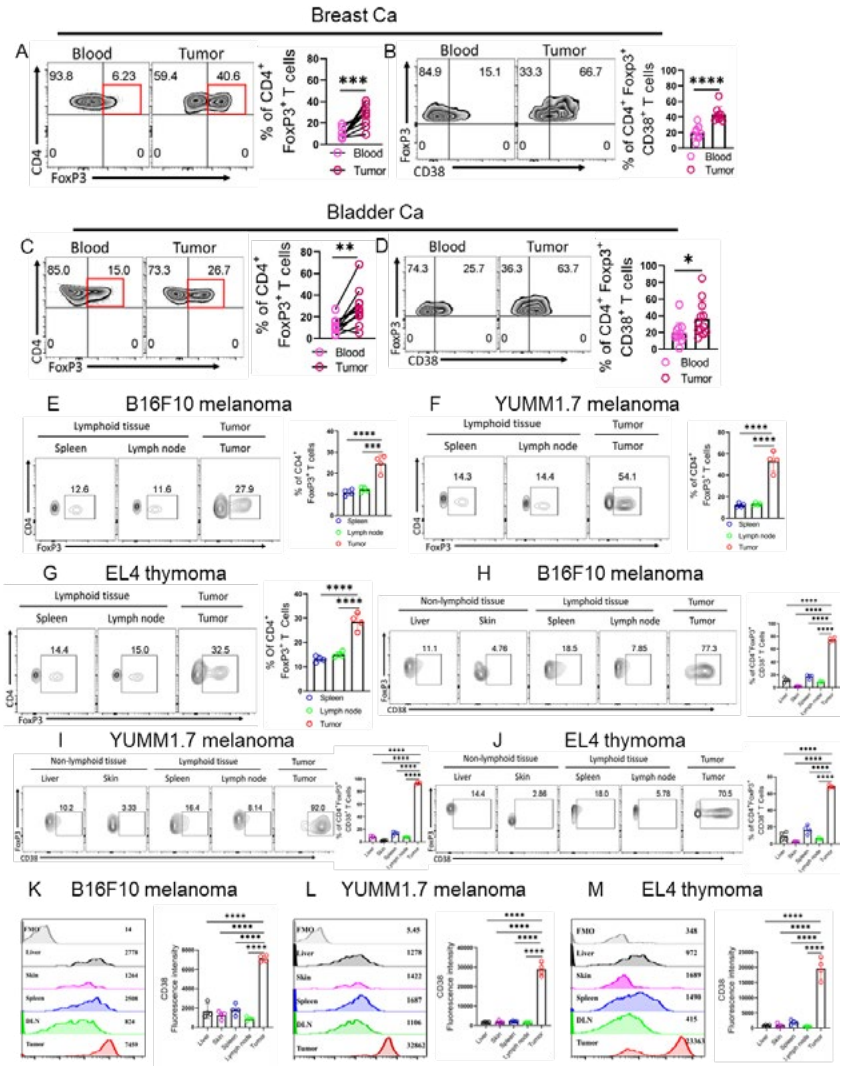


Figure 1: Intratumoral Tregs express CD38. Frequency of Tregs (CD4^{+}FoxP3^{+} T cells) was determined in: (A, C) tumor tissue and paired blood samples from patients bearing (A) breast cancer, (C) muscle-invasive bladder cancer, (E-G) tumor tissue and the spleen from B6 mice bearing 15 days subcutaneously established (E) B16-F10 melanoma, (F) YUMM1.7 melanoma, and (G) EL-4 thymoma. Frequency of FoxP3^{+}CD38^{+} T cells within the Treg compartment (CD4^{+}FoxP3^{+} T cells) was assessed in: (B, D) tumor tissue and paired blood samples from patients bearing (B) breast cancer, (D) muscle-invasive bladder cancer; (H-J) non-lymphoid tissues, lymphoid tissues, and tumor tissue from B6 mice bearing 15 days subcutaneously established (H) B16-F10 melanoma, (I) YUMM1.7 melanoma, and (J) EL-4 thymoma. (K-M) The fluorescence intensity of CD38 was assessed in Tregs from (K) B16-F10, (L) YUMM1.7, and (M) EL-4 thymoma bearing mice. Adjacent bar plots represent cumulative data from nine (A-B), twelve (C-D), and four (E-M) samples. *, P < 0.05; **, P < 0.01; ***, P < 0.005; ****, P < 0.0001.

Next, to assess whether PC-mediated metabolic routing of lactate in gluconeogenesis was key for maintaining the functionality of CD38^{Hi} iTregs, we blocked the enzyme and checked the functionality. Notably, inhibition of PC in CD38^{Hi} iTregs cultured in lactate-media or even in complete media significantly curbed their function, while no such impairment in the functionality was evident upon PDH inhibitor treatment (Fig. 3D and 3E).

Next, we examined whether the intracellular NAD+ pool plays a decisive role. To delineate this, we supplemented NMN while culturing CD38^{Hi} iTregs in lactate media and checked their functionality. We observed that NMN supplementation in CD38^{Hi} iTregs cultured in lactate-rich media improved their mitochondrial OXPHOS and decresed their suppressive function (Fig 3F and 3G). A similar effect was seen when PC, but not PDH, was inhibited in CD38^{Hi} iTregs cultured in lactate media (Fig. 3F). Together, these findings establish the CD38-NAD+ axis as a crucial determinant of Treg metabolic adaptability, enabling them to thrive in the lactate-rich tumor microenvironment.

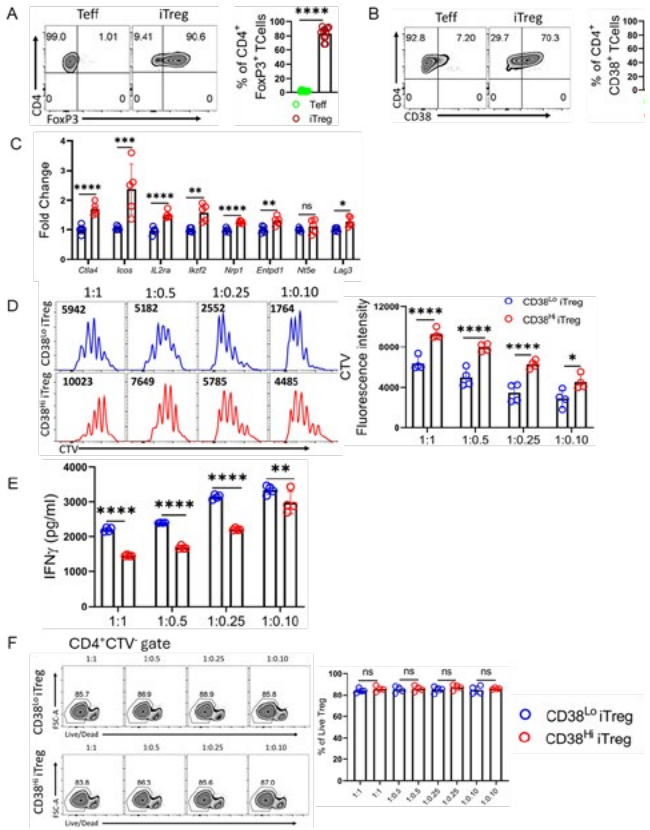


Figure 2: CD38^{Hi} Tregs exhibit superior suppressive activity. (A-B) Naïve CD4^{+} T cells from B6 mice were differentiated into Teff or Tregs, the frequency of CD4^{+} T cells expressing (A) FoxP3 and (B) CD38 expression were assessed. The bar diagram shows cumulative data from eleven experiments. (C) qPCR analysis of various genes in CD38^{Hi} and CD38^{Lo} iTregs. Data are representative of five independent experiments. (D-E) CTV-labeled naïve T cells were activated with anti-CD3/CD28 (1 µg/ml each) in the presence of FACS-sorted CD38^{Hi} and CD38^{Lo} iTregs for three days. (D) CD8^{+} T cell proliferation was assessed via CTV dilution. (E) Supernatant from (D) was used to measure IFN-γ levels. (F) Assessing the percentage of viable iTreg cells (CD4+CTV- gate) after three days of co-culture with CTV-labelled T cells from WT mice. The adjacent bar diagram represents data from four independent experiments. *, P < 0.05; **, P < 0.01; ***, P < 0.005; ****, P < 0.0001; ns, nonsignificant.

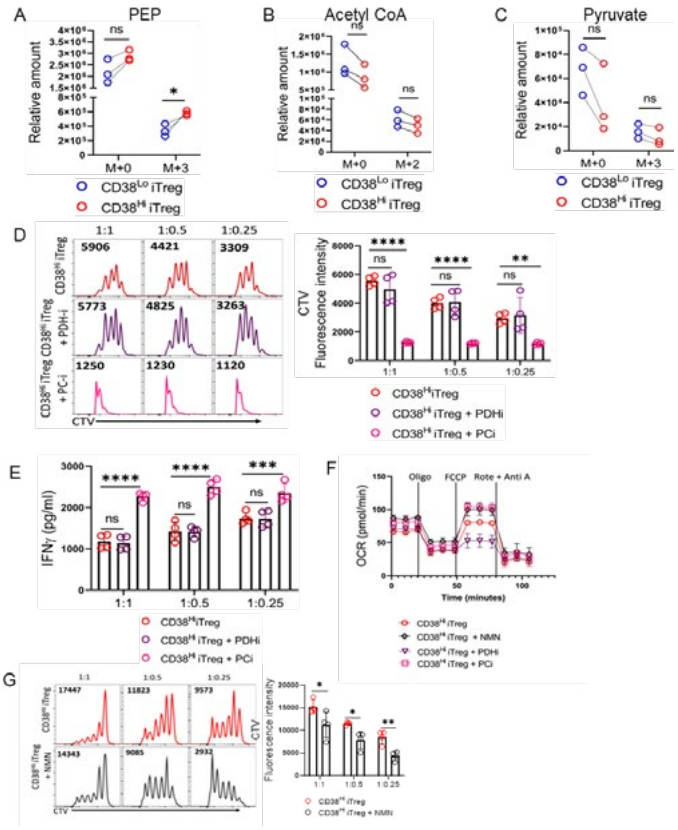


Figure 3: CD38^{Hi}-NAD^{Lo} axis redirects lactate metabolism for the generation of PEP in Tregs. (A-C) Isotopologue distribution for (A) PEP, (B) acetyl CoA, and (C) pyruvate in CD38^{Hi} and CD38^{Lo} iTregs overnight cultured in glucose-free media containing $^{13}C_3$ L-lactate. (D-E) iTregs were differentiated in glucose-free, L-lactate-containing media and sorted into the CD38^{Hi} population. These were then treated overnight with the indicated inhibitors in the same L-lactate-containing media and were used for co-culturing with CTV-labeled naïve T cells in the presence of a T cell activation cocktail (anti-CD3/CD28) for three days and assessed for (D) CD8^{+} T cell proliferation via CTV dilution and (E) measuring IFN-γ levels from the supernatant of the experiment shown in (D). (F) iTregs were differentiated in glucose-free, L-lactate-containing media and sorted into the CD38^{Hi} population before being treated overnight with NMN and indicated inhibitors. Cells were then assessed for OCR under basal condition and in response to the indicated inhibitors. (G) NMN-treated and untreated CD38^{Hi} iTreg differentiated in glucose-free, L-lactate-containing media were co-cultured with CTV-labelled naïve T cells for three days in the presence of anti-CD3/CD28. Proliferation of CD8^{+} T cells was assessed by CTV dilution. The data are representative of three (A-C) and four (D-G) independent experiments. *, P < 0.05; **, P < 0.01; ***, P < 0.005; ****, P < 0.0001; ns, nonsignificant.

Future Research Plans

Mechanistic Dissection of CD38-Driven Epigenetic Remodeling in Tregs. We will investigate how the CD38-NAD^{+} axis influences epigenetic modifications that sustain Foxp3 expression and the suppressive gene program in intratumoral Tregs. This will involve profiling histone modifications and DNA methylation landscapes using ChIP-seq and bisulfite sequencing in CD38^{Hi} vs CD38^{Lo} Tregs, with and without NMN supplementation.

Therapeutic Targeting of CD38^{+} Tregs in Tumors. We will evaluate whether selective targeting of CD38^{+} Tregs using antibody-based depletion or CD38 inhibitors affects anti-tumor immunity in combination with immune checkpoint blockade (ICB). This will be assessed in murine melanoma and bladder cancer models with intact immune systems.

Extramural / CSIR Funding

1. Project title: SMASH-ACT: Small Molecule mTOR modulation for Adoptive T cell Therapy (ACT), Agency: CSIR, Duration: 2024-2026, Sanctioned amount: 69.90 lakhs, Project number: FBR070304
2. Project title: Indian Brest Cancer Genome Atlas, Agency: CSIR, Hq, Duration: 2021-2026, Sanctioned amount: 4990.00 lakhs, Project number: HCP-43 (Co-PI).
3. Project title: Role of endoplasmic reticulum (ER) stress induced UPR signaling in regulating the metabolic fitness and functionality of CD8+ T cells in cancer, Agency: India Alliance DBT Wellcome, Duration: 2020-2024, Sanctioned amount: 359.11 lakhs, Project number: IA/I/19/1/504277

Publications

1. Sarkar I, Basak D, Ghosh P, Gautam A, Bhoumik A, Singh P, Kar A, Mahanti S, Chowdhury S, Chakraborty L, Mondal S, Mukherjee R, Mehrotra S, Majumder S, Sengupta S, Paul S, Chatterjee S*. *CD38-mediated metabolic reprogramming promotes the stability and suppressive function of regulatory T cells in tumor. Science Advances. 2025*. 11(12):eadt2117

Invited Lectures

1. Invited speaker at “Molecular Basis and Mechanisms of Therapy Personalisation in Paediatric Leukaemia”, TMC, Kolkata in collaboration with EMBO, 5-8 February, 2025.
2. Invited speaker at 44th Annual Meeting of the Indian Association for Cancer Research (IACR), CNCI, Kolkata, 16-18 January, 2025.
3. Invited speaker at National Symposium on “Molecular Basis of Life: Health, Disease & Diversity”, Presidency University, 28-30 November, 2024.
4. Invited speaker at 51st Annual International Conference of the Indian Immunology Society, IMMUNOCON-2024, IISc, Bengaluru, 16-20 October, 2024.

Conferences Attended

1. 51st Annual Conference of Indian Immunology Socity: IMMUNOCON-2024, IISc, Bengaluru, 16-20 October, 2024.
2. 44th Annual Meeting of the Indian Association for Cancer Research (IACR), CNCI, Kolkata, 16-18 January, 2025.

Member of Society

1. Member, Technical Expert Committee (TEC), Cancer Disease Biology Program, DBT, Govt. of India (2022-2025)
2. Member, Project Selection Group (PSG), Investigator Initiated Small and Intermediate Grant, ICMR, Govt. of India (2023-2026)

Dr. Shilpak Chatterjee, Principal Scientist

Group Members: Debashree Basak, CSIR-Senior Project Associate; Ishita Sarkar, CSIR-Project Associate II; Puspendu Ghosh, CSIR-SRF; Anwesha Mandal, UGC-JRF; Shaun Mahanti, UGC-JRF; Soham Chowdhury, UGC-JRF

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:

- Developing effective bi-specific CAR-T based therapy for breast and ovarian cancer.
- Development of chimeric bifunctional immunobodies as next generation anticancer therapeutics.
- Developing armed oncolytic Adenovirus carrying suicidal gene recombinant carboxylesterase.

As achievement, 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, specifically the cancer cells overexpressing mesothelin. The same has been observed in RAG1 KO transgenic mice. Based on the RECIST parameters, most mice treated with CAR-T showed a complete response (CR) after a single dose of CAR-T administration in tumor-bearing mice.

Future Research Plans

- In future we will expand CAR-T cells and evaluate the efficacy of CAR-T cells in NSG/ NCG-X mouse model
- CAR-T memory cell and exhaustion markers will be studied.
- We have made biologicals cyto-ab (IL-2-α-PDL1-CH1-IgG1-Fc) which is at the final stage of publication of patent. 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 (3 years). Funding agency: Special Secretary, Science and Technology & Biotechnology, WB. Sanctioned amount: 65,79,000/-. Co-PI. Sanction letter No. 2003 (Sanc.)/ 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. Role: PI. Tenure: Jan 2022-10 April 2024), Sanction amount received: 45,00,000/-. Sanction No. or Ref: 223547/Z/21/Z Dated: 24.01.2022.
3. Advancing Cellular Therapies for Cancers and Inflammatory Disorders: A Comprehensive Indian Initiative (ACT-CID): Sanction amount: 2,99,80,200/- Sanction No: 4/1/ACT-CID/2025-IMD; Dated 21-05-2025 (3 years)
4. Development of Machine Learning (ML)-Deep Learning (DL) and Artificial Intelligence (AI) based diagnostics and data analysis platforms. Budget 1,54,00,000/-

Publications

1. Sarkar, P., Banerjee, S., Saha, S. A., Mitra, P., **Sarkar, S.***. 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 (2023). PMID: 36949118. DOI: 10.1038/s41598-023-30815-5

Invited Lectures

Developing biological based therapeutics (biologics) for the treatment of cancer including breast and ovary. SNU-BioTalk-2025 International Conference on; Symphony of Cellular Signals in Metabolism and Immune Response, Sister Nivedita University (SNU). 16-17 Jan 2025.

Conferences Attended

Developing biological based therapeutics (biologics) for the treatment of cancer including breast and ovary. SNU-BioTalk-2025 International Conference on; Symphony of Cellular Signals in Metabolism and Immune Response, Sister Nivedita University (SNU). 16-17 Jan 2025.

Member of Society

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

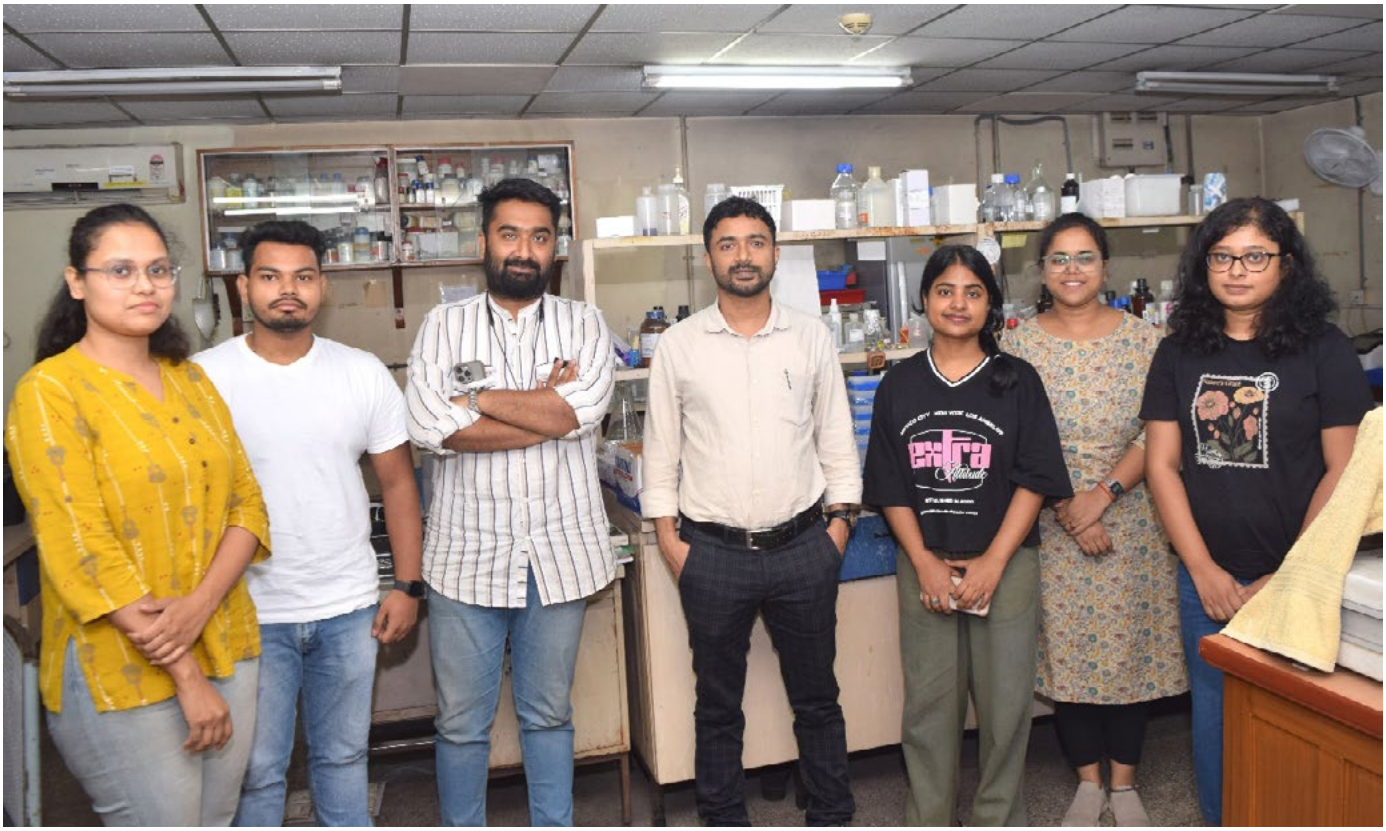
Dr. Siddik Sarkar, Senior Scientist

Group Members: Sarbar Ali saha, CSIR-SRF; Abhishek Swarnakar, DBT-JRF, Arnab Chakrabarty, UGC-JRF; Victor Roy, CSIR-JRF; Susmita Swarnakar, CSIR-SRF

Collaborators: Academic: Dr. Shilpak Chatterjee, CSIR-IICB, Kolkata; Dr. Amitava Sengupta, CSIR-IICB, Kolkata; Dr. Pralay Mitra, IIT Kharagpur; Dr. Mahitosh Mandal, IIT Kharagpur; Dr. Sanchita Goswami, University of Kolkata; Clinical: Dr. Biswaroop Basu, CNCI Kolkata

CELL BIOLOGY AND PHYSIOLOGY DIVISION

The Cell Biology and Physiology division has ten faculty members, who are working in a diverse fields of fundamental and translational biology in different diseases. They are working in various research domains of biology with an aim towards understanding both basic as well as clinical aspects of diseases. Investigations are going on to understand the functions of subcellular organelles and intracellular signalling events in normal as well pathophysiological conditions. Major interests are in the area of metabolic diseases, including cardio-metabolic diseases, diabetes and cancer; neurological disorders, parasitic diseases, reproductive diseases, stem cell biology and lung disorders, which are performed in different systems, like human patients' samples, preclinical animal models, and different primary cell cultures, besides studies based on relevant cell lines. The faculties of Cell Biology & Physiology are further adhered to the different regulatory aspects of gene expression and epigenetic modifications. The faculties have a strong and persistent outlook towards the development of novel therapeutic targets, diagnostics and therapeutic leads. The research groups of this division are also involved in several potential intra-division collaborations, collaborations with other divisions including the scientists from the chemistry division and also with other Institutes across India and abroad. The faculties and their research fellows had an outstanding contribution in the current year in terms of publications, patents and creating new domains of research including initiating new projects with funding from different Government agencies.



Dr. Bijesh P. and his group members

Metabolic Reprogramming via Folate Receptor-Mediated One-Carbon Flux as a Therapeutic Strategy for COPD

Research Activities

Chronic Obstructive Pulmonary Disease (COPD) is a progressive inflammatory disorder marked by alveolar destruction, oxidative stress, and impaired epithelial regeneration. Current therapies mainly focus on symptom management, with limited success in halting or reversing tissue degeneration.

Emerging evidence from our laboratory suggests that one-carbon (1C) metabolism, a critical biochemical network involving folate- and methionine-mediated methyl transfers, plays a vital role in maintaining lung epithelial cell integrity. This metabolic pathway supports nucleotide synthesis, amino acid metabolism, methylation reactions, and redox balance—all essential for regeneration under stress conditions like those seen in COPD.

A key regulatory component of this pathway is Folate Receptor alpha (FOLR1), a high-affinity transporter that facilitates the uptake of folate derivatives required to fuel 1C metabolism. Our findings demonstrate that FOLR1 is highly expressed in alveolar epithelial type II (AEC2) cells, which act as progenitor cells responsible for alveolar maintenance. This suggests a strong metabolic dependency of lung epithelial cells on folate-mediated 1C metabolism, particularly during injury repair and inflammation.

Progress

Differential Expression of FOLR1 in COPD

Single-cell transcriptomic analysis of dataset GSE173896 revealed that FOLR1 is predominantly expressed in lung epithelial populations, with particularly high expression in alveolar epithelial type II (AEC2) cells—known progenitors responsible for alveolar repair and surfactant production. Comparative analysis between healthy individuals, non-COPD smokers, and COPD patients showed that FOLR1 expression patterns were markedly altered in COPD, suggesting a potential disruption in folate uptake mechanisms (Fig,1a). Given FOLR1's role in transporting folate into cells to fuel one-carbon (1C) metabolic pathways, these findings point toward a broader dysregulation of 1C metabolism in COPD pathophysiology. This altered metabolic state may impair nucleotide synthesis, redox balance, and epigenetic regulation, contributing to epithelial dysfunction and impaired lung tissue regeneration in the diseased lung.

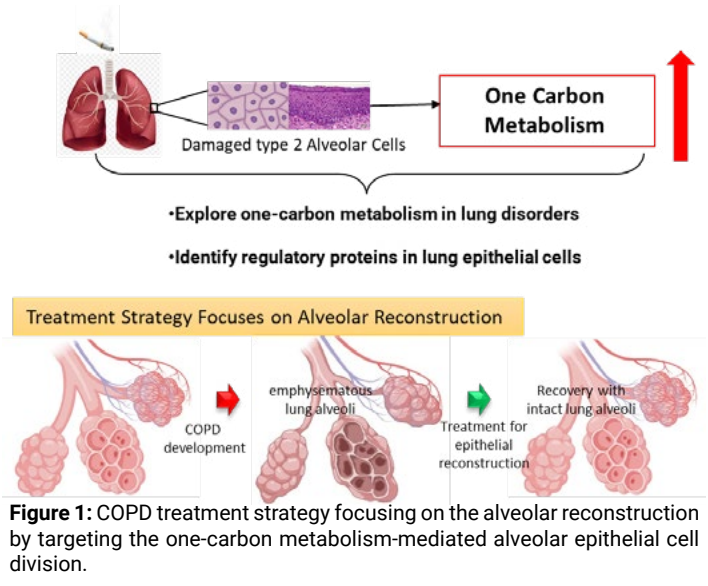


Figure 1: COPD treatment strategy focusing on the alveolar reconstruction by targeting the one-carbon metabolism-mediated alveolar epithelial cell division.

Inflammation-Induced FOLR1 Upregulation

Treatment of A549 alveolar epithelial cells with lipopolysaccharide (LPS), a well-established inducer of inflammatory stress, resulted in a significant upregulation of FOLR1 at both the protein and transcript levels, as demonstrated by Western blotting (Fig.2a) and RT-qPCR (Fig.2b) respectively. This suggests that under inflammatory conditions mimicking COPD-like stress, epithelial cells increase their capacity to import folate, likely to meet the heightened metabolic demands associated with cellular repair, antioxidant defence, and nucleotide synthesis. The induction of FOLR1 in response to LPS underscores its potential role as a stress-responsive transporter that supports one-carbon metabolism during epithelial injury and inflammation.

One-Carbon Metabolism as a Therapeutic Target

To test whether enhancing 1C flux could protect against COPD-like injury, we treated LPS-exposed A549 cells with:

- Dihydrofolate (DHF)
- 5-methyltetrahydrofolate (5-MTHF)
- Folic acid

DHF conferred the strongest protection, significantly restoring cell viability and suggesting that direct support of 1C metabolism can mitigate epithelial damage.

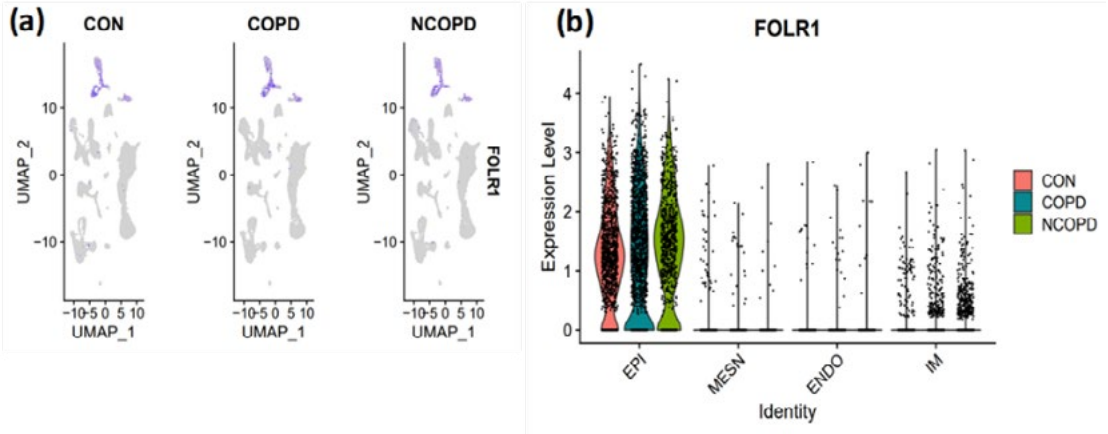


Figure 2: Single-cell RNA-seq analysis of FOLR1 expression in human lung. (a) UMAP showing FOLR1 distribution across controls, non-COPD smokers, and COPD patients. (b) Violin plots of FOLR1 expression across lung cell types. Data from GSE173896

Development of a Stabilized Dihydrofolate Formulation

Recognizing the therapeutic potential of DHF for supporting 1C metabolism, we developed a stabilized DHF formulation using ascorbic acid, sodium copper chlorophyllin, and PEG4000. Formulations were optimized as:

- Encapsulated powders
- Tablets
- Capsules

Stability was confirmed through microbiological assays (AOAC method using Lactobacillus rhamnosus), and the optimized formulation was patented.

Future Research Plans

Building upon the current findings, future efforts will focus on evaluating the therapeutic efficacy of the stabilized dihydrofolate (DHF) formulation in long-term in vivo models of COPD to assess its ability to mitigate chronic inflammation and support lung tissue regeneration. In parallel, we aim to perform metabolic flux analysis of one-carbon (1C) pathway intermediates in both normal and COPD-affected lung epithelium to elucidate metabolic imbalances contributing to disease pathology.

Additionally, we plan to investigate the transcriptional and post-translational regulation of FOLR1, to better understand how its expression is modulated during inflammatory stress and how it integrates with broader cellular signalling networks. Finally, the project will explore potential synergistic interactions between DHF and existing COPD therapeutics, with the goal of developing combinatorial strategies that enhance treatment efficacy and address both symptomatic and regenerative aspects of the disease.

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

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, Complete Application filing date: 26/02/2025, Application No. 202411023759.

PCT Application of patent filed on 19.03.2025, PCT/IN2025/050394.

Dr. Bijesh P., Scientist

Group Members: Sunita Das, UGC-JRF; Anjali E., UGC-JRF; Amrita Gond, UGC-JRF; Ananyo Kumar Ghosh, UGC-JRF; Shreyashree Jana, Project Assistant

Collaborator: Dr. Vikas Singh Chauhan, Chief Scientist, 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.

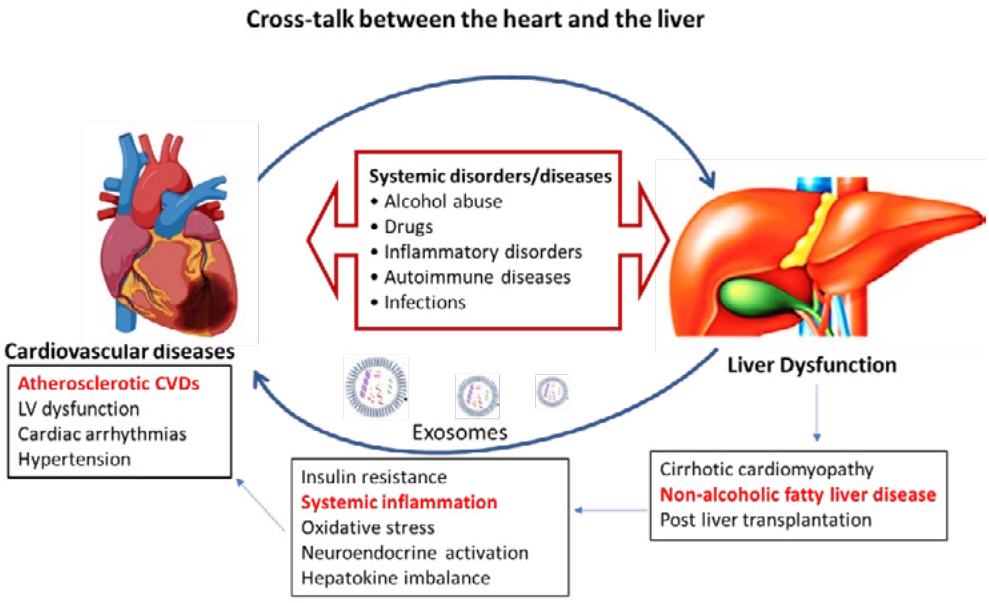
My research aims to elucidate the early molecular events and inter-tissue communication that contribute to the pathogenesis of coronary artery disease (CAD) and non-alcoholic fatty liver disease (NAFLD), with a particular focus on extracellular vesicles.

Progress made

Characterizing Liver-Derived Exosomal Proteome in Atherosclerosis

Small extracellular vesicles (sEVs), or exosomes, are increasingly recognized as critical mediators of intercellular communication in various pathophysiological conditions, including CVDs. Although the liver–cardiovascular axis is clinically relevant, the role of liver-derived sEVs in modulating atherogenesis is poorly understood.

We have successfully isolated exosomes from macrophage-conditioned media and human plasma using ultracentrifugation techniques. Their morphology and size were confirmed via dynamic light scattering (DLS) and cryo-electron microscopy. The western blotting of exosome-specific markers CD63 and TSG101 in human plasma showed the presence of exosomes. Proteomic analysis by LC-MS revealed significant differences in the protein cargo of exosomes derived from control versus cholesterol-treated macrophages. Ongoing studies using ApoE$^{-/-}$ mice aim to map changes in the hepatic exosomal proteome during atherosclerosis progression and to understand the link between hepatic exosomes and atherosclerosis severity.



Evaluation of the role of Plasmalogens on hepatic steatosis-associated 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. Using a high-fat, cholesterol-rich diet (HFCD) rat model, we observed hallmark features of NAFLD and a significant reduction in hepatic plasmenyl ethanolamine (PlsEtn) levels. Our preliminary data suggest that dietary supplementation with plasmalogens may mitigate steatosis and its pro-atherogenic consequences. We have shown that one of the plasmalogens further increased the lipid accumulation significantly, while it alone has no effect. We need to investigate the effect of other plasmalogens, individually and in combination, on steatosis in the hepatocytes. 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.

Uncovering the Role of Calicin in Atherosclerosis

Calicin, originally described as an actin-binding protein specific to spermatozoa, was recently found to be differentially expressed in patients with ST-elevation myocardial infarction (STEMI). Despite its known role in nuclear structure and sperm motility, its function in cardiovascular biology is unknown.

Calicin, initially described as a sperm-specific actin-binding protein, was recently implicated in cardiovascular disease (CVD), with altered expression observed in ST-elevation myocardial infarction (STEMI) patients. To explore its potential role in atherosclerosis, we first confirmed its expression across multiple tissues in ApoE^-/- mice, including the heart, kidney, and testis, by Western blotting—indicating a broader biological relevance. We optimized oxidized LDL (ox-LDL) concentrations to induce foam cell formation in macrophages and determined that 200 µg/mL led to significant lipid accumulation and ~50% cell death. Using this model, we assessed calicin expression at increasing ox-LDL doses. Western blot and confocal imaging revealed a biphasic expression pattern, with calicin upregulated at 100 µg/mL but downregulated at 200 µg/mL, suggesting a dose-dependent regulatory role under lipid stress. Immunoprecipitation and mass spectrometry identified actin and lamin as interacting partners of calicin. Confocal microscopy further showed perinuclear localization and partial colocalization with actin filaments, pointing to a role in cytoskeletal organization and nuclear-cytoskeletal interactions—key processes during foam cell formation and macrophage migration.

These findings suggest that calicin may influence atherogenesis through effects on cytoskeletal remodeling and lipid handling. Its complex expression dynamics and unidentified secretion route highlight the need for mechanistic studies to define its role in atherosclerosis.

Future Research Plans

- Multi-Omics Profiling of Liver-Derived Exosomes
- Perform integrated lipidomic and metabolomic analyses of hepatic exosomes in NAFLD and atherosclerosis models.
- Validate candidate exosomal proteins differentially expressed in CAD and explore their mechanistic roles.
- Molecular Characterization of Calicin in Atherosclerosis
- Investigate co-expression patterns and interacting partners of calicin to elucidate its involvement in pathways regulating inflammation, macrophage and smooth muscle cell function.
- Therapeutic Potential of Plasmalogens and PEDS1 Modulation
- Validate the protective role of plasmalogens in ApoE$^{-/-}$ mouse models of atherosclerosis.
- Assess the effect of PEDS1 overexpression (an enzyme critical for plasmalogen biosynthesis) on hepatic steatosis.
- Develop and test small-molecule agonists of PEDS1 as potential therapeutic agents.

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. Malladi N, Lahamge D, Somwanshi BS, Tiwari V, Deshmukh K, Balani JK, Chakraborty S, **Alam MJ**, Banerjee SK. (2024) Paricalcitol attenuates oxidative stress and inflammatory response in the liver of NAFLD rats by regulating FOXO3a and NFκB acetylation. *Cell Signal* 121:111299.

2. 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.

Md. Jahangir Alam, Scientist

Group Members: Arkya Roy, UGC-JRF; Gopal Dolai, UGC-JRF; Subhadeep Mandal, ICMR-JRF

Collaborators: Dhabalesar Patra, PhD, Structural Biology & Bioinformatics Division, CSIR-IICB, Kolkata; Ramu Adela, PhD, Department of Pharmacy Practice, NIPER-Guahati; Prakas Chandra Mondal, M.D., HOD Apollo Heart Institute, Kolkata

Dr. Joy Chakraborty and his group members

Determining the role of VDAC1 (voltage dependent anion channel 1) on efficient PHB2 (prohibitin 2) exposure during mitophagy

Research Activities

Exposure of inner mitochondrial membrane resident protein PHB2 (prohibitin 2) during autophagic removal of depolarized mitochondria (mitophagy) depends on the ubiquitin-proteasome system. This uncovering facilitates the PHB2 interaction with phagophore membrane-associated protein MAP1LC3/LC3. It is unclear whether PHB2 is exposed randomly at mitochondrial rupture sites. Prior knowledge and initial screening indicated that VDAC1 (voltage dependent anion channel 1) might play a role in this phenomenon. Through in vitro biochemical assays and imaging, we have found that VDAC1-PHB2 interaction increases during mitochondrial depolarization. Subsequently, this interaction enhances the efficiency of PHB2 exposure and mitophagy. To investigate the relevance in vivo, we utilized porin (equivalent to VDAC1) knockout Drosophila line. Our findings demonstrate that during mitochondrial stress, porin is essential for Phb2 exposure, Phb2-Atg8 interaction and mitophagy. This study highlights that VDAC1 predominantly synchronizes efficient PHB2 exposure through mitochondrial rupture sites during mitophagy. These findings may provide insights to understand progressive neurodegeneration.

Future Research Plans

- Determining the relation between mitochondrial dynamics related proteins and VDAC1.
- Identification of the role of VDAC1 on mitochondrial fission site marking
- Quantifying the distribution of VDAC1 in different mitochondrial populations, correlation with the polarization level.

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. 47.9 lakh. (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. 178 lakh (MMP075201).
3. Identification of modulators from natural origins that impede β-amyloid induced proteasome inhibition. Funding agency: Council of Scientific & Industrial Research (CSIR), 2024-2026. 50 lakh (RDS000001).

Publications

1. Roy, M., Nandy, S., Marchesan, E., Banerjee, C., Mondal, R., Caicci, F., Ziviani, E., Chakraborty, J. (2025) Efficient PHB2 (prohibitin 2) exposure during mitophagy depends on VDAC1 (voltage dependent anion channel 1). *Autophagy*, **21**, 897-909.
2. Banerjee, C., Tripathy, D., Kumar, D., Chakraborty, J. (2024) Monoamine oxidase and neurodegeneration: Mechanisms, inhibitors and natural compounds for therapeutic intervention. *Neurochemistry International*. **179**,105831.

Dr. Joy Chakraborty, Senior Scientist

Group Members: Moumita Roy, CSIR-Project Associate; Sumangal Nandy, DBT-Project Associate; Aishi Majumder, UGC JRF; Soumik Kumar Sarkar, UGC JRF

Collaborators: Dr. Deepak Kumar, CSIR-IICB, Kolkata; Dr. Krishnananda Chattopadhyay, CSIR-IICB, Kolkata; Dr. Subhas C. Biswas, CSIR-IICB, Kolkata; Dr. Ranjan Jana, CSIR-IICB, Kolkata

Dr. Partha Chakrabarti and his group members

Role of deubiquitinase JOSD1 in acute and chronic liver disease

Research Activities

We have identified and validated a deubiquitinating enzyme (DUB), JOSD1, as a modulator of cellular apoptosis during periods of hepatic proteotoxicity. Hepatic proteotoxicity can arise due to a plethora of events, of which dysfunction of components of the Ubiquitin-Proteasome pathway is a prominent factor. Bortezomib, which is a proteasomal inhibitor, has been approved for therapy in multiple myeloma patients. However, there have been cases of hepatic toxicity in patients treated with Bortezomib. Taking cue from these, we hypothesized that proteasomal inhibition poses a significant threat to hepatocytes and causes hepatocellular injury. We therefore sought to seek for deubiquitinating enzymes which might play a role in either exacerbating or alleviating hepatocellular injury during periods of proteotoxic stress.

We have individually knocked down 96 DUBs in HepG2 cells and checked for the status of cellular apoptosis and cell viability by fluorescence and luminescence respectively for each DUB under conditions of hepatic proteotoxicity. We stumbled upon JOSD1 whose depletion showed a reciprocal relationship between apoptosis and viability and seemed to mainly exert a protective effect against apoptosis. We then sought to thoroughly validate JOSD1 through diverse assays by either knocking it down or overexpressing it. JOSD1 markedly abrogated apoptosis in HepG2 cells and primary mouse hepatocytes under proteotoxic stress. Further, there was a significant accumulation of JOSD1 around cellular membrane under proteasomal inhibition conditions. We generated a JOSD1 C36A enzymatically inactive mutant and showed that this mutant was unable to exert any protective effect in hepatic proteotoxic conditions. We then sought to look for putative candidates which were working in close association with JOSD1 in bringing about the observed phenotype. We came across SOCS1 whose protein expression levels increased concomitantly with JOSD1 under

proteotoxicity. We performed a series of co-immunoprecipitation studies in HepG2 and primary mouse hepatocytes to confirm JOSD1-SOCS1 interaction. Further, we established that JOSD1 was dependent on SOCS1 to exercise its protective property because depletion of SOCS1 in JOSD1 overexpression condition could not reverse apoptosis whereas overexpression of SOCS1 in JOSD1 depletion conditions could mitigate apoptosis in hepatocytes exposed to proteotoxic stress. We have even validated JOSD1 as a protective molecule in an *in vivo* murinemodel of acute proteotoxicity and showed that knocking down JOSD1 or overexpression of JOSD1 by intravenous adenoviral administration hugely modulated hepatic apoptosis when these mice were given intraperitoneal injection of Bortezomib (Figure 1).

JOSD1 is a lesser-known DUB and not much has been studied about it. Our study is unique in its essence because we are reporting the role of JOSD1 for the first time in hepatocytes under a certain kind of stress. We have integrated the reported studies on JOSD1 into our study and shown how each aspect plays its part in protecting hepatocytes from apoptosis under proteotoxic stress. We believe that our findings are of significant translational importance as JOSD1 can emerge as a potent candidate for abrogating hepatocellular injury in extensive proteotoxic conditions.

Future Research Plans

- Discovery of repertoire of DUBs which could potentially mitigate drug induced liver injury or chronic proteotoxicity.
- Delineate detailed mechanistic underpinnings of DUB-mediated hepatoprotection.
- Chart out potential translational paths by targeting DUB class of enzymes.

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. Supekar R, Sarkar J, Chakrabarti P, Biswas S. (2025) Diagnostic challenges due to hepatitis B virus surface antigen mutations outside the major hydrophilic region. *Arch Virol.* **170**:71.
2. Datta D, Kundu R, Basu R, Chakrabarti P*. (2024) Pathophysiological hallmarks in type 2 diabetes heterogeneity (review). *Diabetol Int.* **16**:201-222.
3. Chowdhury S, Sen A, Das D, **Chakrabarti P**. (2024) Deubiquitinase JOSD1 tempers hepatic proteotoxicity. *Cell Death Discov.* **10**:405.
4. Maity SK, Das Sharma A, Sarkar J, Chaudhuri T, Tantia O, Chakrabarti P. (2024) Adipose tissue-derived adipsin marks human aging in non-type 2 diabetes population. *BMJ Open Diabetes Res Care*.**12**:e004179.
5. Mandal P, Paul D, Sharma H, Saha S, Chakrabarti P, Goswami RK. (2024) Structure-Activity Relationship Study of Biselyngbyolide B Reveals Mitochondrial Fission-Induced Cytotoxicity in Cancer. *ACS Med Chem Lett*. **15**:696-705.

Patents

Quinazolinones Derivatives For Treatment Of Non-Alcoholic Fatty Liver Disease, Preparation And Use Thereof. Talukdar Arindam, **Chakrabarti Partha**, Sarkar Dipayan, Chowdhury Saheli, Goon Sunny, Das Subrata, Das Nirmal, Sarkar Dipika. International Application No. PCT/IN2021/050621, dated 25 June 2021; Priority Application No.: 202011027502 dated 29 June 2020. WO2022003712. Indian patent granted on 26.2.2025

Invited Lectures

1. Therapeutic Opportunities in Steatotic Liver Disease. JISCONPH, Kolkata, 21.11.2024
2. Proteostasis in Steatotic Liver Disease, Serampur College, 11.2.25
3. Heterogeneity in Type 2 Diabetes, NRS Medical College, Kolkata, 8.2.2025

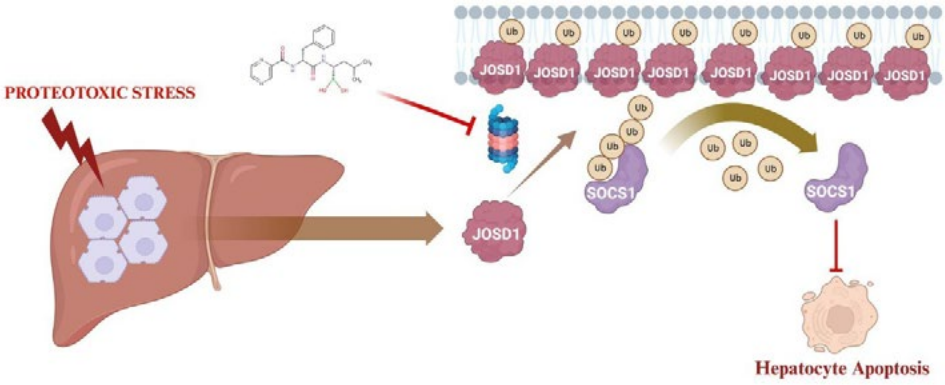


Figure 1. Schematic of the hepatoprotective mechanism of JOSD1. Chronic proteotoxic stress or Bortezomib-induced proteasomal inhibition leads to accumulation of monoubiquitinated JOSD1 on the plasma membrane where it deubiquitinates SOCS1 and prevents hepatocyte death.

Dr. Partha Chakrabarti, Senior Principal Scientist

Group Members: Saheli Chowdhury, 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; Supriyo Bera, CSIR project SRF; Asmita Bhar, DBT project JRF

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

Dr. Prem Prakash Tripathi and his group members

Transient Neurogenesis and Long-Term Depletion of Neural Progenitors in the Dentate Gyrus After Kainic Acid-Induced Seizures

Research Activities

The adult mammalian hippocampus, particularly the dentate gyrus (DG), retains a unique capacity for neurogenesis—an intrinsic response to diverse pathological insults, including neurodegeneration and injury. This regenerative process is thought to underlie limited but potentially significant neuronal repair and functional recovery. However, the long-term sustainability and consequences of this endogenous regeneration remain largely unexplored. In our study, we investigated the dynamics of hippocampal neurogenesis in response to excitotoxic injury using the kainic acid (KA)-induced status epilepticus (SE) model, which simulates key aspects of human temporal lobe epilepsy and neurodegeneration. This well-established in vivo model enabled us to examine the acute regenerative responses and the subsequent chronic effects on the neurogenic niche.

Following kainic acid-induced seizures, we observed a robust activation of the neurogenic cascade within the subgranular zone (SGZ) of the dentate gyrus. Immunohistochemical analyses revealed significant proliferation and migration of neural stem/progenitor cells (NSCs), as evidenced by BrdU incorporation and co-localization with early neuronal markers such as TuJ1 and mature neuronal markers such as NeuN. The presence of BrdU+TuJ1+ and BrdU+NeuN+ cells at the injury sites in CA3 and CA1 subfields confirmed that newly generated neurons had not only emerged from the SGZ but also migrated to the damaged hippocampal areas, suggesting an active, albeit transient, attempt at structural and functional restoration.

To better understand the impact of KA-induced seizures, we assessed neuronal loss across hippocampal subfields, particularly focusing on CA1 and CA3. Using TUNEL staining to detect apoptotic DNA fragmentation, we found extensive neuronal death primarily within the pyramidal layers of these regions, supporting the premise that KA administration induces excitotoxicity via overstimulation of glutamate receptors. This localized damage appears to be a key trigger for subsequent neurogenesis within the DG.

To quantify neurogenesis temporally, BrdU was administered to adult mice experiencing SE, either over a 3-day or 7-day period, beginning on the 3rd or 5th day post-KA treatment. Brains were harvested and analyzed shortly after the final BrdU injection. Our results showed a marked increase in BrdU+ cell numbers within the DG compared to controls, confirming that seizures substantially elevate cellular proliferation in the neurogenic niche. These findings corroborate earlier reports indicating seizure-induced neurogenic bursts as a reparative response.

To elucidate the long-term fate of neural progenitors born in the acute phase after SE, a pulse-labeling strategy was employed on the third day post-KA. Mice received multiple BrdU injections over 12 hours and were subsequently sacrificed 45 days later. Analysis of hippocampal sections at this time point revealed increased numbers of BrdU+ cells, indicating survival and differentiation of early progenitors. Co-labeling with TuJ1 and NeuN further verified the presence of both neuroblasts and mature neurons, suggesting that these early-activated progenitors contribute to neuronal replacement and integration into the hippocampal circuitry.

Despite this initial regenerative burst, long-term consequences were also evident. At 240 days post-KA treatment, we assessed the expression of several key markers of neural stem and progenitor cell activity, including Ki67, HopX, and Sox2. All three markers showed significantly diminished expression within the DG of KA-treated animals when compared to age-matched controls. These data imply that the early, seizure-induced proliferation of progenitor cells may lead to an eventual depletion of the finite NSC pool, resulting in reduced neurogenic capacity in aged animals. To further explore this hypothesis, we evaluated the continued maturation and survival of neurons generated from intermediate progenitor cells (IPCs) over time. BrdU+NeuN+ cells were quantified at the 240-day mark, revealing a substantial decline in newly generated neurons in KA-treated mice compared to controls. This long-term reduction suggests a progressive impairment of the neurogenic niche, likely due to premature exhaustion of stem cell reserves and altered microenvironmental cues.

We extended our investigation by conducting a longitudinal analysis of proliferative and neurogenic marker expression from day 10 to day 240 post-SE. The expression of Ki67 and PCNA declined significantly over time in KA-treated animals, indicating a sustained suppression of cell proliferation. Notably, while control animals showed expected age-related declines, the rate and extent of reduction were significantly greater in the KA group. By day 240, quantitative analyses showed a profound suppression of neurogenesis-related markers, highlighting the long-term detrimental effects of early-life SE on the hippocampal neurogenic niche.

Future Research Plan

- Our future investigations aim to characterize the morphological and functional transformations of various hippocampal cell types following SE. Specifically, we plan to examine whether early activation of radial NSCs (HopX+GFAP+) leads to their conversion into reactive astrocytes (S100β+GFAP+), signifying a shift toward a gliogenic fate at the expense of neurogenesis. Such a transformation could contribute to the loss of regenerative potential in the hippocampus and perpetuate a cycle of inflammation, scarring, and functional decline.

- Additionally, we propose to explore whether the observed alterations in neurogenesis correspond with changes in hippocampus-dependent cognitive functions. A battery of behavioral tests—including novel object recognition, spatial memory tasks, and assessments of mood-related behaviors—will be employed to evaluate the functional impact of neurogenic niche disruption. Parallel investigations into hippocampal synaptic plasticity, including long-term potentiation (LTP), may offer mechanistic insights into how impaired neurogenesis translates to cognitive deficits.

- In summary, our findings delineate a biphasic response of the hippocampal neurogenic niche to kainic acid-induced seizures. In the acute phase, there is a strong but transient neurogenic activation, potentially aimed at neuronal repair. However, this initial burst appears to come at a cost—long-term depletion of the progenitor pool and impairment of sustained neurogenesis. These outcomes suggest that while the adult brain harbors intrinsic regenerative capabilities, their overactivation in pathological contexts may lead to premature exhaustion of the niche and compromised repair potential later in life.

- Understanding the cellular and molecular mechanisms governing this transition from neurogenic activation to exhaustion will be critical for designing targeted interventions. Future therapeutic approaches may need to balance the promotion of neurogenesis with strategies that preserve the long-term integrity and self-renewal capacity of the neural stem cell population. Ultimately, such insights will be vital for developing effective treatments for neurodegenerative disorders, traumatic brain injuries, and epilepsy-related cognitive impairments.

Extramural / CSIR Funding

Evaluation of Neuroprotective potential of Brahmi Ghrita, Panchgavya Ghrita and Ayush 56 in epilepsy model, its functional significance and mechanism (GAP-479), Agency- CCRAS, Ministry of Ayush (2024-2026) (PI) 44 Lakhs

Publications

1. Bose, S., Saha, P., Alam, M.T., Chatterjee, B., Sarkar, M., Dixit, A.K., Kumar, D., Pathak, R.K., Tripathi, P.P., Srivastava, A.K. (2025) Inhibition of DNA polymerase eta-mediated translesion DNA synthesis with small molecule sensitises ovarian cancer stem-like cells to chemotherapy. *Br J Pharmacol*.

2. 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.

Patents

A recombinant construct for screening drugs against sars-cov-2 spike protein Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava, filing date 01/02/2025, US Patent App. 18/704,638.

Dr. Prem Prakash Tripathi, Senior Scienstist

Group Members: Jhilik Dey, UGC-SRF; Sreyashi Chandra, Project Associate; Rahul Mallick, CSIR-SRF; Aniket Dey, CSIR-JRF; Minakshi Biswas, Project Assistant

Collaborators: Amit Srivastava, 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

Cloning of *msrA* and *ms* in pETDuet-1 vector is being undertaken.

Amplification of *ms* and *msrA* from genomic DNA of *S.* Typhimurium has been successful using the designed primers. The amplified PCR products were gel purified using gel extraction kit.

The next steps of cloning which involve RE digestion, ligation, transformation *etc* are being carried on.

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

Book Chapters

Sarkhel, R, Mahawar, M. (2024) SFRR- INDIA: Discover 2024, International conference on "Developments in the science of oxidative stress and redox medicine", Abstract Book, BARC, Mumbai.

Member of Society

1. Member, Society of Veterinary Biochemists and Biotechnologists of India (SVBBI), Bhubaneshwar, India, Life membership.
2. Member, Indian Poultry Science Association (IPSA), India, Life membership.

Dr. Ratanti Sarkhel, Scientist

Group Members: Ms. Puja Kundu, UGC- JRF

Dr. Rupasri Ain and her group members

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

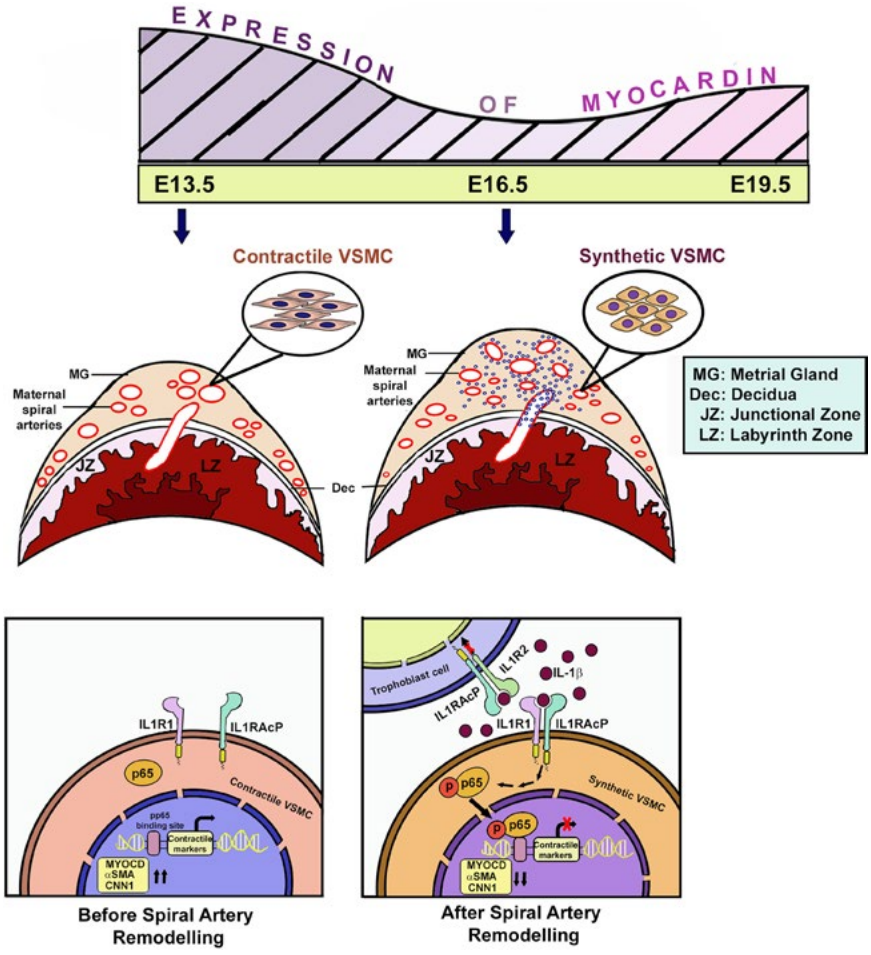
Research Activities

We are interested in how early trophoblast development is regulated by non-coding RNAs, 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.

IL1β-NFκβ-Myocardin signaling axis governs trophoblast-directed plasticity of vascular smooth muscle cells

Vascular smooth muscle cell (VSMC) plasticity is fundamental in uterine spiral artery remodeling during placentation in Eutherian mammals. Our previous work showed that the invasion of trophoblast cells into uterine myometrium coincides with a phenotypic change of VSMCs. Here, we elucidate the mechanism by which trophoblast cells confer VSMC plasticity. Analysis of genetic markers on E13.5, E16.5, and E19.5 in the rat metrial gland, the entry point of uterine arteries, revealed that trophoblast invasion is associated with downregulation of MYOCARDIN, α-smooth muscle actin, and calponin1, and concomitant upregulation of Smemb in VSMCs. Myocardin overexpression or knockdown in VSMCs led to upregulation or downregulation of contractile markers, respectively. Co-culture of trophoblast cells with VSMCs decreased MYOCARDIN expression along with compromised expression of contractile markers in VSMCs. However, co-culture of trophoblast cells with VSMCs overexpressing MYOCARDIN inhibited their change in phenotype, whereas, overexpression of transactivation domain deleted MYOCARDIN failed to elicit this response. Furthermore, the co-culture of trophoblast cells with VSMCs led to the activation of NFκβ signaling. Interestingly, despite producing IL-1β, trophoblast cells possess only the decoy receptor, whereas, VSMCs possess the IL-1β signaling receptor. Treatment of VSMCs with exogenous IL-1β led to a decrease in MYOCARDIN and an increase in phosphorylation of NFκβ. The effect of trophoblast cells in the downregulation of MYOCARDIN in VSMCs was reversed by blocking NFκβ translocation to the nucleus. Together, these data

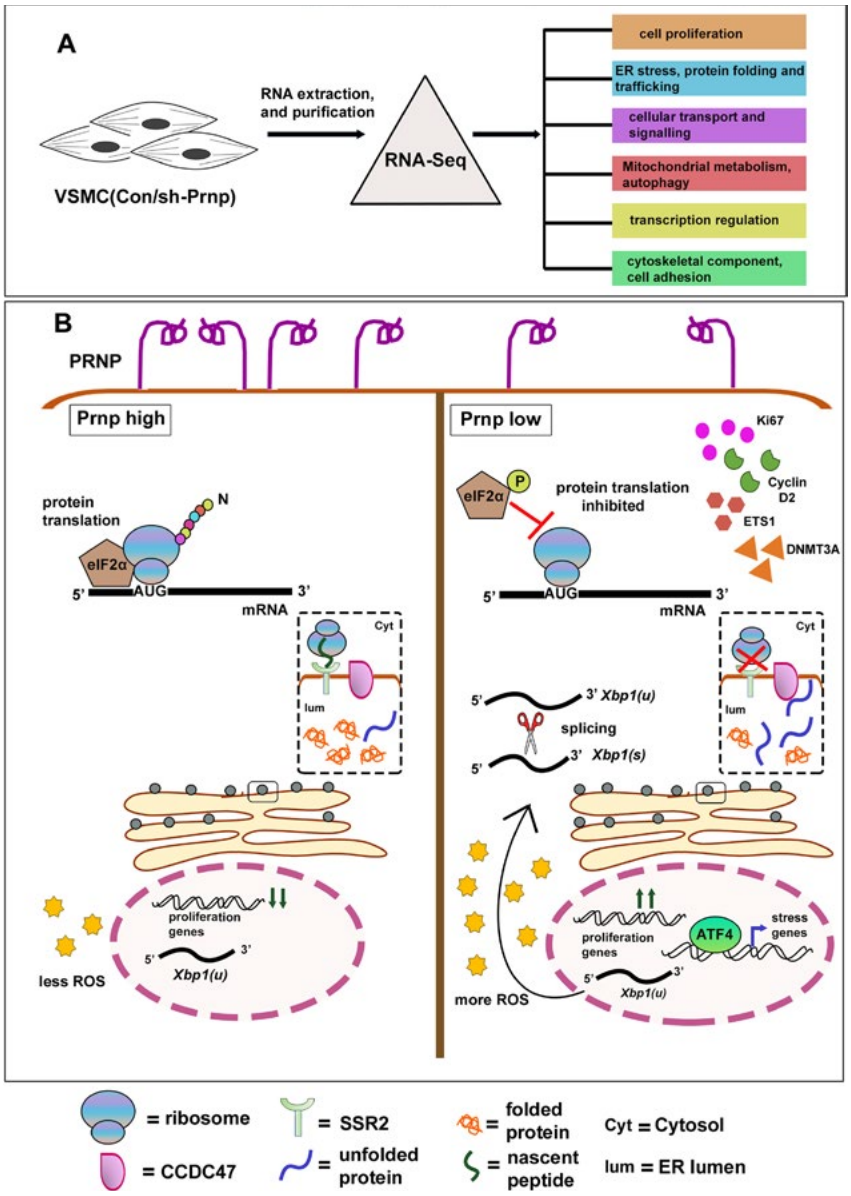
highlight that trophoblast cells direct VSMC plasticity, and trophoblast-derived IL1-β is a key player in downregulating MYOCARDIN via the NFκβ signaling pathway.



This study highlights that trophoblast cells direct VSMC phenotype switching by downregulating MYOCARDIN. In addition, trophoblast-derived IL-1β is one of the molecular triggers of this important physiologicalevent. Our results demonstrated that activation of IL-1β signaling leading to NFκβ phosphorylation and its translocation to the nucleus is pivotal in the downregulation of MYOCARDIN. Furthermore, MYOCARDIN is a key regulator of VSMC plasticity, leading to their de-differentiation.

Pleiotropic Function of Cellular Prion Protein: Encompassing Endoplasmic-Reticulum Stress, Cell Proliferation in Vascular Smooth Muscle Cells

Cellular prion protein (PRNP) has been implicated in various physiological processes in different cell types, for decades. Little has been known how PRNP functions in multiple, yet related processes within a particular system. In our current study, with the aid of high-throughput RNA-sequencing technique, we have presented an overall transcriptome profile of rat vascular smooth muscle cells (VSMCs) with Prnp knockdown. Fifty-one genes were found to be differentially regulated, of which, genes involved in cell proliferation and endoplasmic reticulum (ER) stress pathway, show significant upregulation. That PRNP negatively regulates VSMC proliferation, has been demonstrated using immunoblot assays, BrdU incorporation assay and Ki-67 immunofluorescence staining. As revealed from our RNA-Seq data, ATF4, a downstream effector of the PERK arm of ER stress pathway is upregulated upon RNA interference of Prnp in VSMCs. As a result, the expression of the functional phosphorylated isoform of translation initiation factor eIF2α (p-eIF2α) is elevated. Additionally, we also showed that downregulation of Prnp leads to excess intracellular ROS accumulation, subsequently leading to splicing of Xbp1 mRNA and triggering unfolded protein response (UPR) within the cell. Therefore, our findings highlight that PRNP directly or indirectly modulates an array of biological processes and plays a pivotal role in preserving the equilibrium between excess proliferation and optimal endoplasmic reticulum function in VSMCs.



Schematic representation of a glimpse of cellular events regulated by PRNP in VSMCs. (A) Sequencing of whole RNA extracted from control and Prnp downregulated VSMCs reveals several crucial biological processes to be directly or indirectly regulated by PRNP. (B) Under normal condition, when PRNP levels are high, cells undergo controlled proliferation with proper ER function, and protein folding. Lower levels of PRNP in VSMCs, leads to increased expression of proliferation genes (Ki67, Cyclin D2, ETS1, DNMT3A). Increased proliferation takes a toll on ER health and function thus inducing ER stress. The transcription factor ATF4, a downstream effector of the PERK pathway, starts synthesizing stress-response genes. With the phosphorylation of eIF2α the protein translation machinery immediately comes to a halt. Decreased levels of PRNP also causes more ROS generation, and accumulation inside the cell. This in turn causes the splicing of the Xbp1 transcript in the cytosol. Two ER-resident proteins SSR2 and CCDC47 respectively inhibit any newly synthesized nascent peptide to enter the ER lumen whilst the already misfolded and unfolded proteins are being re-folded.

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 by cellular rendezvous involving TS cells, VSMCs and endothelial cells of the spiral arteries.

Extramural / CSIR Funding

1. Odd-skipped related-1 in cardiac hypertrophy. Department of Biotechnology (DBT), 2024-27, (BT/PR50045/CMD/150/86/2023).
2. Decoding the epigenetic foot-print in vascular smooth muscle cells induced by trophoblast cells: Implications in placental morphogenesis. Department of Biotechnology (DBT), 2024-27, (BT/PR49910/MED/97/642/2023).
3. Long non-coding RNA signature and function in trophoblast stem cell differentiation. Department of Biotechnology (DBT), 2024-27, (BT/PR51209/MED/31/474/2023).

Publications

1. Bose, R., Ghosh, M., Ain, R. (2025) Pleiotropic Function of Cellular Prion Protein: Encompassing Endoplasmic-Reticulum Stress, Cell Proliferation in Vascular Smooth Muscle Cells. *J Cell Biochem*. **126:** e30692.
2. Das P, Bose R, Paul M, Nandy D, Basak T and Ain R (2024) IL1β-NFκβ-Myocardin signalling axis governs trophoblast-directed plasticity of vascular smooth muscle cells. *FASEB J*. **38**: e23637.

Invited Lectures

1. FOXO4 and its transcriptional targets inhibit ferroptosis in trophoblast cells: Implications in IUGR. University of Delhi. International Conference on Reproductive Sciences and Molecular Medicine: Innovations in Therapeutics and Technologies (ICRSMM-2024) and 41st Annual Meet of Society for Reproductive Biology and Comparative Endocrinology (SRBCE), November, 2024.
2. Decoding cell-cell communication during spiral artery remodelling. CSIR-IICT, Hyderabad. International Conference on Reproductive Health Science with Emphasis on Innovation, Integration, and Implementation. February, 2024.
3. Invasive trophoblast cells: Guardian of cell-cell communication in placental morphogenesis. ACTREC, Navi Mumbai, 46th Annual meeting of Indian Society of Cell Biology, January, 2024.

Conferences Attended

46th Annual meeting of Indian Society of Cell Biology, ACTREC, Navi Mumbai, January, 2024.

Dr. Rupasri Ain, Chief Scientist

Group Members: Tamal Kanti Gope, CSIR-SRF; Swarnali Dey, UGC-SRF; Priyanka Das, UGC-SRF; Madhubanti Ghosh, CSIR-SRF; Poulomi Sarkar, CSIR-SRF; Debankur Pal, CSIR-SRF; Md Arsadullah Ansari, CSIR-JRF; Shreya Deb, WISE-Kiran JRF; Dr. Sarbani Saha, WISE-Kiran Post-doctoral fellow.

Dr. Sib Shankar Roy and his group members

Molecular mechanisms and pathophysiology of cancer metabolism

Research Activities

Metabolic alterations are the key features of tumor cells that are acquired by the cells to adapt unfavorable conditions that exist in Tumour microenvironment (TME). Both intrinsic and extrinsic factors may concurrently contribute to influence cellular bio-energetics and mutations in oncogenic transcription factors alters signalling networks, eventually contributing to metabolic reprogramming. Among the important oncogenic transcription factors, proto-oncoprotein Ets1 hailing from the Ets family, regulates several aspects of cancer, including angiogenesis, metastasis, resistance to chemotherapy, etc. Several TME-derived factors assist the developing tumour cells to gain numerous survival advantages. Our present research aims to comprehend how Ets1 regulates glycolytic genes followed by metabolic state of cancer cells in response to a key TME-derived signal. The relevance of structural and functional alterations in mitochondria, the primary site of bioenergetic modulations within the cellular system is directly linked with oncogenesis in tumour cells. Considering this we focused on ETS1 in regulating the mitochondrial dynamics in the context of cancer progression. Modulating the function of transcription factors 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 on ETS1-DAXX interactions was performed that mediate diverse aspects of carcinogenesis.

Alterations in lipid metabolism have immense importance developing carcinogenic. Lipogenesis as well as the oxidation of fatty acids (FAO) are crucial components of de-regulated lipid metabolism. Considering this, we studied the possible interactions of adipocytes and cancer cells as well as unvelled the detailed mechanism of SREBP1 and CPT1-mediated oncogenic advancement. The role of carnitine palmitoyil transferase 1(CPT1) in regulating FAO during oncogenesis have been studied in our laboratory and it is important considering its therapeutic importance.

One of the most effective strategies for managing cancer is metabolic targeting and nutrient transporters as well as ion exchangers. In this light, studying the solute carrier family of proteins that are involved in glutamine (essential nutrient of tumor cells) or metabolite transfer through mitochondrial membrane or plasma membrane of tumor 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. Taken together, our laboratory focuses on understanding the metabolic alterations at different layers that are directly or indirectly associated with tumorigenesis.

Aims and Objectives

- Implications of mitochondrial structure-function aberrations on metabolic fate of cancer cells and associated oncogenesis.
- The role and regulation of Ets1 oncogenic transcription factor in oncogenesis.
- The implications of nutrient/metabolite transporters on tumorigenesis and identification of potential therapeutic targets for therapeutic intervention
- The regulation Carnitine Palmitoyiltranferase-1 in regulating altered fatty acid oxidation in tumour cells.

Work Achieved

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. 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.

Oncogenic transcription factor in metabolic alteration: 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 transcriptional 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.

Altered Fatty Acid Oxidation via CPT1A promotes epithelial-to-mesenchymal transition in ovarian cancer

Metabolic alterations are increasingly recognized as fundamental features of cancer. Recent studies have highlighted the involvement of altered fatty acid oxidation (FAO) at different stages of tumor development. As the rate-limiting enzyme of FAO, CPT1 plays a crucial role in these metabolic adaptations in cancer cells. However, the regulation of CPT1 expression and activity in tumor cells still requires detailed investigation. Our studies reveal that CPT1A, a variant of CPT1, is significantly upregulated in ovarian cancer (OC) and correlates with poor prognosis. Inhibition of CPT1A, either by siRNA-mediated knockdown or by etomoxir, reduces the migratory and invasive properties of the OC cells. CPT1A exerts these effects by modulating the expression of epithelial-to-mesenchymal transition (EMT) associated genes at transcriptional and protein levels. Growth factors like transforming growth factor beta (TGFβ) are abundant in the tumor microenvironment and modulate the metabolic profile of tumors, thereby promoting EMT. Our findings demonstrate that TGFβ treatment increases the rate of FAO in ovarian cancer cells. Mechanistically, TGFβ mediates this effect by enhancing CPT1A expression and its enzymatic activity in OC cells through an AMPK-dependent pathway. Additionally, we identified NRF2 as a potential transcriptional regulator of CPT1A within the context of TGFβ-AMPK signaling. Finally, inhibiting CPT1A successfully attenuates TGFβ-induced EMT in ovarian cancer cells. Cumulatively, our study underscores the role of CPT1A-mediated FAO in facilitating ovarian cancer progression through TGFβ-induced EMT.

Future Research Plans

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. In recent years inhibitors/modulators of different metabolic pathways have earned significant attention from the oncologists, due to their importance. Many small moleculue inhibitors of different pathways/molecular targets are in clinical trial and there are a lot of hope in these molecules in terms of future therapeutics. Our laboratory is also interested in extending this study to culminate towards a translational output.

Extramural / CSIR Funding

CSIR 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" Sanction No. 8/26/HCP-40/2021-TMD-IND INT; Duration: 1/4/21 to 31/3/26

Publications

1. Chatterjee, P., Ghosh, D., Chowdhury, S., Roy, SS. (2024) ETS1 drives EGF-induced glycolytic shift and metastasis of epithelial ovarian cancer cells. *BBA - Molecular Cell Research*, **1871**, 119805.
2. Ghosh, S., Tanbir, E., Mitra, T., Roy, SS. (2024) Unveiling stem-like traits and chemoresistance mechanisms in ovarian cancer cells through the TGFβ1-PITX2A/B signaling axis. *Biochemistry & Cell Biology*, **102**,1–16.

Book chapter

Shreya Bandopadhyay, Udit Dey, Parna Chakraborty, Pallabi Debnath, Subhadip Kundu, Debabrata Laik, Sib Sankar Roy* (2024) The Role of Matrix Metalloproteinases MMP2 and MMP9 in Ovarian Cancer Progression; Chapter-9; Handbook of Proteases in Cancer: Cellular and Molecular Aspects; Ed by Sajal Chakraborti, eBook Published 13 December 2024; eBook ISBN9781003394716; CRC Press; DOIhttps://doi.org/10.1201/9781003394716.

Invited lectures

1. Chaired a session of 44th Annual Meeting of the Indian Association for Cancer Research (IACR), held at Biswa Bangla Convention Centre, Kolkata, 16-18 January, 2025.
2. Invited Lecture as Resource person in Animal Science, Regional Science Congress, Govt of West Bengal, held at Rampurhat College, January 10, 2025. Title of the talk: 'Mechanistic Understanding and Therapeutic Strategies of Women-Centric Cancer.'
3. Acted as Resource Person on Cancer Biology, Ayush CME and delivered lecture on Ayush CME held at CSIR-IICB, during February 03-08, 2025. Title of the Talk: 'Altered metabolism of tumor cells: the causes, consequences and therapeutic interventions.'
4. Invited Lecture at National Symposium on Cancer Biology and Management, organized by CCSAHDR, in collaboration with NASI, India, held at Sister Nivedita University, on July 23, 2024. Title of the talk: 'Metabolic Adaptations Acquired by the Tumour Cells'.
5. Invited lecture, Conference on Microbiology, MTIM-2024, held at St Xaviers College, during October 04-05, 2024, Title of the talk: 'Metabolic Reprogramming In Tumour Cell.'
6. Plenary Lecture, National Symposium on Physiology and Annual Meeting of Physiology Society of India (Physicon-2024), held at Tripura University, Agartala, during November 15-17, 2024. Title of the Talk: 'Metabolic Reprogramming in Tumor Cells: Mechanism and Translational Implications Towards Disease Management.

Dr. Sib Sankar 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

Collaborators: Satinath Mukhopadhyay, SSKM Hospital, Kolkata, India; Dr. A. Mukherjee, PhD, KolGOTrg, Kolkata; Dr. S. Chakraborty S, CSIR-IICB, Kolkata.

Dr. Subhas C. Biswas and his group members

Neurodegenerative Diseases: Understanding pathophysiology to identify potential therapeutic targets

Research Activities

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

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.

Underlying cause of PD is severe loss of the dopaminergic neurons in the substantia nigra pars compacta (SNpc) of the midbrain. These neurons are responsible for producing dopamine, which is necessary for basal ganglia mediated control of motor functions. Loss of dopamine results in the characteristic symptoms of PD, including tremors, rigidity, gait and difficulty in walking. The etiology of PD is not clearly known, but hereditary and environmental factors are implicated. A few genes have been found to be responsible for the familial type of the disease; most cases of PD are sporadic. While treatments are available to help manage its symptoms, there is still much work to be done in terms of finding a cure or prevention of the disease.

Cdc25A phosphatase is activated and mediates neuronal cell death in a model of PD

Extensive research findings indicate that when post-mitotic neurons are exposed to various apoptotic conditions such as lack of trophic factors, DNA damage, exposure to Aβ, and oxidative stress, they leave the G_0 state of the cell cycle and activate cell cycle proteins abnormally. This activation can be fatal to the neurons. One of the initial responses observed is the activation of G1/S cyclin-dependent kinases (Cdks), such as Cdk4. Among the cell cycle regulators implicated across these neurodegenerative disease models, the dual-specificity phosphatase Cell division cycle 25A (CDC25A) plays a key role in activating CDKs at the G1/S transition. Cdc25A is a dual-specificity phosphatase that cleaves phosphate groups from phosphorylated tyrosine and serine/threonine residues to activate Cdks activity at the G1-S transition. A variety of normal cells and tissues express Cdc25A during early embryonic development and in adults. In the postmitotic stage, cells that are destined to become neurons exit the cell cycle and enter a quiescent state. In proliferating cells, many genes that are vital for cycle completion are upregulated during the G1-S transition. Phosphatases remove inhibitory tyrosine/threonine phosphates from Cdks in order to activate cyclin-dependent kinases (e.g., Cdk4, Cdk2, etc.). Cdc25A is responsible for this crucial step during the G1-S transition. In recent studies, evidence suggests that Cdc25A level and activity increases during neuronal death induced by Camptothecin, NGF deprivation, and beta-amyloid.

Our observations indicate that Cdc25A is rapidly elevated, activated and plays a required role in PD relevant model of neuron death. Cdc25A acts as a regulator of Rb phosphorylation and E2F1 mediated PUMA-Caspase3 activation in neuron death in response to 6-OHDA treatment. These observations have important implications for our understanding of the intricate network of signaling pathways involved in the process of cell death and may have potential therapeutic applications for diseases characterized by aberrant cell cycle activation that leads to neurodegeneration. Further studies aimed at targeting Cdc25A could lead to the development of new treatments that may prevent or slow the progression of these devastating neurodegenerative disorders. In a complementary study, we have recently shown that newly synthesized molecules that inhibit Cdc25A phosphatase activity block neuronal cell death caused by NGF deprivation and 6-OHDA. While more *in vivo* and clinical research is needed to fully understand the implications of our observations, these findings represent a promising avenue of research that may ultimately lead to new therapies for patients suffering from PD (Figure 1).

Development of serum-free primary astrocyte culture to study ER stress and inflammation in response to Aβ

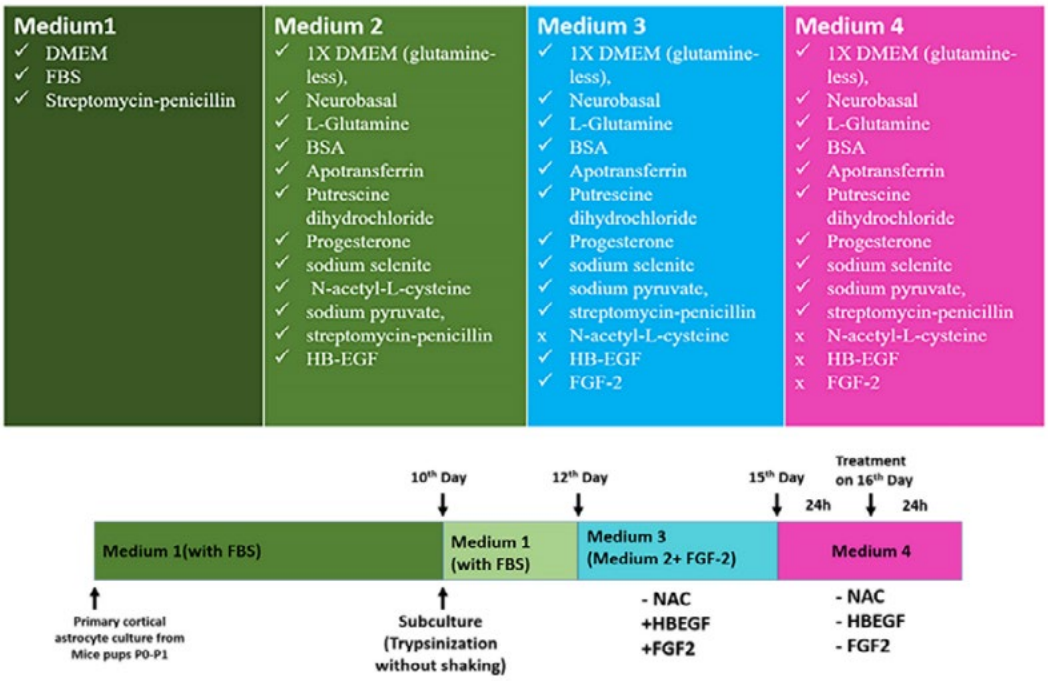
Astrocytes become reactive, contributing to neuroinflammation, impaired amyloid-beta (Aβ) clearance, and synaptic dysfunction in AD. Aβ accumulation induces endoplasmic reticulum (ER) stress in neurons and glial cells, activating the unfolded protein response (UPR), which, when prolonged, disrupts neuron function and promotes neurodegeneration. In astrocytes, ER stress further impairs Aβ clearance and may exacerbate inflammation. Although the blood-brain barrier (BBB) restricts access to brain tissue, some serum components like hormones can still enter and influence brain activity. Pathological conditions may increase BBB permeability, allow more serum entry, and affect brain cells.

How subtle ER stress leads to inflammatory responses in diseased condition, remains elusive. Studying the interplay between ER stress and inflammatory responses in astrocytes is critical for integrative mechanistic understanding of these pathways in AD. Although there are well-established methods for culturing neurons to study ER stress responses in vitro, current literature lacks cell culture protocols dedicated to study ER stress responses in astrocytes. Most current astrocyte culture models use serum, which introduces variables that can interfere with studying disease mechanisms like ER stress as well as neuroinflammation. This study aimed to develop a serum-free murine cortical astrocyte culture to more accurately investigate Aβ-induced ER stress and inflammation. Existing serum-free methods are noy suitable for certain experimental questions, highlighting the need for an improved, reliable model.

A serum-free primary cortical astrocyte culture model was developed without N-acetyl-L-cysteine (NAC) and growth factors to study ER stress and inflammation triggered by Aβ. Initially, astrocytes were cultured in serum-containing Medium 1 for 10 days, reaching ~90% confluency. After removing microglia via orbital shaking, the astrocytes were trypsinized and transferred to serum-free Medium 2. However, cells deteriorated and died by 72 hours. Replating cells in Medium 1 restored viability, and switching to Medium 3 (without NAC) followed by Medium 4 (without NAC and growth factors) on day 16 resulted in healthy astrocytes with typical branched morphology.

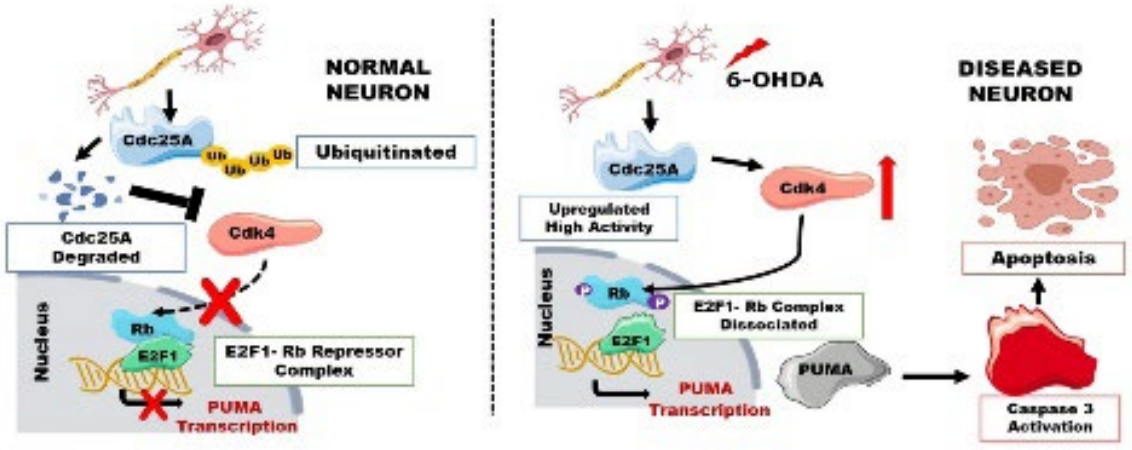
To assess ER stress, astrocytes were treated with 1.5 µM Aβ42-1 at 6 ,3 ,0, and 24 hours. In Medium 2, Aβ did not induce significant phosphorylation of eIF2α, a key ER stress marker. However, in Medium 3 (NAC removed), Aβ treatment led to increased eIF2α phosphorylation at 24 hours, indicating late-onset ER stress.

TNF-α levels were measured to evaluate inflammation. In Medium 3, Aβ treatment did not significantly alter TNF-α expression at any time point. When astrocytes were cultured in Medium 4 (without growth factors), Aβ exposure caused a significant increase in



TNF-α expression at 24 hours, suggesting that the absence of growth factors unmasks Aβ-induced inflammatory responses.

In astrocytes cultured in serum-free, exposure to Aβ1-42 led to time-dependent changes in reactivity and inflammation. Western blot and immunofluorescence analyses showed a significant increase in GFAP expression and corrected total cell fluorescence (CTCF) at 24 hours, alongside a morphological shift toward a more fibrous shape, indicated by an increased cell perimeter. These findings suggest enhanced astrocyte reactivity at later stages of Aβ exposure. Additionally, gene expression analysis revealed an early upregulation of anti-inflammatory markers (Ptx3, S100a10, Sphk1), indicating a protective response, which transitioned to a pro-inflammatory state at 24 hours with elevated expression of C3, Iigp1, and Ggta1. This temporal pattern suggests that astrocytes initially respond to Aβ with protective signaling but shift to a detrimental, inflammatory phenotype with prolonged exposure.



Future Research Plans

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

Publications

Das AK, Biswas SC (2024). Cdc25A phosphatase is activated and mediates neuronal cell death by PUMA via pRB/E2F1 pathway in a model of Parkinson's disease. *Biochimica et Biophysica Acta (BBA)-Molecular Cell Research* **1871**, 119848.

Invited Lectures

1. Alzheimer's disease: reactive astrocytes play a key role in disease pathogenesis. 38th Annual Meeting of Society of Neurochemistry, India (SNCI), Panjab University, Chandigarh. 26th – 28th September, 2024.
2. ICAM-1 reprograms microglia to ameliorate amyloid pathology and cognitive functions in a model of Alzheimer's disease. XLII Annual Meeting of the Indian Academy of Neurosciences. NIMHANS, Bengaluru. 11th – 14th November, 2024.

Conferences Attended

1. 38th Annual Meeting of Society of Neurochemistry, India (SNCI), Panjab University, Chandigarh. 26th – 28th September, 2024.
2. XLII Annual Meeting of the Indian Academy of Neurosciences NIMHANS, Bengaluru. 11th – 14th November, 2024.

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).

Awards

Elected Fellow of National Academy of Sciences, India (NASI), Bhopal, Dec 2, 2024

Dr. Subhas C. Biswas, Chief Scientist

Group Members: Kusumika Garami DST RA (Women Scientist); Diptesh Roy, CSIR-SRF; Angshuman Murmu, UGC-JRF; Ananya Mondal, UGC-JRF; Nimai Gorai, UGC-JRF

Collaborators: Dr. P. K. Gangopadhyay, KPC MC&H, 1F, Raja S C Mullick Road, Kolkata; Dr. A. Biswas A, Bangur Institute of neurosciences, 52/1A, SN Pandit Road; Dr. K. Cm Ghosh, Calcutta National Medical College & Hospital; Dr. J. Chakraborty, CSIR-IICB, Kolkata; Paul A, CSIR-IICB, Kolkata; Dr. Biswadip Banerjee, CSIR-IICB, Kolkata

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

Identification of Inflammatory Goblet cells in lung disease

I demonstrated the presence and functional relevance of a previously unvalidated inflammatory goblet cell subtype ($iNOS^{+}Muc5AC^{+}$) in airway disease pathogenesis. Prior to this, Goblet 2 cells had only been predicted from single-cell RNA-seq studies (Braga et al., 2019) without biological confirmation. Through Rad50 knockdown models, I showed that epithelial plasticity under inflammatory stress leads to the emergence of immune-like goblet cells expressing chemokines (CXCL10, CXCL11) and iNOS, promoting neutrophilia. Furthermore, I elucidated Rad50's novel role as a molecular gatekeeper linking Nrf2 and NFκB pathways to maintain epithelial lineage integrity. These findings position Rad50 as a central regulator preventing epithelial immune transdifferentiation, offering new therapeutic insights for chronic inflammatory diseases such as COPD and asthma. This work advances the understanding of epithelial barrier dysfunction and immune plasticity, providing a new mechanistic framework supported by chemokine profiling, histopathology, and flow cytometry analyses.

Unraveling the molecular landscape of RXRβn COPD: Implications for PNEC hyperplasia and airway repair

I identified Retinoid X Receptor gamma (RXRγ) as a critical regulator of lung homeostasis and emphysema protection. Our findings demonstrated a significant reduction of RXRγ in COPD patient lungs and neutrophil elastase-induced murine emphysema models. Knockdown of RXRγ in naïve mice induced spontaneous emphysema-like features, accompanied by pulmonary neuroendocrine cell (PNEC) hyperplasia and elevated CGRP levels, mirroring human COPD pathology. Transcriptomic profiling revealed that RXRγ loss upregulates olfactory receptor genes, a hallmark of PNEC expansion. Mechanistically, RXRγ was shown to transcriptionally regulate ROBO2, preventing PNEC dysregulation. Therapeutically, pharmacological blockade of CGRP, MMP-12, or neutrophil elastase successfully reversed emphysematous injury. Additionally, we found that docosahexaenoic acid (DHA), an endogenous ligand of RXRγ, was depleted in COPD patients, and DHA supplementation restored RXRγ levels and improved lung injury outcomes in both naphthalene and neutrophil elastase-induced models. This work revealed a novel RXRγ–PNEC–CGRP axis in COPD pathogenesis and opened new avenues for therapeutic interventions targeting epithelial repair.

Development of bioavailability platforms for nutrient absorption studies in Millets

As part of a collaborative project involving ICAR-IARI, NABI, and CSIR-IICB, I contributed significantly to developing experimental platforms for assessing nutrient bioavailability from pearl millet landraces (P701 and Garwal Ki Dhani). Focusing on Objective 3 of the project, we established a mice-based feeding model to systematically evaluate iron, zinc and polyphenol absorption. Our findings demonstrated that P701 millet significantly enhanced iron storage, as evidenced by a twofold increase in liver iron absorption, threefold higher ferritin levels and fourfold higher hepcidin levels compared to controls. Additionally, P701 millet improved intestinal villi length and immune function (dense white pulp in spleen), without inducing adverse histopathological changes. These outcomes offer critical insights into the nutritional superiority of specific millet varieties and their potential for addressing mineral deficiencies. This work, achieved through a strong multi-institutional collaboration, advances bioavailability research and supports the development of nutri-rich millet-based food products.

Discovery of a Novel Isothiocyanate derivative (SCS-OCL-381) for protection against Acute Lung Injury

I contributed to the development and mechanistic evaluation of SCS-OCL-381, a novel synthetic isothiocyanate derivative, for therapeutic intervention in acute lung injury (ALI). Using a murine model of LPS-induced ALI, we demonstrated that SCS-OCL-381 significantly alleviates lung injury by stabilizing the Scaffold/Matrix-Associated Region-Binding Protein 1 (Smar1) and inhibiting NF-κB p65 phosphorylation. This stabilization led to suppression of pro-inflammatory cytokines (IL-6, TNF-α, KC, IL-17), reduced neutrophil infiltration and preservation of alveolar-capillary barrier integrity. Complementary in vitro studies with THP-1 macrophages confirmed that SCS-OCL-381 modulates NF-κB activation and cytokine production. The targeted action of SCS-OCL-381 on the Smar1-NF-κB axis presents a promising, selective anti-inflammatory strategy for acute and chronic lung diseases like COPD and asthma, offering advantages over broad immunosuppressants like corticosteroids. This contribution enhances the translational prospects for small-molecule therapeutics in respiratory inflammation.

Smar1 in COPD Pathogenesis and Therapeutic Modulation

I guided the thesis work of my student, which uncovered the critical role of Scaffold/Matrix-Associated Region-Binding Protein 1 (Smar1) in COPD pathogenesis. Through detailed studies, we demonstrated that Smar1 levels are significantly reduced in human COPD lungs, long-term cigarette smoke-exposed mice, and elastase-induced emphysema models. Smar1 knockdown in mice resulted in spontaneous emphysema-like features mediated through IL-17 secretion by airway epithelial cells and the CGRP/MMP-12 axis originating from pulmonary neuroendocrine cells (PNECs). We also validated Smar1's direct regulation of IL-17 gene expression through chromatin immunoprecipitation. Importantly, sulforaphane, a natural isothiocyanate, rescued Smar1 levels and mitigated lung injury in both naphthalene and elastase models. This work highlighted Smar1 as a central regulator of lung homeostasis and established it as a promising therapeutic target for emphysema and COPD. This achievement not only advanced our research portfolio but also significantly contributed to student mentorship and capacity building in translational pulmonary biology.

Novel discovery of lipofibroblasts in Idiopathic Pulmonary Fibrosis (IPF)

I identified the previously unrecognized role of lipofibroblasts in the progression of idiopathic pulmonary fibrosis (IPF), contributing significantly to the expanding understanding of fibroblast heterogeneity in lung disease. Traditionally thought to be benign lipid-storing cells, our findings demonstrated that lipofibroblasts can transdifferentiate and acquire pro-fibrotic phenotypes under pathological conditions, thereby promoting fibrotic remodeling of the lung parenchyma. This discovery shifts the paradigm of fibroblast biology in IPF by highlighting the plasticity of mesenchymal cell subsets and opens new avenues for therapeutic targeting of fibroblast reprogramming mechanisms. By elucidating lipofibroblast involvement in fibrogenesis, this work provides a critical conceptual advancement in lung fibrosis research.

CAR-T cell strategy for Idiopathic pulmonary fibrosis

We aim to develop CAR-T cells targeting integrin α8 and CD-90 for treating bleomycin-induced lung fibrosis, a model for human IPF. First we involve validating THY1 (CD90) and ITGA8 as myofibroblast markers through immunofluorescence histochemical studies and flow cytometry-based immunophenotyping. Subsequently, bispecific CAR-T cells targeting THY1 and ITGA8 will be developed and tested for specificity in vitro. Then we will evaluate lung-specific CAR-T cells in mouse models of IPF, assessing targeting efficacy and therapeutic impact post-intratracheal delivery. Selected targets, THY1 and ITGA8, exhibited high expression in myofibroblasts of IPF lungs, validated through analysis of human protein atlas data. This comprehensive approach identifies THY1 and ITGA8 as promising targets for CAR-T cell therapy in IPF, showcasing the potential for precision-guided treatments to address the complex pathology of lung fibrosis and advance IPF management. We are in the process of in vitro validation followed by in vivo validation strategies.

Bioengineering the Metabolic Network of CAR T Cells with GLP-1 and Urolithin A to Improve Persistence and Anti-Tumor Activity (Teamwork and collaborative project output)

As part of a collaborative team effort, I contributed to the development of metabolically reprogrammed CAR (MCAR) T cells through combined activation of autophagy and mitophagy pathways using GLP-1 receptor agonists (semaglutide) and Urolithin A. This strategy enhanced mitochondrial metabolism, promoted $CD8^+$ memory T cell formation and significantly improved CAR T cell persistence and anti-tumor efficacy in vitro and in xenograft models. Additionally, we engineered GLP-1-secreting CAR T cells (MCAR T-2), which maintained long-term memory and exhibited robust anti-tumor effects even under tumor re-challenge while reducing the risk of cytokine release syndrome. This work establishes metabolic reprogramming as a powerful strategy to enhance CAR T cell therapy durability, offering novel insights for improving outcomes in solid and hematologic cancers. The project exemplifies successful interdisciplinary collaboration between immunology, metabolism and therapeutic engineering teams.

Future Research Plans

- Validate inflammatory goblet cells in human/mouse lung samples and target Rad50-Nrf2-NFκB signaling to restore epithelial integrity.
- Advance RXRγ-based therapies (DHA, CGRP blockers) for COPD and explore PNEC plasticity through multi-omics.
- Develop bispecific CAR-T cells targeting THY1/ITGA8 for lung fibrosis and assess safety in IPF models.
- Enhance CAR-T efficacy via metabolic reprogramming using GLP-1 and Urolithin A for solid tumors and fibrotic lungs.
- Target lipofibroblast reprogramming in IPF using lineage tracing and epigenetic inhibitors.
- Translate millet bioavailability findings into nutritional interventions for lung health.
- Strengthen translational pipelines via IICB-TRUE-industry collaborations for cell therapies and nutraceuticals.

Extramural / CSIR Funding

1. Modern innovative solutions for Environmental/ Occupational Lung Health challenges using Clinical and Pre-clinical strategies (Mission Lung), CSIR, MLP-137, 2020-25, 169 lakh.
2. The steroid sensitizing role of RXR-gamma, a nuclear receptor, in the pathogenesis of emphysema, DST-SERB, GAP432, 2021-2024, 35 Lakhs
3. Development of Genetically Engineered 'Off-the-shelf' and Inducible CAR-T Cells for Cancer Therapeutics, DBT Multi-institutional, GAP 448, 2023-2026, 55 Lakhs
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, GAP 451, 20.5 Lakhs

Publications

Akhtar A, Shakir M, Ansari MS, Divya, Faizan MI, Chauhan V, Singh A, Alam R, Azmi I, Sharma S, Pracha M, Uddin IM, Bashir U, Shahni SN, Chaudhuri R, Albogami S, Ganguly R, Sagar S, Singh VP, Kharya G, Srivastava AK, **Mabalirajan U**, Roy SS, Rahman I, Ahmad T. (2025) Bioengineering the metabolic network of CAR T cells with GLP-1 and Urolithin A increases persistence and long-term anti-tumor activity. *Cell Rep Med.* **6** :102021.

Patents

1. Encapsula dietary supplement ted dihydrofola ation as effective te formulation for nutraceutical supp—202411023759 Application No (as Co-inventor)
2. Dihydrofolate for hypoglycemic activity," and was filed in the United States Patent and Trademark Office on May 31, 2023, as application 18/326,450 **(as Co-inventor)**

Dr. U. Mabalirajan, Principal Scientist

Group Members: Joytri Dutta, UGC-SRF; Sabita Singh, UGC-SRF; Archita Ray, CSIR-SRF; Atmaja Karmakar, CSIR-SRF; Antara Baidya, CSIR-SRF

Collaborators: Dr. Amit Kumar Srivastava, Senior Scientist, CSIR-IICB, Kolkata; Dr. Parthasarathi Bhattacharyya, Institute of Pulmocare & Research, Kolkata; Dr Anigra Dasgupta, BR Singh Hospital, Sealdah, Kolkata; 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 multi-drug resistant pathogenic bacteria globally.

Dr. Chandrima Shaha

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

Research Activities

The goal was to systematically analyze the complex host-pathogen networks in trypanosomatid parasites and explore potential drug candidates. Our studies use the *Leishmania* parasite, a unicellular organism and a challenging pathogen responsible for significant health problems in the four eco-epidemiological regions of the world (Southeast Asia, the Americas, East and North Africa). As reported by WHO, 700,000–1 million new cases are reported annually. With increasing urbanization, conflicts, the spread of the disease to new areas, and the emergence of cutaneous forms of the disease, it is essential to analyze the potential for new drugs, along with a thorough examination of the complex relationship between the parasite and the host. Approximately, 75% of drugs developed to treat infectious diseases have origins in nature, and many people globally utilize plant-based therapies for various ailments. For parasitic diseases, numerous plant-derived products are currently used for treatment. The renewed interest in natural products in both academia and industry is partly driven by recent technological advancements that highlight the potential of using natural phytochemicals as pharmaceuticals in the future. Established plant-based drugs may also be repurposed for different applications. The wide variety of novel structures from plant-based compounds presents the opportunity to create appropriate, non-toxic products through combinatorial changes. It is essential to identify products that can be repurposed while also considering the synthesis of new products based on relevant structural information.

Our analysis demonstrates that multiple drugs used for parasites target the mitochondria. In drug development, mitochondria are recognized as significant pharmacological targets due to their crucial role in energy regulation. Disrupting energy generation results in irreversible cell damage. Therefore, compounds capable of affecting mitochondrial function are attractive candidates. We employed a search strategy where two electronic databases, PubMed and Google Scholar, were explored over a period spanning years 1985 to 2024 with 'plants' and '*Leishmania*' as keywords. About 1718 results were listed. Based on the titles, we performed a selection of articles, subsequently evaluating the abstracts for eligibility, followed by assessing the full texts for relevance. From

here, we extracted 160 references for further analysis. The inclusion/study selection criteria for plant extracts with good anti-leishmanial effects targeting the mitochondria having prioritized those already tested in humans or animals. Possible compounds tested only *in vitro* but targeting the mitochondria of the parasite were also evaluated. The plant-based compounds that target the parasite's mitochondria include artemisinin and chloroquine, two anti-malarial drugs that affect mitochondria and demonstrate strong anti-leishmanial effectiveness in both *in vitro* cultures and *in vivo* animal models. Quinolones, coumarins, and quercetin are additional compounds with leishmanicidal properties that disrupt mitochondrial activity to effectively eliminate parasites in animal models of the disease and could be considered potential drugs. The evaluation has been published (Shaha, C. Expert Reviews in Molecular Medicine, 27, e15, 1–15, https://doi.org/10.1017/erm.2025.8).

Future research plans

The *Leishmania* parasite is a unicellular organism that undergoes cellular apoptosis. Related organisms also do the same. It is of interest to see how the *Leishmania* parasite and other related organisms adopted this process of death during evolution. The mechanisms underlying this process are important to delineate as that could reveal important targets. A review of such mechanisms will be performed. The following topics will also be analyzed: a) Identification of possible new drugs from plant sources and b) Promising molecules as anti-leishmanials from synthetic compounds.

Extramural / CSIR Funding

National Academy of Sciences funding for JC Bose Distinguished Chair Professorship and the Indian National Science Academy for INSA Senior Scientist (Since Sept. 2024).

Publications

Shaha C (2025). Plant-derived products as anti-leishmanials which target mitochondria: a review. *Expert Reviews in Molecular Medicine*, **27**, e15, 1–15 https://doi.org/10.1017/erm.2025.8 (earlier in press, since published).

Invited Lectures

1. Bacteriological Research in British India: Its Impact. Asiatic Society Seminar to observe 150th birth year of Prof. U.N. Brahmachari. May 28, 2024.
2. Our cells as our medicine. Translational Research for Society and Sustainability. KIIT Deemed to be University, Bhubaneswar. June 14, 2024.
3. Magic of being alive: the story of our cells. Ramakrishna Mission Institute of Culture, Popular lecture, Kolkata. June 25, 2024
4. Invaders, hosts and survival: the beauty of cellular struggle, IACS, Kolkata. September 18, 2024.
5. What is right and what is wrong? – Scientific Ethics". IICB. October 3, 2024.
6. The Joy of Being a Scientist – Siksha-o-Anushandhan University, 19th SOAFAL – IV Oration. December 28, 2024.
7. Science communication in current times. Lecture at ISNA Annual General Meeting. March 3, 2025.
8. Journey of a scientist: from living cells to cell death, NEIST Jorhat, March 10, 2025.

Meetings Attended

1. As Member, Research Council Meeting, National Institute of Oceanography, Goa. April 1, 2024.
2. As Member, Governing Council - Indian Association for the Cultivation of Science, Delhi. April 18, 2024
3. As Chair, Rashtriya Vigyan Puraskar Meeting. New Delhi, April, 28, 2024.
4. As Member, WAST Council Meeting, Kolkata, May 30, 2024.
5. As Member, Indian Institute of Science, Promotions Assessment Committee Meeting. June 21, 2024.
6. As Panel discussant. Bose Stat at 100, S. N. Bose National Centre for Basic Sciences, Kolkata. WQST. July 17-19, 2024,
7. As Member, Indian Institute of Science, Promotions Assessment Committee Meeting. September 20,
8. As Member, Indian Institute of Science, Promotions Assessment Committee Meeting. December 6, 2024.

9. As Member, WAST Council Meeting. December 17, 2024,
10. As Chair of David Goltzman lecture, Sister Nivedita University, Kolkata, International conference on “Symphony of Cellular Signals in metabolism and immune response” January 16-17, 2025.
11. As Member, Council Meeting, Indian Statistical Institute, Kolkata,January 23, 2025,
12. As Distinguished Chair of the lecture session “Cell Signalling 1” at IABS-2025 Conference, Indian Association for the Cultivation of Science. February 6-8, 2025.
13. As Member, Book Release of Biography of Chandrima Shaha at INSA, New Delhi. March 8, 2025.
14. As Member, Indian Institute of Science, Promotions Assessment Committee Meeting. March 13, 2025,
15. As Member, WAST Council Meeting. March 24, 2025.

Member of Society

1. Chair, Research Advisory Board, National Council of Science Museums, Ministry of Culture.
2. Chair, Rashtriya Vigyan Puraskar 2025, Govt. of India.
3. Member, ISI Council.
4. Member, ISI, Policy planning and evaluation committee.
5. Member, SAC, National Institute of Plant Genome Research. New Delhi,.
6. Member, Research Council, CSIR-National Institute of Oceanography, Goa
7. Member, Promotion and Assessment Committee, Indian Institute of Science, Bangalore.
8. Member, Bose Institute Council.
9. Member, Academic Advisory Council, Indian Institute of Technology, Gandhinagar
10. Member, Leadership Conclave, Indian Institute of Technology, Gandhinagar
11. Member, Governing Body, INSA Women Associates Committee.
12. Member, Core Committee of the Digital Archive in Science, Birla Industrial Technological Museum.

Dr. Nahid Ali and her group members

Targeting *Leishmania donovani* kinases: Diagnostic, vaccine, and therapeutic advances centered on LdAIRK and Hesperadin

Research Activities

In *Leishmania* species, kinases play crucial roles in regulating key cellular processes such as cell cycle progression, parasite differentiation, and virulence, making their inhibition a potentially transformative strategy for disease intervention. Among these, Repressor of Differentiation Kinase 2 (RDK2), Aurora Kinase (LdAIRK), and *Leishmania*-Activated C-Kinase Antigen (LACK) are particularly noteworthy. These kinases, with molecular weights of 49, 36, and 34 kDa respectively, are highly conserved across *Leishmania* species and life stages. They are central to parasite survival, mediating essential functions related to cell division and developmental transitions. Our study provides compelling evidence supporting the diagnostic and prognostic utility of three *Leishmania donovani*-derived kinase-based recombinant antigens—RDK2, LACK, and LdAIRK—for visceral leishmaniasis (VL) and post-kala-azar dermal leishmaniasis (PKDL) across endemic regions like India and Brazil in human hosts and canine leishmaniasis (CanL) across Brazil. Among them, LdAIRK emerged as the most promising candidate, demonstrating superior sensitivity and specificity in ELISA, urine-based assays, and rapid test formats. Its performance surpassed that of widely used rK39-based tests, particularly in detecting active disease, monitoring treatment response and identifying PKDL cases. Importantly, the successful transition of these antigens into field-friendly dipstick and lateral flow platforms underscores their potential for real-world deployment. The strong immunoreactivity of LdAIRK in canine samples further supports its role in zoonotic surveillance and control efforts. While limitations exist—including the need for broader cohort validation and performance assessment in asymptomatic and co-infected individuals—this work establishes a robust foundation for next-generation diagnostic tools. Future efforts should prioritize field trials, antigen refinement and multiplex assay development to fully harness the clinical and public health impact of these kinase antigens.

VL remains a pressing global health challenge, particularly in resource-limited regions, due to limitations in current treatments and the absence of an effective human vaccine. While CanL vaccines offer partial protection, human vaccines require higher efficacy

and durable immunity. Our study highlights a rational vaccine design approach targeting LdAIRK—a conserved, parasite-specific protein—combined with potent adjuvants (MPLA, R848, and 3M-052) in cationic liposomes to enhance antigen delivery and Th1-skewed immunity. By leveraging skin-resident dendritic cells and synergistic Toll-like receptor agonists, the formulation aims to stimulate robust CD4+ and CD8+ T-cell responses and macrophage activation. Subcutaneous delivery, though challenging, was optimized using this platform to simulate realistic immunization routes. Overall, this strategy offers a promising pathway toward developing a safe, effective and field-deployable vaccine for human VL, capable of overcoming immune evasion by *Leishmania* and improving protection in endemic populations.

Hesperadin, a known inhibitor of mammalian Aurora kinase B, has shown promising anti-parasitic activity across various protozoan species. Our study establishes the anti-leishmanial potential of hesperadin, a mammalian Aurora kinase B inhibitor, by demonstrating its ability to disrupt the cell cycle and induce death in *L. donovani* promastigotes. The primary mechanism appears to be mitotic catastrophe, characterized by cell-cycle arrest at the G2/M checkpoint, nuclear abnormalities, and the formation of polyploid cells with micronuclei. These changes result from the inhibition of LdAIRK, an Aurora kinase homolog essential for proper mitotic progression. Alongside this, hesperadin-induced mitochondrial stress—marked by initial hyperpolarization followed by depolarization, reactive oxygen species accumulation, and ATP depletion—contributed to parasite death. Although classical markers of apoptosis such as phosphatidylserine externalization, caspase activation, and DNA fragmentation were observed, they were either partial or delayed, suggesting a non-canonical form of apoptosis combined with necrotic features. The modest effect of broad-spectrum inhibitors like z-VAD-fmk and EGTA further implies the involvement of diverse proteases, including calpains, cathepsins, and metacaspases, in the downstream execution of cell death. Notably, the intracellular amastigote form was more sensitive to hesperadin, highlighting its therapeutic promise. However, the relatively high IC_{50} in promastigotes underscores the need for improved drug delivery. Overall, hesperadin exerts a complex, multi-pathway cytotoxic effect on *L. donovani*, primarily driven by mitotic disruption, with mitochondrial and protease-mediated components contributing to the downstream death cascade.

In summary, our study highlights the critical role of *Leishmania* kinases—particularly LdAIRK—in parasite survival and disease progression, demonstrating their strong potential as diagnostic and prognostic biomarkers for VL and PKDL. The superior performance of LdAIRK-based assays over existing tests, along with its applicability in canine surveillance, underscores its translational value. Additionally, the targeted vaccine strategy leveraging LdAIRK combined with immune-stimulating adjuvants offers a promising avenue for developing an effective human VL vaccine. Furthermore, the identification of hesperadin as a potent inhibitor of LdAIRK establishes a novel therapeutic approach by inducing mitotic catastrophe and mitochondrial dysfunction in *L. donovani*. Collectively, these findings advance the field of leishmaniasis research by providing new tools and targets for diagnosis, vaccination and treatment.

Future Research Plans

- Develop a subunit recombinant vaccine containing gp63, EF1-α, and CPC antigens with T-cell epitopes, delivered via MPLA-bearing cationic liposomes, and evaluate immune responses and protection in animal models.
- Assess the vaccine potential of the native and recombinant LACK antigen from *L. donovani* by comparing its efficacy to gp63 in liposomal formulations and studying its immunogenicity in mouse models of visceral leishmaniasis.
- Advance the use of PC-SA cationic liposomes in cancer therapy by targeting tumor immune evasion mechanisms, reducing immunosuppressive cytokines, and delivering peptide therapies to inhibit mutant p53 and improve drug sensitivity.
- Further develop and scale up the PC-SA–amphotericin B liposomal formulation for visceral leishmaniasis and fungal infections, conduct preclinical toxicity studies, and progress toward regulatory approval and clinical trials in collaboration with industry partners.

Extramural / CSIR Funding

1. Awarded a Sir J. C. Bose Fellowship under DST research grant, of Rs. 47,39,783/- project entitled “Exploration of recognized potent antigen and liposomal tools to design a defined subunit T cell vaccine and chemotherapy against VL” from 2022-2024.
2. Submitted a DHR-ICMR research grant, in collaboration with Dr. Susanta Kar and Dr. Vahab Ali, of Rs. 2,92,96,032/- for the project entitled “IND enabling studies on a novel liposomal amphotericin B for treatment of Kala-azar and fungal infections”, 2025.

Publications

1. Chhajer R, Bhattacharyya A, **Ali N**. 2024. Cell Death in *Leishmania donovani* promastigotes in response to Mammalian Aurora Kinase B Inhibitor- Hesperadin. Biomedicine and Pharmacotherapy. 177:116960. doi: 10.1016/j.biopha.2024.116960.
2. Bhattacharyya A, Chhajer R, Ejazi SA, Kamran M, Gayen S, Rahman M, Goswami RP, Pandey K, Das VNR, Das P, Silva FO, Costa DL, Nery Costa CH, **Ali N**. 2025. The potential of *Leishmania donovani* Aurora kinase in the diagnosis of Indian and Brazilian visceral leishmaniasis patients. Microbiology Spectrum. Apr 16: e0324724. doi: 10.1128/spectrum. 03247-24.
3. Bhattacharyya A, Didwania N, Ejazi SA, Chhajer R, Gayen S, Rahman M, Goswami RP, Pandey K, Das VNR, Das P, da Silva, FO., Costa, DL., Costa, CHN., **Ali N**. 2025a. Recombinant *Leishmania*-activated C kinase as a novel antigenic candidate for immuno-diagnosis of visceral leishmaniasis occurring in India and Brazil. Infectious Diseases of Poverty. (Accepted).

Book Chapters

Bhattacharyya, A, Ali, N, Gayen, S. 2024. diagnostic approaches for neglected tropical diseases in West Bengal: A comprehensive review in Current Advances in Microbiology. Published by Dr. Rajyasri Neogy, Vijaygarh Jyotish Ray College, Kolkata. ISBN: 978-81-969267-6-2.

Invited Lectures

1. Topic: Targeting phosphatidylserine for cancer therapy: A novel strategy with cationic liposomes.

   Venue: Zoology for Ecosystem and Human Health, University of Kalyani, Kalyani West Bengal, India, 22nd April, 2024.
2. Topic: Novel Liposomal Amphotericin B for Treatment of Kala-azar and Fungal Infections and Rapid Diagnostic Test for Detection Of Visceral Leishmaniasis (Kala-azar).

   Venue: DHR Meeting For Clinical Trials, New Delhi, India, 3rd May, 2024.
3. Topic: A novel strategy for the therapy of leishmaniasis and cancer targeting phosphatidylserine.

   Venue: 1st National Conference on Emerging Trends in Bioscience Research (ETBR) Department of Biological Sciences, Aliah University, India, 5th February, 2025.
4. Topic: Innovation in diagnosis and therapy of kala-azar for better disease management.

   Venue: International Health Conference Theme: "Transforming Global Health: Tracking Neglected Tropical Diseases (NTDs)" ICESCO HQ, Rabat Kingdom of Morocco, 17-19th February, 2025.

Conferences Attended

1. International Conference on Scope of Microbiology Beyond Academia: Industry Entrepreneurship and More, 5th to 6th April, 2024 at Vijaygarh Jyotish Ray College, Kolkata, India.
2. Zoology for Ecosystem and Human Health, University of Kalyani, Kalyani West Bengal, India, 22nd April, 2024.
3. DHR Meeting for Clinical Trials, New Delhi, India, 3rd May, 2024.
4. 1st National Conference on Emerging Trends in Bioscience Research (ETBR) Department of Biological Sciences, Aliah University, India, 5th February, 2025.
5. International Health Conference Theme: "Transforming Global Health: Tracking Neglected Tropical Diseases (NTDs)" ICESCO HQ, Rabat Kingdom of Morocco, 17-19th February, 2025.

Member of Society

1. Life member of Society of Biological Chemists
2. Life member of Indian Immunological Society
3. Life member of Indian Science Congress

4. Member of Molecular Immunology Forum
5. Life member of Chemical Biology Society
6. Member of Scientific Investigation Board (SIB) at CSIR-IICB, 1st October 2024.

Awards

Received **FIRST PRIZE** for poster presentation "Recombinant LACK revealed as a novel antigenic candidate for immuno-diagnosis of human visceral leishmaniasis." Bhattacharyya, A and Ali, N. At International Conference on Scope of Microbiology Beyond Academia: Industry Entrepreneurship and More, 5th to 6th April, 2024 at Vijaygarh Jyotish Ray College, Kolkata, India.

Prof. Nahid Ali, J.C. Bose Fellow, INSA Honorary Scientist

Group Members: Ms. Nicky Didwania, Senior Project Associate (JCB); Mr. Anirban Bhattacharyy, Senior Research Fellow (ICMR)

Collaborators: Mehebubar Rahaman, MD and Rama Prosad Goswami, MD, Department of Tropical Medicine, School of Tropical Medicine, Kolkata, West Bengal, India; Krishna Pandey, MD, Vidya Nand Ravi Das, MD, Pradeep Das, MD, Department of Molecular Biology, Rajendra Memorial Research Institute of Medical Sciences, Patna, Bihar, India; Fernando Oliveira da Silva, PhD, Dorcas Lamounier Costa, PhD, Carlos Henrique Nery Costa, PhD, The Federal University of Piauí (UFPI), Teresina, Piauí, Brazil.

Dr. Saikat Majumder and his group members

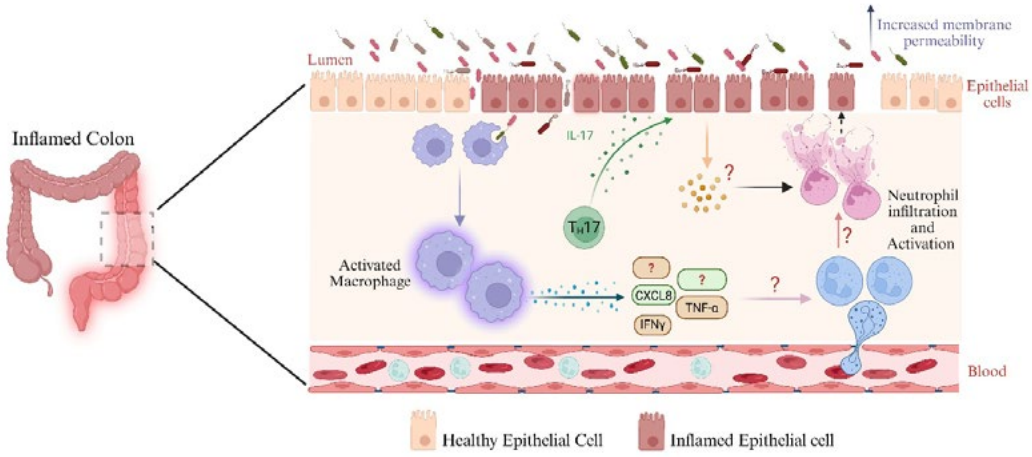
Understanding the stromal cell–immune cell interactions during autoimmune inflammatory diseases

Research Activities

Accumulating evidence from our research and that of others indicates a complex interplay between immune cells and non-immune stromal cells. The pathogenesis of numerous autoimmune disorders has been shown to originate from or be influenced by subtle interactions between these two cell types. To enhance our understanding of this intricate class of disorders, our research focuses on the heterogeneity of non-immune stromal cells within the lymph node and non-lymphoid tissues under both homeostatic and inflammatory conditions, particularly in the context of autoimmunity. Understanding these complex relationships may shed light on the increasing prevalence of autoimmune diseases in India and pave the way for the creation of innovative treatments for their prevention and management.

Specifically, our research aims to elucidate how aberrant IL-17 signaling contributes to neutrophil-driven inflammation in Type 1 Diabetes, with a focus on mechanisms such as cytokine-mediated β-cell stress, oxidative damage, and altered antigen presentation. By dissecting these complex pathways, we aim to identify potential therapeutic targets that could modulate IL-17–neutrophil interactions and mitigate disease progression.

An additional focus is to identify the intricate interplay between IL-17A, neutrophils, and the gut microbiome in the pathogenesis of Ulcerative Colitis. We seek to recognize key microbial signatures and immune pathways that exacerbate disease, emphasizing how IL-17A–driven neutrophilic inflammation compromises intestinal barrier integrity and immune tolerance. Furthermore, we aim to define the role of the Th17/IL-17 axis in Salmonella-induced mucosal inflammation and tissue injury.



Future research plans

- Thorough understanding of the interactions between stromal cells and immune cells during inflammatory and autoimmune diseases, as well as the creation of stromal cell-directed therapies for the treatment of disease.
- How does host metabolism influence host-pathogen dynamics? Identification of signaling pathways/ key transcription factors that drive metabolic reprogramming in the context of infection.
- Design and Development of novel CAR-T constructs against rheumatoid arthritis.

Extramural / CSIR Funding

1. Elucidating the role of aberrant IL-17-neutrophil axis in driving Type 1 diabetes pathogenesis. Indian Council of Medical Research (ICMR), 2024-2027, 73.2 Lakhs (IIRPSG-2024-01-05953; GAP-491).
2. Investigating the IL-17A-neutrophil axis and microbiome interactions in the pathogenesis of Ulcerative Colitis: Toward targeted Immunotherapies. Anusandhan National Research Foundation (ANRF) PM-ECRG, 2024-2027, 61.5 Lakhs (ANRF/ECRG/2024/005340).

Publications

Sarkar I, Basak D, Ghosh P, Gautam A, Bhoumik A, Singh P, Kar A, Mahanti S, Chowdhury S, Chakraborty L, Mondal S, Mukherjee R, Mehrotra S, **Majumder S**, Sengupta S, Paul S, Chatterjee S. CD38-mediated metabolic reprogramming promotes the stability and suppressive function of regulatory T cells in tumor. ***Sci Adv***. 2025 Mar 21;11(12): eadt2117.

Invited Lectures

1. Delivered an online lecture on *T cell Immunity: subsets, cytokines, and their roles in health and disease* in the Faculty Development Program at Neotia University, Kolkata of 25th February, 2025.
2. Delivered a lecture on *Basic Immunology* to disseminate the basic biology knowledge to the school students at Lakshminarayanpur Sitanath High School, South-24 Parganas, West Bengal. The event was a part of CSIR JIGYASA 2.0 program: Virtual Lab Integration (HCP-0101).

Dr. Saikat Majumder, Senior Scientist

Group Members: Lagnajita Chakraborty, UGC-JRF; Ritabrata Roy, UGC-JRF

Collaborators: Dr. Partha Chakraborti, Senior Principal Scientist, CSIR-IICB, Kolkata; Dr. Shilpak Chatterjee, Principal Scientist, CSIR-IICB, Kolkata; Dr. Aditi Chandra, Saha Institute of Nuclear Physics, Kolkata; Dr. Ajitesh Roy, Ramakrishna Mission Seva Pratishthan, Kolkata; Dr. Rajib Sarkar, IPGME&R, SSKM Hospital, Kolkata

Dr. Sourish Ghosh and his group members

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

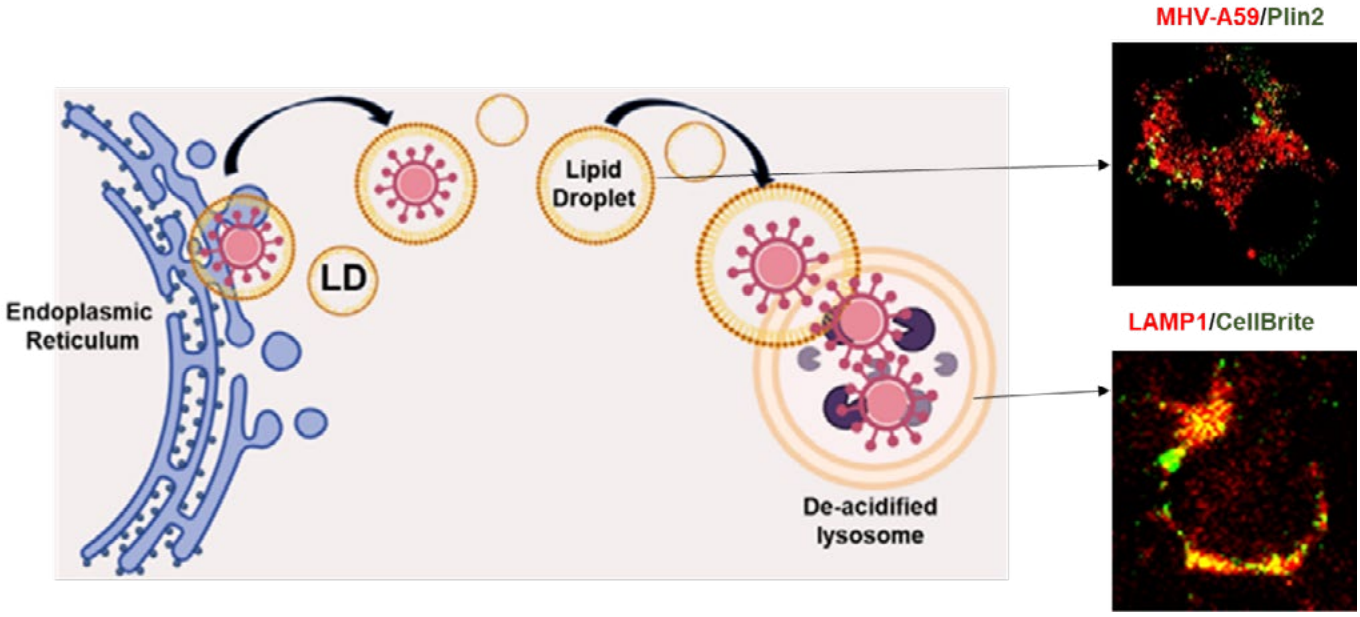
Research Activities

Our lab investigates unconventional mechanisms by which neurotropic and enteric viruses hijack host cell pathways for egress, trafficking, and transmission. We focus on lipid droplets (LDs) and extracellular vesicles (EVs) as key organelles in viral dissemination. Our studies reveal that β-coronaviruses exploit LDs for ER-to-lysosome trafficking and exit via non-lytic lysosomal exocytosis. Separately, we uncovered that Japanese Encephalitis Virus is released in small EVs through an ESCRT-independent pathway regulated by nSmase-2 and ceramide metabolism. We are currently exploring how LDs regulate EV biogenesis and viral egress, aiming to identify host-pathogen interactions that enable immune evasion and persistent infection.

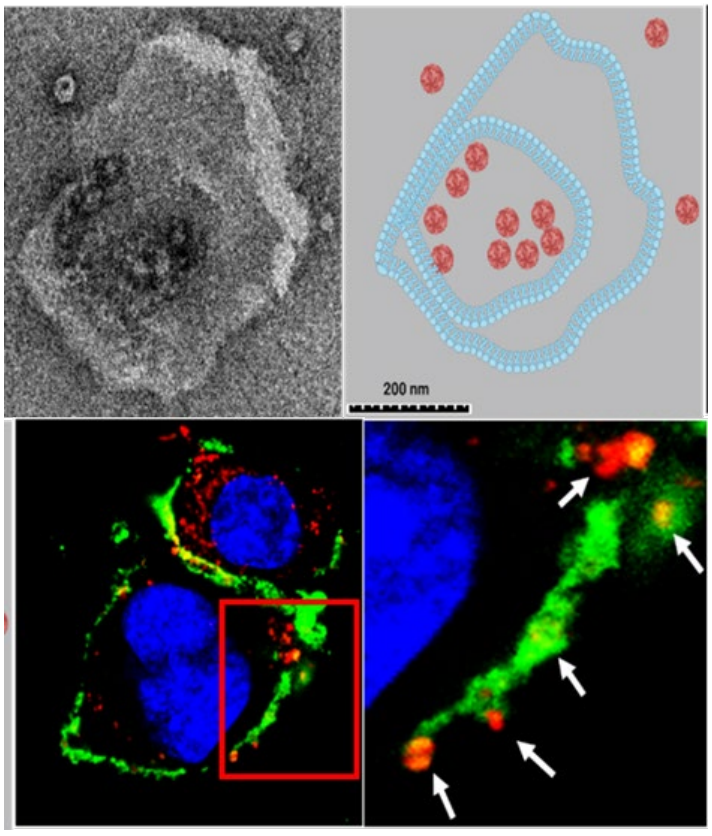
A. Lipid Droplets in Viral Trafficking and Egress

We have established a research focus on various β-coronaviruses, including MHV-A59, Human Coronavirus OC43, and SARS-CoV-2. Our findings reveal that after assembly and maturation, these viruses are transported from the ER inside lipid droplets (LDs), which facilitate their trafficking to lysosomes. Due to the expression of specific coronavirus proteins such as ORF3A and E, which act as viroporins, lysosomes become de-acidified, preventing viral degradation. These altered lysosomes are then transported to the plasma membrane, enabling viral release via lysosomal exocytosis—a non-lytic egress mechanism that helps the virus evade immune detection. We have established this through high resolution imaging studies and flow cytometry.

We have also identified the precise contact points between LDs and lysosomes that enable viral transfer. Currently we are interested to know whether LDs apart from intracellular trafficking of viruses have role in viral exocytosis or transmission.



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



For the first time, we have discovered that Japanese Encephalitis Virus (JEV), a member of the Flavivirus family, egresses within small extracellular vesicles (~200 nm in size). Our characterization confirms these vesicles as exosomes, which transport an average of 3–5 viral particles per vesicle, starting 18 hours post-inoculation in neuronal cells. Confocal imaging reveals the pinching-off process of these vesicles from the host membrane, with viral puncta visibly stained using the red PKH26 dye. This finding highlights a novel, non-lytic mode of JEV egress, potentially facilitating immune evasion and enhanced viral dissemination.

Through our research we have observed that these viruses are getting packaged inside small EVs by ESCRT-independent pathway mediated by nSmase-2 and Ceramide Kinase. We have also observed that LDs also have a role to play in regulating the expression of nSmase-2 and viral egress through small EVs, hence. Currently we are exploring the molecular mechanism of this pathway.

Future Research Plans

- Defining role of Lipid Droplets in viral infection and transmission.
- Identifying advantages of EV-mediated viral transmission.

Extramural / CSIR Funding

1. 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)
2. Tuning Lipid Droplets for Antiviral Interventions in Brain. DBT Call for Neuroscience, 2024-2027, 79.4 Lakhs, (BT/PR51484/MED/122/359/2024)
3. 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)
4. Vesicular Transmission of Flavivirus & Its Role in Neurodegeneration, CSIR- FBR Project, 2024-2027, 69.4 Lakhs.

List of Publications

1. Sarkar A, Ghosh S*. SARS-CoV-2 persistence: A potential catalyst for age-associated neurodegenerative diseases. Advanced Neurology. 2024. (Cover Page).
2. Dhar S, Ghosh S*. Innate Immune Sensors Spying Microbial Hideouts! OAS1 - 'Stalwart Defender' or 'Hidden Enemy'? Journal of Cellular Immunology. 2024

Invited Lectures

1. Organellar & Membrane Trafficking held at IISER, Pune, October, 2024.
2. "Microbes: Miracle or Menace; Innovation for health, environment & industry", RKMV, Centenary College, Rahara, March, 2025

Member of Society

Member of 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; Suparna Dhar, DBT-JRF; Bhaghyasree Mullick, UGC-JRF; Tamoghna Chakraborty, UGC-JRF

Collaborators: Prof. Jayasri Das Sarma, IISER, Kolkata; Dr. Sheetal Gandotra, CSIR-IGIB, New Delhi; Dr. Kesavardana Sannula, IISC, Bengaluru; Dr. Vineet Chaudhary, AIIMS, New Delhi; Dr. Mohammed Saleem, NISER, Bhubaneshwar; Dr. Dilip Kumar, Ashoka University, Haryana; Dr. Arindam Talukdar, CSIR-IICB, Kolkata; Dr. Subhas C. 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. We had previously published (***Int J Infect Dis*, 2022**) that COVID-19 serums during Wuhan and Delta waves were highly cross-reactive in Dengue virus (DENV) serological tests and could neutralize dengue (all serotypes) causing less dengue during 2020-21 globally. We have then showed that subsequent Omicron wave serums (due to >30 spike mutations) became 50% less cross-reactive in DENV Ab tests. They could still neutralize DENV serotypes 1, 2 & 4 but possibly caused worldwide surge of DENV 3 due to ADE (***J Med Microbiol*, 2024**).

2. We have provided multiple pieces of evidence that conversely, dengue immunity had been protective against *betacoronaviruses* including SARS-CoV-2 and played a major role in reduced mortality due to COVID in dengue endemic regions like Southeast Asia. Pre-pandemic DENV antibodies neutralized MHV-1, a murine betacoronavirus in plaque reduction assay as well as SARS-CoV-2, also a betacoronavirus in surrogate VNT (***J Med Virol*, 2024**).

3. We have recently published that the number of observed cases of **occult hepatitis B virus infection (OBI)** in eastern India has been increasing. Here, HBsAg/S gene mutations were identified in apparently healthy individuals with OBI, and the S protein variants from these patients were characterized *in vitro*.

Plasma samples from 217 healthy blood donors were collected from three different regions in eastern India and screened for hepatitis B virus (HBV) infection using a nucleic acid amplification test and immunoassays for serological markers. S protein variants found in positive plasma samples were characterized using a liver cell line.

Twenty-nine of the 217 plasma samples tested, were positive for HBV DNA but negative for hepatitis B surface antigen (HBsAg) and antibody to HBV core antigen (anti-HBc). Sequencing of the HBV S gene revealed a novel S protein mutation (L173H) in an area outside the major hydrophilic region. Known OBI-associated mutations (S34L, P178R); a mutation resulting in a stop codon at position 196, associated with lamivudine-resistance; the substitution I81T, and a dual mutation (G145A and Q101H) were also identified.

S proteins containing these mutations, produced by transfection of human hepatoma (Huh7) cells with recombinant plasmids, were undetectable or gave significantly weaker signals than the wild-type control, despite similar levels of S mRNA production for the mutant and wild-type plasmids. **The OBI cases in this study were unexpectedly seronegative**. In vitro analysis revealed that the mutations identified here caused the virus to evade immunodetection using commercial immunoassays, thereby rendering a large portion of the population "silently" infected with HBV (***Arch Virol*, 2025**). In congruence with above results, we had also provided evidence of "silent" HBV infection (OBI) in **Psoriasis, Vitiligo, and *Pityriasis Rosea*** clinical skin disease cases from Kolkata, suggestive of an auto-immune pathology due to chronic exposure to HBV (**IJD, 2024**).

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

1. Study of infection dynamics of Leishmania donovani in the presence of Lepsey NLV1 virus: Role of the virus in patho-biogenesis of Kala-azar and its remediation. ICMR, 2024-27, 113.46 Lakhs, IIRP-0959-2023.
2. Vesicular transmission of Flavivirus & its role in neurodegeneration. CSIR, 2024-2026, 69.44 Lakhs, FBR070305 (Co-PI).

Publications

1. Supekar R., Sarkar J., Chakrabarti P., Biswas S. (2025). Diagnostic challenges due to hepatitis B virus surface antigen mutations outside the major hydrophilic region. ***Archives of Virology* 170**, 71. https://doi.org/10.1007/s00705-025-06256-y.
2. Supekar R., Roy S., De A., Biswas S. (2024). Evidence of "Silent" Hepatitis B Virus Infection in Psoriasis, Vitiligo, and *Pityriasis Rosea* Cases: A Pilot Study. ***Indian Journal of Dermatology* 69**, 422. DOI: 10.4103/ijd.ijd_4_24.
3. Sarker S., Dutta C., Mallick A., Das S., Das Chowdhury C., De A., Gorai S., Biswas S. (2024). Dengue virus (DV) non-cross-reactive Omicron wave COVID-19 serums enhanced DV3 infectivity in vitro. ***J Med Microbiol*. 73**, 001852. https://doi.org/10.1099/jmm.0.001852
4. Mallick A., Sukla S., De A., Biswas S (2024). Evidence support that dengue virus can impart broad-spectrum immunity against betacoronaviruses in dengue endemic regions. ***J Med Virol.* 96**, e29771. https://doi.org/10.1002/jmv.29771

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 (2023); Patent No. KE 1006/Kenya (2024).

Awards

Fellow by election, West Bengal Academy of Science & Technology (WAST), 2025.

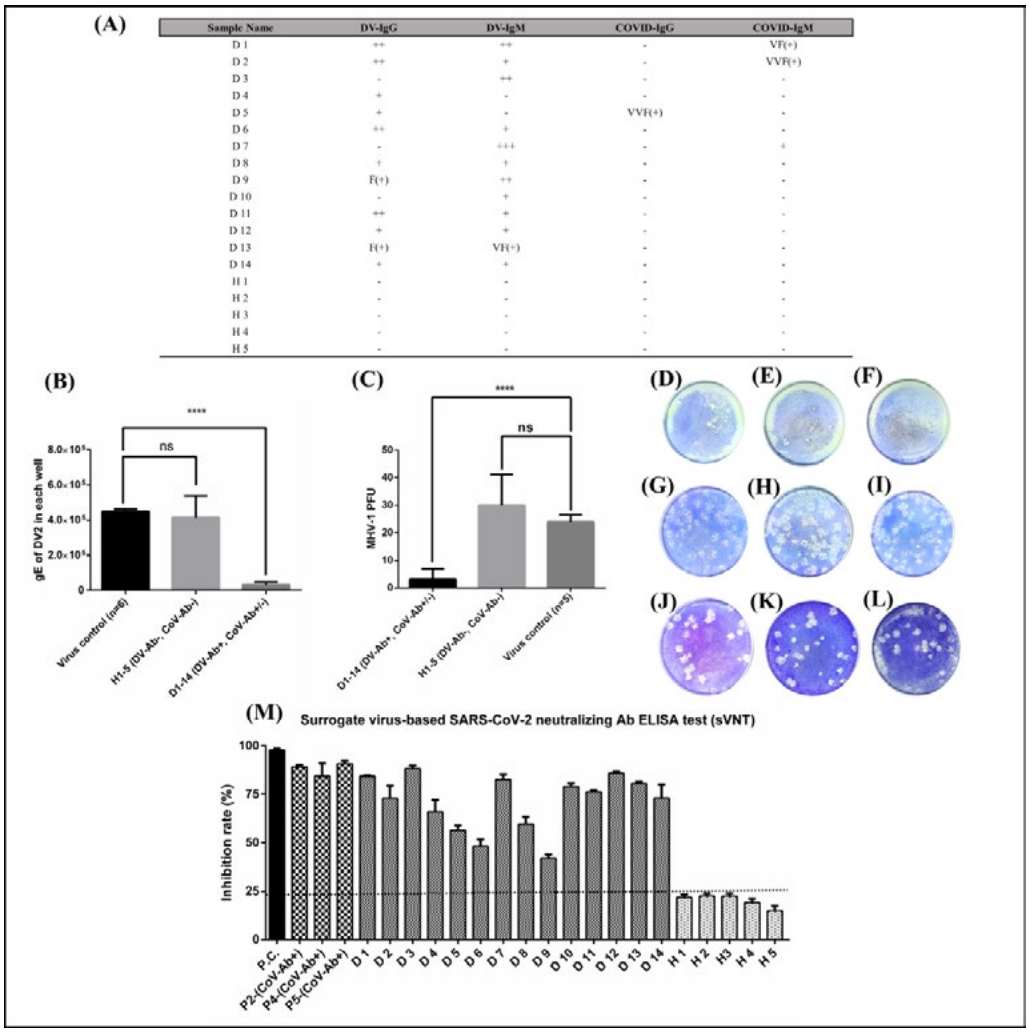


Figure 1: MHV-1 plaque reduction neutralization test (PRNT) and SARS-CoV-2 surrogate virus neutralization test (sVNT) by COVID-19 predated DV serum samples. **(A)** Serological characterization of COVID-19-predated DV-infected and DV non-infected human serum samples by DV and SARS-CoV-2 LFIAs. **(B)** 2D bar graph of VNT of DV-2 where virus titre (mean ± SD) decreased significantly (P<0.0001) by cross-reactive pre-pandemic DV serum samples. **(C)** 2D bar graph representing plaque counts (mean ± SD) from the PRNT assays where significant reduction in PFU was also observed (P < 0.0001). **(D-F)** MHV-1 plaque reduction on L2 cell sheet by COVID-19 predated DV infected patients' serum samples (D1-3). **(G-I)** MHV-1 plaques on L2 cell sheet post-incubation with COVID-19 predated dengue non-infected control serum samples (H1-3). **(J-L)** Plaques were formed on L2 cell sheet, at 48 h after MHV-1 infection (virus control). P values were calculated from minimum three counts for each condition (titres/plaque counts), by two tailed, unpaired t test at 95% level of confidence. **(M)** Surrogate virus-based SARS-CoV-2 neutralizing Ab ELISA test (sVNT) to determine the neutralizing potential of test serum samples. COVID-19 pre-dated DV serum samples (D1-14) showed comparable neutralization pattern as the pandemic SARS-CoV-2 serum samples (P2-, P4- and P5-CoV-AB+ serum samples) or the positive control (P.C.), supplied in the ELISA kit. The control human serum samples (H1-5) could not prevent MHV-1 plaque formation and showed 15-23% inhibition percentage in the sVNT ELISA. The highest inhibition percentage of 23% (H2) observed among the five control human serum samples, was taken as the cut-off (dotted line) of the sVNT ELISA. Each column represents mean ± SD from three replicates for each test sample and the positive control (P.C.) supplied in the ELISA kit.

Dr. Subhajit Biswas, Senior Principal Scientist

Group Members: Abinash Mallick, CSIR-SRF; Chiroshri Dutta, CSIR-SRF; Supratim Sarkar, CSIR-SRF; Sayantan Das, UGC-SRF; Pritam Dey Sarkar, UGC-JRF; Dr. Priyanka Dhar, CSIR-RA; Dr. Sonali Khan, CSIR-PA; Dr. Rudra Chhajer, ICMR-RA; Dr. Paroma Mitra-ICMR-PA

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 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
- Evolution of cargo transport by dynein motors: a potential anti-malaria drug target. Department of Biotechnology (DBT), 2025-2028, 100 Lakhs, BT/PR42978/BMS2/156/1/2024

Publications

Das S, Manna A, Majumdar O, Dhara L. M-*O*-M mediated denaturation resistant P2 tetramer on the infected erythrocyte surface of malaria parasite imports serum fatty acids. **iScience.** 2024 Apr 16;27(5):109760. doi: 10.1016/j.isci.2024.109760. PMID: 38726364; PMCID: PMC11079477.

Conferences Attended

Apicomplexan Parasites Virtual Symposium (Apicomplexa2025-), January 2025 ,23-22, Chaired by Prof. Vern B. Carruthers, University of Michigan Medical School, MI, USA

Dr. Sudipta Das, Ramalingaswami Fellow and Assistant Professor (AcSIR)

Group Members: Dipon Ghosal, Project Associate-II

Dr. Sujoy K. Das and his group members

Anti-Virulent and Immunomodulatory Nano-on-Nanodroplets to Combat Refractory Biofilm Infection

Research Activities

Biofilm-associated chronic wound infection caused by *Staphylococcus aureus* often causes major life-threatening complications including inflammation, tissue damage, and accounts for an annual death of ≈17 million globally. The irreversibly adhered bacterial cells of the biofilms are held accumulated by a self-secreted hydrated extracellular polymeric substances (EPS) matrix hindering the penetration and diffusion of different antimicrobials including antibiotics, leading to the development of antimicrobial resistance (AMR). Bacterial infection usually instigates the innate immune response as the first line of host defense leading to the pro-inflammatory microbicidal activity. Upon infection, these macrophages differentiate into M1 or pro-inflammatory phenotype which are remarkably characterized by the increased levels of proinflammatory cytokines. However, the highly acidic and H_2O_2-rich microenvironment of bacterial biofilm intervened with these macrophage responses by secreting a large quantity of pore-forming endotoxins, which led to an alteration in the cellular permeability, causing their membrane dysfunction. In this manner, the entire host defense innate immune response remains compromised with inhibited phagocytosis and induced macrophage damage. The advancement of nanotechnology-based antibiofilm agents has emerged as excellent therapeutics for the disruption of these notorious biofilms.

Inspired by the fusogenic property of the nanodroplets and immunomodulatory functions of the metal nanoparticles, a target specific nano-on-nanodroplets were engineered as an anti-virulent and immunomodulatory therapeutics against the *S. aureus* biofilm microenvironment, activating macrophage polarization and phagocytosis to eradicate the biofilm biomass. These innovative nano-on-nanodroplets were prepared through the synthesis of cetylpyridinium chloride (CPC) functionalized silver nanoparticles (AgNPs) on the template of nanodroplets (**Figure 1**). The as-synthesized nano-on-nanodroplets (C-AgND) (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 specific binding of C-AgND neutralizes the negatively charged EPS layer, causing their destabilization followed by penetration of the nanoformulation into the biofilm matrix, killing the persister cells. Consequently, C-AgND eliminates the virulence property of the *S. aureus* biofilm through α-hemolysin neutralization. C-AgND promotes a strong immunomodulatory effect by polarizing macrophages into their M1 phenotype to induce phagocytosis of the disintegrated biofilm-released residual cells, rejuvenating the host's innate immune responses. Further the results demonstrated significant up-regulation of iNOS expression after the treatment

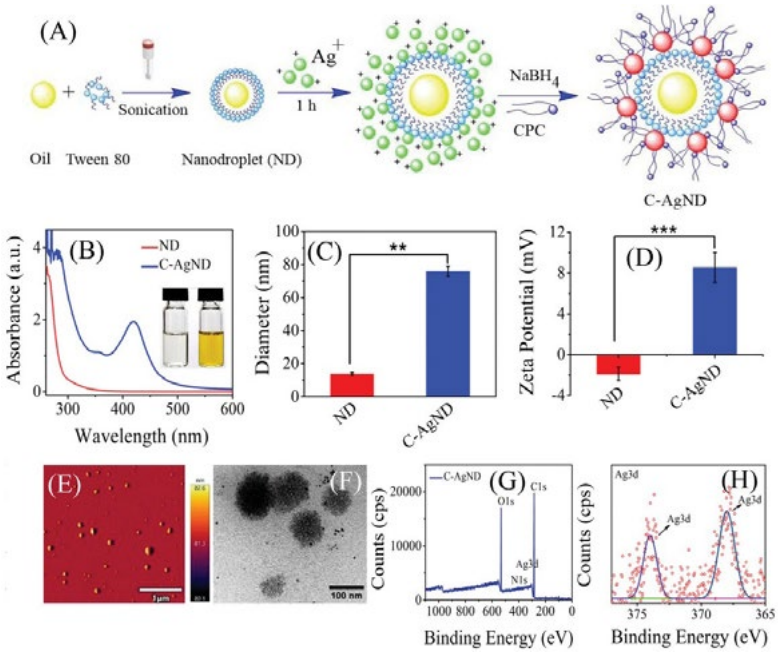


Figure 1: Synthesis and characterization of C-AgND. Schematic presentation and chemistry (A) of the synthesis of novel nano-on-nanodroplets (C-AgND). UV–vis spectra (B) of ND and C-AgND; the inset images exhibit the colored physical images of ND and C-AgND. DLS measurements (C) of ND and C-AgND. Zeta Potential values (D) of ND and C-AgND. AFM image (E) of C-AgND. HRTEM image (F) of C-AgND. XPS survey spectra (G) of C-AgND. High-resolution XPS spectrum (H) of Ag 3d spectra of C-AgND.

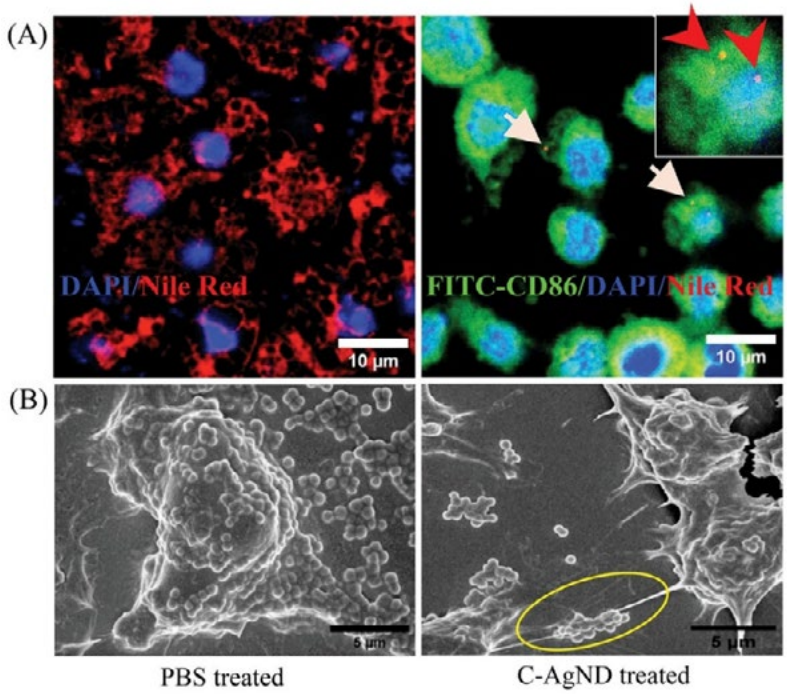


Figure 2: C-AgND-induced phagocytosis by macrophage cells. Immunofluorescence staining (A) and FESEM analysis (B) exhibiting bacterial phagocytosis after C-AgND treatment to macrophages, Scale bar, 10 and 5 µm respectively. Red arrows in the right panel inset and white arrows in the right panel depict the bacterial cells engulfed within the macrophages. Yellow circle depicts the antigen presentation ability of the macrophage cells engulfing the bacteria.

with C-AgND, suggesting that C-AgND had the potential to be an intrinsic immunomodulator to polarize the macrophages into their M1 phenotype. The release of proinflammatory cytokines further accelerate the antibiofilm immune responses and trigger the phagocytosis. The CLSM and FESEM images (**Figure 2**) demonstrated phagocytic efficacy of the C-AgND-induced M1 macrophages. In the M0 macrophages, the biofilm infection caused the bacterial cells to bind to the entire surface of the macrophages, causing structural deformation and dysfunction of the macrophages, and thus impaired their phagocytic efficacy. In nonstrast, C-AgND treatment induced macrophage polarization from M0 to M1 having increased antigen-presenting ability favoring the engulfing of the bacterial cells inside the macrophage cells. The ex vivo skin wound infection model further illustrates an excellent biofilm eradication efficacy of C-AgND in comparison to the commercial ones, rendering them to be a promising replacement of existing antibiofilm agents in clinical application.

Future Research Plans

- **Novel drug delivery system using microneedle patch**

Microneedle technology has 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.

Extramural / CSIR Funding

1. Hemostat – A Lifesaving Bandage for Faster Bleeding Arrest (BT/AIR0711/PACE-17/19), BIRAC, Govt. of India, 46.65 lakh, 2023-2025.
2. Development of antimicrobial peptide tagged nanoformulation for targeted combination therapy against *Pseudomonas aeruginosa* (STBT-13015/3/2024-WBSCST SEC)**,** DSTBT, Govt. of West Bengal, 28.13 lakh, 2023-2026.

Publications

1. Bose, S., Das, S.K. (2025) Biofilm Microenvironment-Sensitive Anti-Virulent and Immunomodulatory Nano-on-Nanodroplets to Combat Refractory Biofilm Infection Through Toxin Neutralization and Phagocytosis. *Adv. Healthcare Mater*. ***14***, 2403528.
2. Choudhary, P., Ramalingam, B., Bose, S., Das, S.K. (2025) Antibacterial and safe chitosan–graphene hydrogel films: a promising nanotherapeutic for Staphylococcus aureus wound infections. *Biomater. Sci*. ***13***, 639-658.
3. Choudhary, P., Ramalingam, B., Shaw, A, Das, S.K. (2025) Nanoengineered and highly porous 3D chitosan-graphene scaffold for enhanced antibacterial activity and rapid hemostasis. *Int. J. Biol. Macromol*. ***306***, 141521.

Member of Society

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

Dr. Sujoy K Das, Principal Scientist

Group Members: Somashree Bose, UGC SRF; Sivanghi Parhi, DBT SRF; Arpita Mukherjee, UGC SRF; Avishek Shaw, DBT JRF; Nourin Parvej, Project JRF; Soumyajit Nandi, PA

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 Imbalance of cortisol and dehydroepiandrosterone (DHEA) level was observed in several infectious diseases and high plasma cortisol levels were also found in human visceral leishmaniasis. However, the mechanism remains ambiguous. In *L. donovani*-infected BALB/c mice, we observe increased cortisol versus decreased DHEA levels coincide with high organ parasite burden and anti-inflammatory cytokines along with increased 11β-hydroxysteroid dehydrogenase (11βHSD1) expression. DHEA treatment in J774 and THP-1-derived macrophages restrains *L. donovani*-induced cortisol levels by inhibiting 11βHSD1 expression that increases pro-inflammatory and decreases anti-inflammatory mediators, thereby lowering intracellular parasitemia. In infected THP-1-derived macrophages, DHEA reciprocally regulates glucocorticoid receptors (GR) - GRα and GRβ expression, increasing GRα/GRβ heterodimers, which antagonize GRα homodimer binding on IL-10, DUSP-1 and IκBα promoters. Finally, *L. donovani* induces PPAR-γ binding on 11βHSD1 promoter by lipophosphoglycan, which drives cortisol production. Collectively, our observations identify DHEA as a potent immunomodulator which inhibits cortisol-mediated immunosuppression and GRβ induction to counteract GRα-anti-inflammatory signalling.

Understanding the crosstalk between mitochondrial OXPHOS and alternative activation/immunosuppression of macrophages during experimental visceral leishmaniasis

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. 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

Extramural / CSIR Funding

1. Facility Creation Project (FCP) entitled "National Facility for Secondary and Tertiary (Preclinical validation) screening of small molecules and phytopharmaceuticals against India's dominant diseases (CSIR FCP).
2. Towards discovery and development of novel drugs and pharmaceuticals (Ministry of Earth Sciences, Govt. of India,)

Publications

1. Seth, A., Dutta, M., Sarkar, R., Prusti, P., Katiyar, S., Kar, S. (2025) DHEA counteracts Leishmania donovani-induced cortisol:GR signaling-mediated immunosuppression and anti-inflammatory bias. The Journal of Infectious Diseases. (Online ahead of print).
2. Qamar, T., Misra, D.P. & Kar, S. Semaphorins and its receptors: Emerging cellular biomarkers and therapeutic targets in autoimmune and inflammatory disorders. (2025) Life Sciences. 361:123281

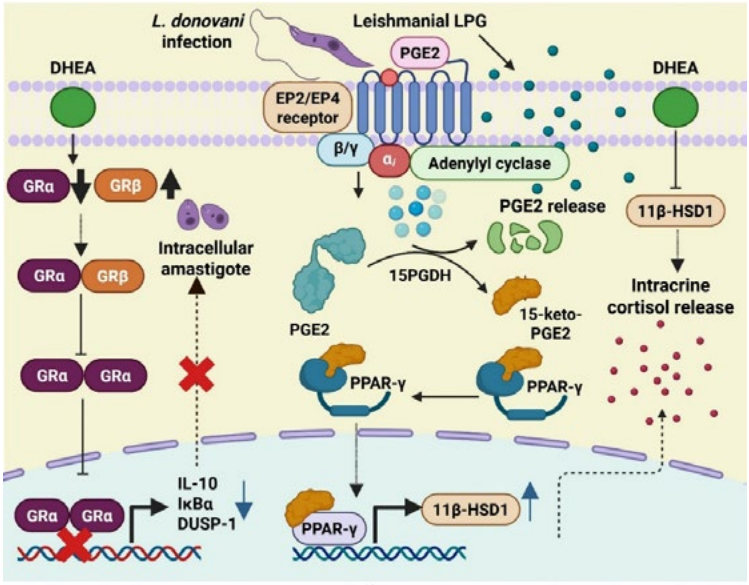


Figure 1: A diagrammatic depiction of how DHEA administration exerts immunomodulatory effect by reciprocal regulation of GRα/GRβ isoforms in human THP-1-derived macrophages, leading to marked increase in heterodimers that antagonize GRα homodimer binding on positive GRE of upstream promoter regions of key anti-inflammatory mediators namely: IL-10, DUSP-1 and IκBα that may support parasite persistence. In addition, DHEA also exhibits direct inhibitory effect on 11βHSD1 enzyme, thereby lowering its expression. The figure further demonstrates how *L. donovani* LPG induces production of PGE2 which, converts into 15keto-PGE2, providing ligands for activation and nuclear translocation of PPAR-γ receptor. The latter then consequently binds to 11βHSD1 promoter, increasing its expression and cortisol release. However, DHEA treatment serves to directly inhibit 11βHSD1 enzyme expression, which may potentially lower intracellular cortisol production and reduce ligands for anti-inflammatory GR signalling.

Invited Lectures

Invited lecture delivered at KARYASHALA National Workshop on Human Metagenomic Sequencing Data Analysis: Emphasis on Health and Disease on a 7-day hands on workshop held at the BRIC-NIBMG campus from 22nd to 28th July, 2024.

Conferences Attended

Molecular Immunology Forum (MIF 2024) meet organized by IISER, Bhopal.

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: Ritika Sarkar, UGC JRF; Prabha Prusti, CSIR JRF; Kashmiri Naaz, CSIR JRF; Ishita Chatterjee, Project associate 1

Collaborators: Dr. Mrigank Srivastava, CSIR-CDRI, Lucknow; Dr. Ajit Chande, IISER, Bhopal

Dr. Umesh Prasad Singh and his group members

Discovery of therapeutics against viral diseases and cancer

Research Activities

Our endeavour has been towards development of therapeutic from natural sources/synthetic compounds. Our focus is mainly antivirals for dengue and SARS-Cov2 and cancer.

We have obtained several unnatural amino-acid-containing peptide leads with IC_{50} of about 1-2 μM against dengue virus NS3/NS2B protease. The design focuses on metabolic stability of these peptides in human plasma for increased half-life, which is one of the main problems with peptide-based therapeutics. If successful, it can potentially be a first-in-class non-coded amino acid based peptide as a therapeutic agent against dengue.

We have also been trying to find some new molecules against colorectal cancer from natural products. In this direction, through our theoretical computational studies using some of the targets of colorectal cancer like MDM2, followed by natural product isolation and testing in cancer lines. We have successfully identified two limonoids — Swietenine (**1**) and Swietenolide (**2**) — from the seeds of *S. macrophylla* (Pal et al., 2023). Both these compounds showed strong anti-colorectal cancer (CRC) activity in lab tests using the HCT-116 cell line, with IC_{50} values of 10.5 μM (5.96 μg/ml) and 5.6 μM (2.7 μg/ml), respectively. We showed that these compounds activity works through the inhibition of mouse double minute 2 (MDM2) homolog (Fig. 1).

Importantly, the activity of compound **2** (IC_{50} = 5.6 μM) is almost the same as that of the standard anti-cancer drug 5-fluorouracil (5-FU; IC_{50} **= 5 μM).** This finding is uncommon for natural products as usually they show very low activity. Compounds **1** and **2** are 8.5 to 15.6 times more active than the crude chloroform extract of the identified plant *S. macrophylla*.

Our further studies showed that the Selectivity Index (S.I.=CC_{50}/IC_{50}), which measures how many folds it is selective for particular targetted cell-lines (here colorectal cancer) compared to normal cancer cells. The S.I. was found to be 7 for compound **1** and 13 for compound **2**, much higher than the extract's S.I. (~2) against CRC. This suggests that both compounds, especially compound **2**, could serve as promising agents against human colorectal cancer. Further studies, which would require enhancing the potency of

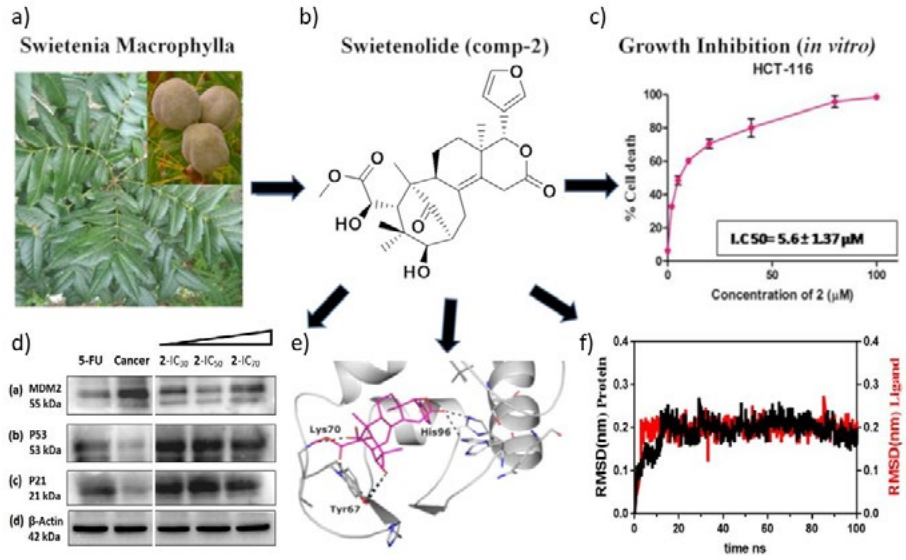


Figure 1: The graphical abstract, shows (a) the plant *S. Macrophylla* (leaves) and also its fruits (in brown colour) from which the limonoids were isolated. (b) The scheme of the most active molecule (Swietenolide, the compound **2** is shown. (c) The curve shows the increase in % cell death with increasing concentration of compound **2**. (d) The comparative change in expression levels of MDM2, P53, P21 due to treatment with compound **2** at different concentrations. The expression levels in +ve control (5 FU treatment at 5 µM) and –ve control (no treatment, cancer cell-line), and expression level of housekeeping protein β-actine are also shown. (e) The docking studies shows the theoretical binding pose of compound **2** (in stick model, magenta) with target protein MDM2 active site (shown as cartoon, in grey colour). Some of the residues of MDM2 active site are shown as stick model and are labelled. (f) The MD simulation studies showing RMSD of the protein (MDM2) and the bound ligand (compound 2) during 100 ns simulation time.

these molecules significantly are underway to develop these molecules/analogues as potential colon cancer therapeutics.

In another collaborative work we explored the potential of melatonin as anti-gastric cancer therapeutic. Cancer cells mainly use glucose as their energy source. As a result, high blood sugar (hyperglycemia) can make them grow more aggressively. Hence, in this collaborative study (Chatterjee et al., 2024), we explored the potential of melatonin to counter this aggressive growth in AGS cells, a human gastric cancer cell line, under high-glucose conditions.

Melatonin reduced cell proliferation in a dose-dependent manner, altered MMP-9 and TIMP-1 expression, and arrested cells in the G0/G1 phase by binding to the ATP site of CDK-2, inhibiting its kinase activity. It also decreased cyclin D1, cyclin E, CDK-4, and CDK-2 expression.

These findings suggest that melatonin has strong anti-gastric cancer potential and could be considered for future treatments of gastric cancer in patients with hyperglycemia.

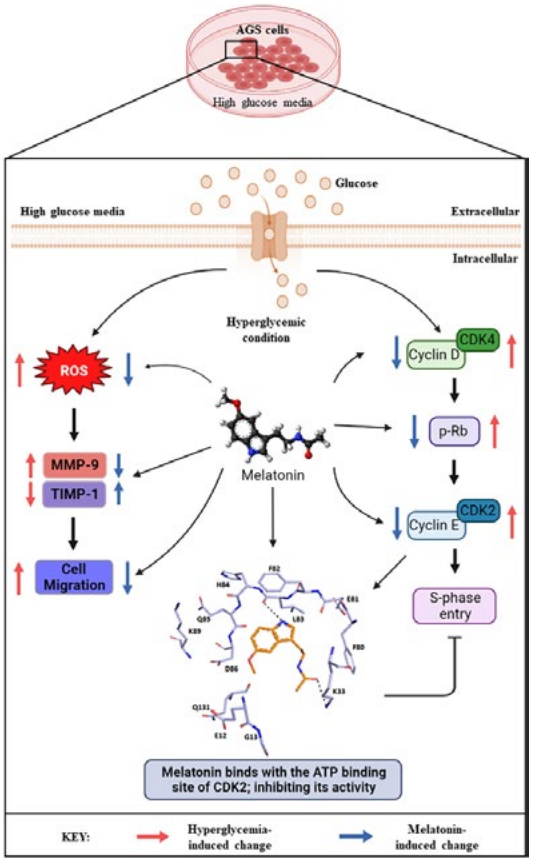


Figure 2: The graphical abstract showing the overall design of the study and its findings.

Future Research Plans

- Since, we have already 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. We further plan to do animal testing to develop them further.
- The natural product based anti-cance molecules also hold promise due to its reasonable good potency and high selectioty for cancer. In a collaborative effort we would like to do further SAR based on this natural product to enhance its potency and do its pre-clinical development towards a possible clinical candidate.

Extramural / CSIR Funding

1. CSIR Phytopharmaceutical Mission (Phase III), CSIR, 2024-2026, 145.56 lakhs, (MMP075201)
2. Towards discovery and development of novel drugs and pharmaceuticals, CSIR–Deep ocean mission, 2024-2027, ~ 900 lakhs (one of Co-PIs).
3. Establishing of *in vitro* dengue protease activity based high throughput screeningplatform and discovery of synthetic and/or natural product based protease inhibitorsfor dengue virus. [OLP-118]. CSIR-IICB, 2024-25, 10 Lakhs.

Publications

1. Chaudhary, S.; Rai, R. N.; Jyothi, D.; Singh, U. P.; Kumar, (2024) A. Solid-State Green Synthesis of Two (1:1) Organic Intermolecular Compounds; Their Physico-Chemical, Thermal, Single Crystal Growth, and Atomic Packing Studies. *Mater. Chem. Phys. 322*, 129541. https://doi.org/10.1016/J.MATCHEMPHYS.2024.129541.
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.* 908–895 ,(2) *82*. https://doi.org/10.1007/S12013-024-01241-9.
3. Pal, P. C.; Nag, S.; Jyothi, D.; Das, S.; Saha, K. Das; Singh, U. P. (2024) 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.* 2104–2097 ,(12) *38*. https://doi.org/10.1080/14786419.2023.2233045.

Invited Lectures

Structural and Computational Studies for Discovery and Development of Therapeutics against some Viral Proteins, Central University of South Bihar, One Week Short Term Prog (Interdisciplinary) on 'Bioinformatics and Biological Research' March 29-24th 2025.

Conferences Attended

Thematic Conclave on Mental Health and Wellbeing" as part of the "One Week One Theme" (OWOT) initiative. CSIR-IICB, November 11-12, 2024

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: Purna Chandra Pal, NIPER SRF; Abhishek Lahiri, CSIR-SRF; Deeti Jyothi, CSIR-GATE-SRF; Sudesna Das, CSIR-SRF; Riya Baral, ICMR, 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. Kishan Gopal, Sr. Principal Scientist, IMTECH, Chandigarh; Dr. Snehasikta Swarnakar, CSIR-IICB, Kolkata

Dr. Upasana Ray and her group members

Dengue virus NS1 protein differentially modulates expression of multiple liver cell proteins in favour of virus pathogenesis

Research Activities

Non-structural protein NS1 is an important pathogenic protein for Dengue and other similar viruses. Liver function gets modulated during Dengue infection displaying various pathological signs. As liver is an important organ affected by Dengue infection, our laboratory studies molecular mechanisms of Dengue virus NS1 mediated pathogenesis in liver. NS1 has both intracellular as well as extracellular isoforms and thus NS1 can participate in mediating virus related pathogenic effects in diverse ways.

Previously, we had performed next-generation sequencing to generate a transcriptome profile of liver cells over-expressing Dengue virus NS1 protein. Currently, we are interested in studying the role of NS1 in modulating liver cell factors in favour of virus pathogenesis, therapeutic target identification and therapeutic candidate designing. Broadly we are studying roles of NS1 in modulation of cell surface receptors; coagulopathy and vasculopathy; mitochondrial function and lipid metabolism.

Our laboratory has been engaged in addressing the following research questions:

- Understanding the molecular mechanisms of NS1 mediated modulation of cellular receptors and implications on virus infection and pathogenesis.
- Understanding the role of NS1 in modulation of mitochondrial function and its role in mediating virus pathogenesis.
- Understanding the mechanism of NS1 mediated dysregulation of factors related to coagulation cascade.

NS1 mediated modulation of cellular receptors and implications on virus pathogenesis

Earlier we had demonstrated that Dengue virus NS1 leads to upregulation of specific cell surface receptors on liver cells. We found that out of the upregulated receptors, PHB1 and PHB2 were interacting directly with the viral envelope protein leading to enhanced viral entry under NS1 overexpression. Also, we demonstrated that both PHB1 and PHB2 exist together in the envelope and plasma membrane protein interaction complex. Although PHB1 and PHB2 were upregulated under NS1 overexpression in liver cells, when we checked for the modulation of PHB1 and PHB2 on other cell types we observed that upregulation could be found in some while in others the levels were unaffected. Thus, role of NS1 mediated upregulation of PHB1 and PHB2 leading to enhancement of virus infection appears to be tissue specific.

Details: Earlier it was shown that Dengue virus envelope binds to PHB1 and PHB2 and upregulation of PHB1/2 after Dengue NS1 upregulation in liver cells leads to enhanced entry of envelope protein. Previously, upregulation of PHB1/2 was demonstrated under the transient NS1 overexpression. We first confirmed if PHB1 and PHB2 were also upregulated under virus infection (Figure 1).

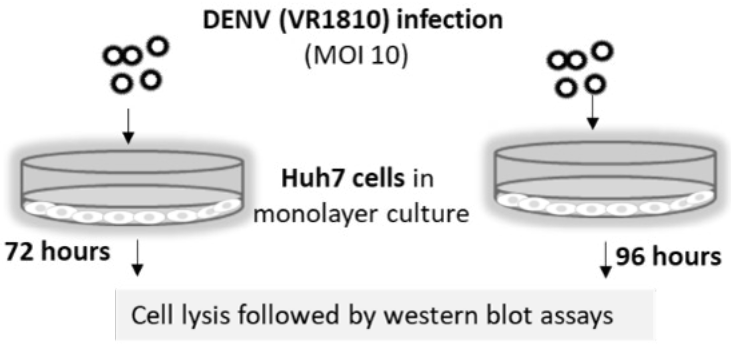


Figure 1: Experimental set up of virus infection Huh7 cells

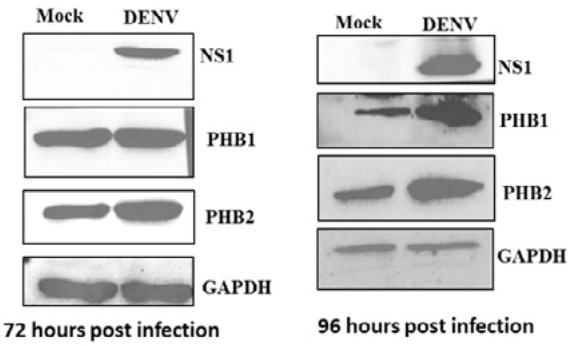


Figure 2: Effect of Dengue virus infection on PHB1 and PHB2 in assay to validate PHB1/2 overexpression

Huh7 cells were infected with Dengue virus (serotype 2) for either 72 hours (3 days) or 96 hours (4 days). Cells were harvested and cell lysate was used to perform western blot assays for PHB1 and PHB2. Both PHB1 and 2 were found to be upregulated (Figure 2). Upregulation was more prominent at 96 hours post infection.

We also verified the upregulation of PHB1 and 2 in AG129 mice model infected with Dengue virus (Figure 3).

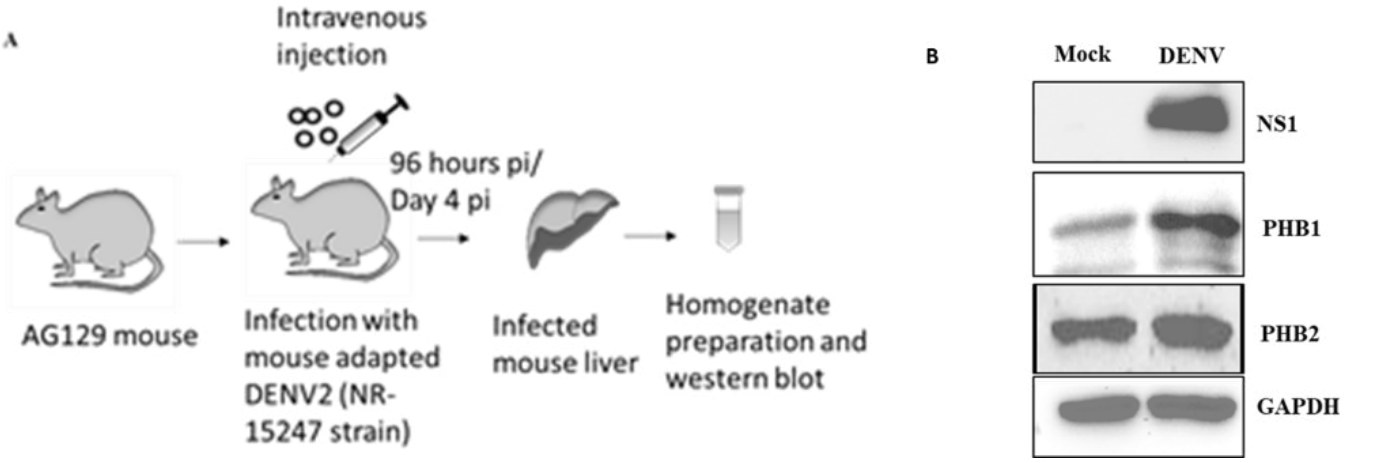


Figure 3: Effect of Dengue virus infection on PHB1 and PHB2 in AG129 mice infected with Dengue virus. (A) Experimental set up (B) Western blot assay. DENV: Dengue virus; pi: post-infection

4 days post-infection liver was used to prepare liver cell homogenate and western blot assays were performed to check the status of PHB1 and PHB2 levels. We found that both PHB1 and PHB2 were upregulated due to Dengue infection in AG129 mice.

To study/ characterize and target envelope, PHB1/2 interaction we first checked if PHB1 and PHB2 occur together while envelope binds the cell surface prohibitins. For this we Huh7 cells were used to prepare plasma membrane extract. Plasma membrane extract was allowed to bind with Dengue virus (serotype 2) envelope protein. Anti-PHB2 antibody was used to pull down the envelope-plasma membrane protein complex. Presence of envelope protein and PHB2 was confirmed using western blot assay. Also, anti-PHB1 antibody was used to perform western blot to check the presence of PHB1 in the complex. We found that Dengue envelope protein binds PHB1 and PHB2 as a single complex (Figure 4). We are preparing a manuscript using this data with other data that was generated earlier.

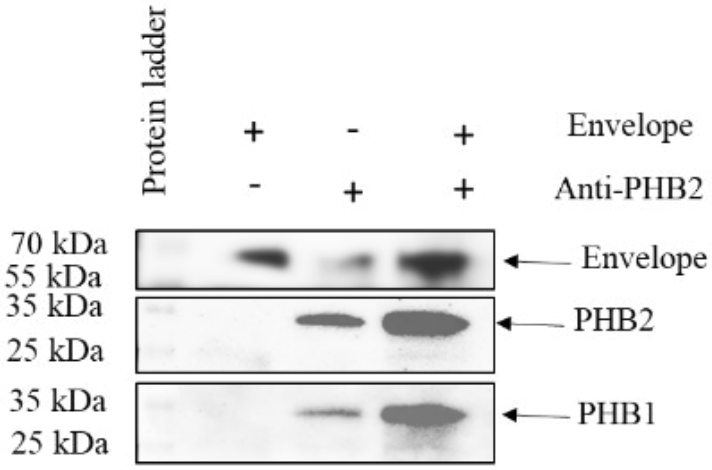


Figure 4: Immuno-pulldown assay of Dengue envelope-plasma membrane protein complex

Further, envelope and PHB1/2 proteins were docked to select the best fit binding complex and MD simulation studies were performed in collaboration with Dr. Saikat Chakrabarti to confirm if the complex is stable. Based on the molecular docking, peptides were designed. These peptides will further be used to validate the interaction interface.

NS1 mediated modulation of mitochondrial function

PHB1/2 are also found in mitochondrial membrane. Considering the important roles of PHB1/2 in mitochondria, we checked the effect of NS1 on mitochondrial PHB1/2. We have shown that PHB1 and PHB2 incorporation in liver cell mitochondria were also getting modulated implying possible dysregulation of mitochondrial function. We observed that NS1 co-localized with mitochondria indicating possible translocation of cytoplasmic NS1 to mitochondria. At present we only know that NS1 exists with mitochondria. We are performing deeper studies to check if NS1 exist on the mitochondrial surface or NS1 enters mitochondria.

NS1 mediated dysregulation of factors related to coagulation cascade

We have shown earlier that NS1 overexpression or virus infection leads to downregulation of some of the coagulation factors belonging to the common pathway of the coagulation cascade including factor I, V, X and XIII. It is known that fibrinogen or coagulation factor I gene expression gets modulated by IL6. In our study we have found that IL6 receptor on the liver cell surface gets downregulated due to NS1 overexpression. As IL6 uses IL6 receptor to gain entry in hepatocytes, downregulation of IL6 receptor can lead to reduced expression of fibrinogen thus contributing to coagulopathy. IL6 has many other important roles and dysregulation of IL6 receptor can thus potentially disrupt many cellular functions. IL6 receptor has two subunits, IL6R alpha and gp130. We found that both the receptor subunits got downregulated due to virus infection and NS1 overexpression.

Further studies are ongoing to understand the molecular mechanisms behind NS1 mediated cellular pathogenesis. Details: IL6 receptor has two subunits, IL6Rα and gp130 (Figure 5).

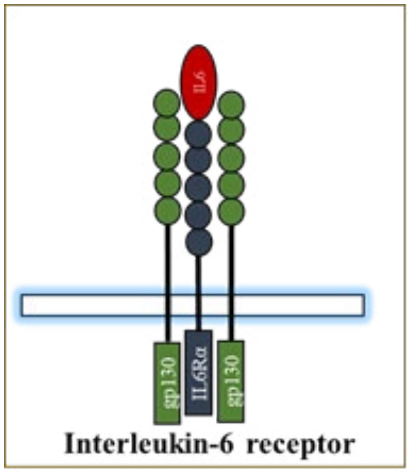


Figure 5: IL6 receptor subunits

In our transcriptomics data, IL6 receptor was seen to be downregulated under NS1

overexpression. We first validated the transcriptomics data by checking the levels of both IL6Rα and gp130 in Huh7 cells overexpressing Dengue NS1 (serotypes 2) using western blot assays. Our data revealed that both the subunits of IL6 receptor get downregulated due to NS1 overexpression (Figure 6).

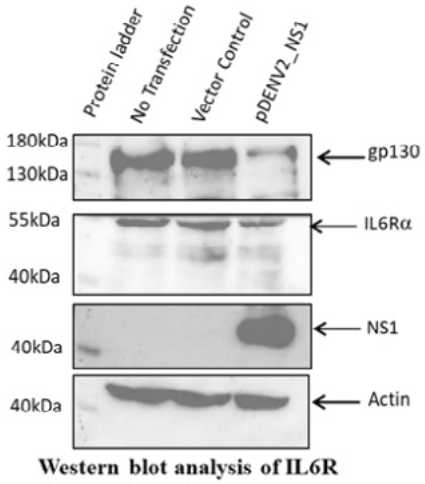


Figure 6: Western blot assay to assess Huh7 cells

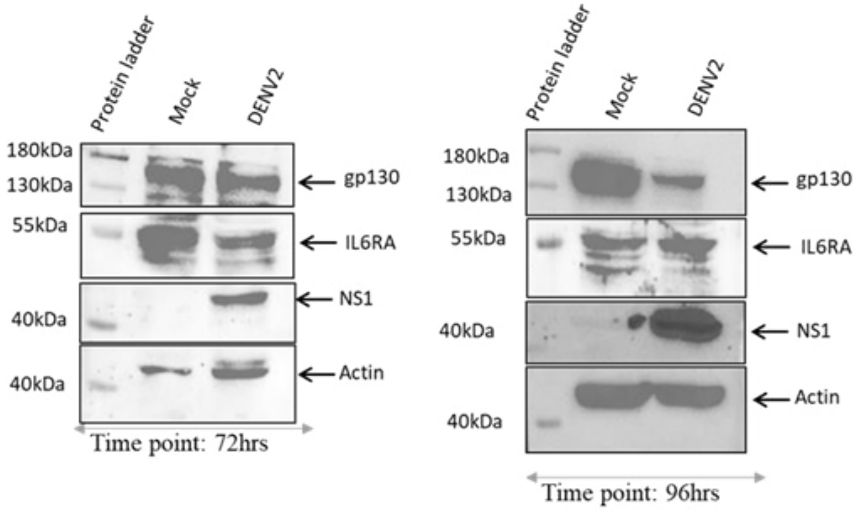


Figure 7: Validation of IL6 receptor modulation in DENV2 infected levels of IL6 receptor subunits

As Dengue virus has other proteins as well, during natural Dengue infection, NS1 will not be present in isolation. Thus, we wanted to validate the downregulation of IL6 receptor subunits in the presence of all other proteins of Dengue virus. For the same, we performed virus infection assays. Huh7 cells were infected with Dengue virus for 72 hours and 96 hours followed by harvesting the cells, cell lysate preparation and western blot assays (Figure 7). We observed that the two subunits of IL6 receptor were getting downregulated. IL6Rα levels got downregulated at 72 hours and became normal by 96 hours i.e. after 4 days of infection. After 4-5 days Dengue patients start recovering. Thus, at present we assume that IL6Rα levels getting close to mock might represent a situation akin to that of recovery phase.

Further, from our transcriptomics data of genes modulated due to NS1 overexpression in Huh7 cells, we have shortlisted transcription modulators of IL6 receptor. This preliminary data will be further validated to understand the mechanism of regulation of IL6 receptor subunits.

Future Research Plans

In future we will further study the role of NS1 mediated modulation of serum PHB1 and PHB2 in virus pathogenesis. We will check the effect of NS1 overexpression on mitochondrial structure to relate with pathogenic effects on liver function. We have shortlisted other soluble receptors as well that got differentially modulated in our transcriptpmics study. We will now try to validate the expression of those soluble receptors so as to widen our understanding about the mechansims of disease pathogenesis. All our research will help us identify targets for molecular intervention with an objective of management of disease severities.

Extramural / CSIR Funding

1. OLP118 project (CSIR-IICB) with following work packages:

   Project package 1: Characterizing PHB1/2 receptor-Dengue envelope protein interaction interface for designing anti-NS1 induced entry enhancement inhibitors

   Project package 2: Characterizing the NS1 mediated modulation of IL6 receptors in liver cells and effect of IL6 receptor modulation on IL6 entry and liver cell function with special focus on coagulopathy.

2. Role of Dengue virus NS1 induced modulation of soluble receptors from liver in progression of virus pathogenesis (Project submitted to DBT)

3. NS1-mediated modulation of Prohibitin 1 and 2 and its impact on mitochondrial function in hepatocytes during dengue infection (Project submitted to ICMR)

Publications

1. Das, S., Mallik, M. H., Chattopadyay, P., Mallick, S., Karmakar, D., Ghora, S., Begum, F., Chatterjee, B., Thagriki, D. S., Srivastava, A. K., & Ray, U. (2024). Dengue virus NS1 leads to downregulation of HNF4 alpha in liver cells resulting in a decrease in coagulation factors I, V, X, and XIII, contributing to coagulopathy. Journal of virology, 98(12), e0141824. https://doi.org/10.1128/jvi.01418-24.

2. Begum, F., Chandra, S., Mallik, M. H., Dey, J., Tripathi, P. P., & Ray, U. (2024). A SARS-CoV-2 peptide antigen purified from bacteria and displayed in a high-density repetitive manner on a virus-like particle could generate anti-SARS-CoV-2 neutralizing antibodies unlike free peptide. Biochemical and biophysical research communications, 739, 150579. https://doi.org/10.1016/j.bbrc.2024.150579

Patents

A recombinant construct for screening drugs against SARS-CoV-2 spike protein. Upasana Ray, Feroza Begum, Prem Prakash Tripathi, Amit Kumar Srivastava, (United States of America-Publication Number:20250003966; Republic of Korea-Publication Number:1020240099336; China-Publication Number:118355125; Brazil-Publication Number:112024008107; Europe-Publication Number:4423281; Japan-Publication Number:2024541032)

Invited Lectures

1. Viruses and vaccine (Invited talk for biology section). Invited by regional task-force of the Inter-Academy Panel for Women in STEMM (IAP-WiSTEMM), which is a joint initiative of the three national science academies of India - the Indian National Science Academy (INSA), the Indian Academy of Sciences (IASc), and the National Academy of Sciences, India (NASI), Satyendra Nath Bose National Centre for Basic Sciences (SNBNCBS, Sector-III, Salt Lake, Kolkata) (February, 2025)
2. Viruses and vaccine strategies. Invited talk for Refresher course in Life Sciences -MMTTC-Central University of Kerala (January 2025)
3. Novel insights into the role of Dengue virus NS1 in mediating virus pathogenesis. Invited talk at 'The Genomics Analysis & Technology Conference Lite (East)', 2024 by Bencos Healthcare Solutions, Kolkata (August, 2024)

Conferences Attended

The Genomics Analysis & Technology Conference Lite (East)', 2024 by Bencos Healthcare Solutions. Kolkata (August, 2024)

Member of Society

Life member of Indian Virological Society (2025)

Awards

'Indian Immunology Society- Women in science' recognition by Indian Immunology Society (2025)

Dr. Upasana Ray, Principal Scientist

Group Members: Feroza Begum, CSIR-SRF (recently received her provisional PhD degree); Sandeepan Das, CSIR-SRF (recently received her provisional PhD degree); Md Hasan Mallik, UGC-JRF; Subhadip Ghora, UGC-JRF; Prabhat Lama, UGC-JRF

Collaborators: Dr. Partha Chattopadhyay, Head, Department of Medicine, Sagore Dutta Medical College and Hospital, Kamarhati; Dr. Dhableshwar Patra, Senior Scientist, CSIR-IICB, Kolkata; Dr. Saikat Chakrabarti, Senior Principal 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. 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.

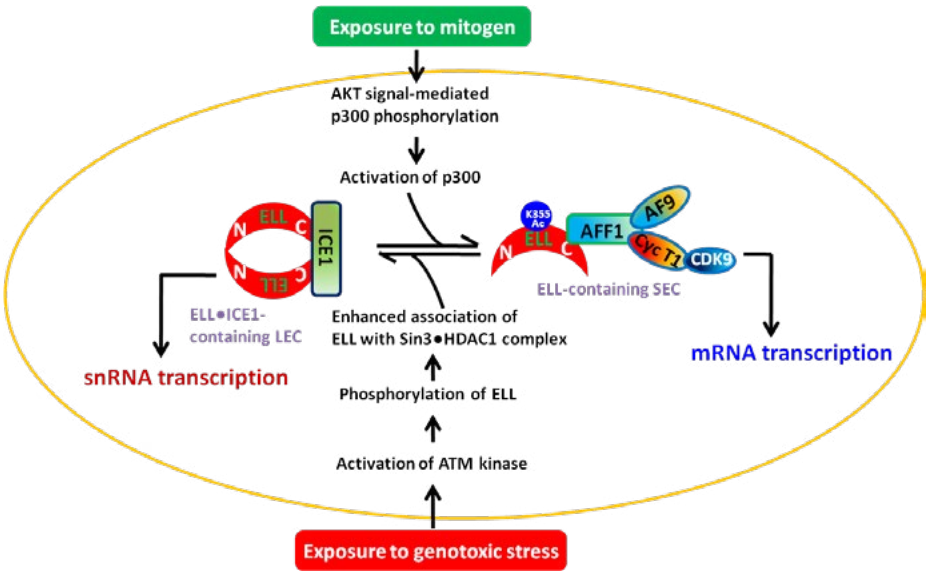
Aims and Objectives

- Detailed studies on role of p300 autoacetylation in global regulation of context-dependent transcription within mammalian cells.
- Mechanistic understanding of role of selective association of ELL components of SEC complex in regulation of global mRNA and snRNA gene transcription.

- Mechainstic understanding of regulation of SEC functions in context-dependent global transcription within mammalian cells.

Work Achieved

Dynamic partitioning of a critical elongation factor between SEC and LEC regulates cellular mRNA and snRNA transcription



Human RNA polymerase II (Pol II) regulates transcription of significant number of global mRNA and snRNA genes by involving Super Elongation Complex (SEC) and Little Elongation Complex (LEC) respectively. However, underlying mechanisms of these differential involvements of Pol II are not known. In this study, we show that human ELL, through its dynamic differential association within SEC and LEC, controls expression of target mRNA and snRNA genes by regulating Pol II recruitment. Mechanistically, we show that p300-mediated acetylation of Lysine 355 (K355) residue favors ELL monomerization and corresponding ELL●SEC formation and mRNA transcription; and reciprocally, HDAC1-mediated deacetylation favors dimerization and subsequent ELL●LEC formation and snRNA transcription; and *vice versa*. Physiologically, we show that whereas, mitogen treatment enhances AKT signaling-dependent p300-mediated ELL(K355) acetylation leading to increased ELL●SEC assembly and mRNA transcription, genotoxic stress causes ATM-mediated ELL phosphorylation-dependent deacetylation of ELL(K355) by Sin3●HDAC1 complex causing enhanced ELL●LEC assembly and snRNA transcription.

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

Overall model depicting functional regulation of expression of mRNA and snRNA genes in a context-dependent manner that involves p300-mediated acetylation of ELL at K355 residue and deacetylation by Sin3A●HDAC1 complex. Upon exposure to mitogen that promotes growth and proliferation of cells, through activation of signalling, human p300 gets phosphorylated by Akt at key Ser1834 (S1834) residue that activates its autoacetylation resulting in activation. Upon activation, p300 acetylates ELL at K355 residue that causes its monomerization leading to enhanced association with SEC components and transcriptional activation of growth and proliferation-related genes. This enhanced association with SEC also causes reduced interaction with LEC components leading to decreased expression of snRNA genes. On the contrary, treatment of cells with genotoxic reagent that causes ATM kinase-mediated phosphorylation of ELL. This phosphorylation, in turn, enhances ELL interaction with Sin3A●HDAC1 complex leading to its deacetylation. The deacetylated ELL forms dimer and thus reduces its interaction with SEC and concomitantly enhances interaction with LEC components for simultaneous reduction of expression of mRNA and increased expression of snRNA genes 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 / CSIR Funding

1. 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. Wellcome-Trust DBT India Alliance Senior Fellowship 2023-28, 450 Lakhs, (IA/S/22/1/506227).
2. Mechanistic understanding of tumor suppressor role of human EAF1 in renal cell carcinoma through regulation of selective

expression of apoptotic genes. CSIR-FIRST, 2024-26, 99 Lakhs, FIR070304.

3. 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 Lakhs, (CRG/2022/000756).

Publications

Talukdar, P., Pal, S., Biswas, D. (2024) Post-translational modification-dependent oligomerization switch in regulation of global transcription and DNA damage repair during genotoxic stress *Nature Communications*. 15(1):4128

Invited Lectures

1. Selective partitioning of a critical elongation factor between SEC and LEC regulates cellular mRNA and snRNA transcription JNCASR, Bangalore, 17th Asian Epigenomics Meeting 15-16th Oct 2024
2. Understanding of Eukaryotic Transcriptional Regulatory Mechanisms and Their Role in Human Diseases" Presidency University, Kolkata, Molecular Basis of Life: Health, Disease and Diversity 28-30th Nov 2024
3. Understanding of Eukaryotic Transcriptional Regulatory Mechanisms Involving Super Elongation Complex and Its Implications in MLL Fusion-mediated Leukemogenesis" TATA Memorial Cancer Center Kolkata and EMBO workshop, TMC, Kolkata 05-07th Feb 2025

Conferences Attended

1. 17th Asian Epigenomics Meeting, JNCASR, Bangalore, 15-16th Oct 2024
2. Molecular Basis of Life: Health, Disease and Diversity, Presidency University, Kolkata, 28-30th Nov 2024
3. TATA Memorial Cancer Center Kolkata and EMBO workshop, TMC, Kolkata 05-07th Feb 2025

Member of Society

Elected member of Guha Research Conference 2024

Awards

Elected Member of Guha Research Conference (GRC) 2024

Dr. Debabrata Biswas, Senior Principal Scientist

Group Members: Arijit Nandy, CSIR-SRF; Prathama Talukdar, ICMR-SRF; Avik Ghosh, CSIR-SRF; Poushali Chakraborty, CSIR-SRF; Pamela Pal, UGC-SRF; Bakul Pal, UGC-JRF; Sherstha Mukhopadhyay, UGC-JRF; Sk. Anzar Hasnain, UGC-JRF; Ekjot Kaur, Project Assistant; Srerupa Roy, Project Assistant; Gaurav K. Bhagat, Research Associate

Collaborators: Benu Brata Das, PhD, Professor, Department of Physical Sciences, Indian Association for Cultivation of Sciences, Kolkata; Kunal Rai, PhD, Professor, Department of Genomic Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

Dr. Smrutisanjita Behera and her group members

Investigation of the function of Extracellular Vesicles (EVs) and bacterial Outer membrane vesicles (OMVs) in rice and *Xanthomonas oryzae pv.oryzae* interaction

Research Activities

The aim of our work is to understand the early signalling events that occur during the interaction between Rice and its bacterial pathogen *Xanthomonas oryzae pv oryzae* (*Xoo*). *Xoo* causes up to 80% of crop loss in India. Plant pathogens can develop resistance against chemical pesticides and antimicrobial compounds by deploying mechanisms for efflux of pesticides, enzymatic degradation, target site mutation, and target site overexpression. To provide a sustainable resistance against Xoo, a basic understanding of Xoo Rice interaction is necessary. In this context, we explored the communication between rice and Xoo through Xoo-released Outer Membrane Vesicles (OMVs). We have isolated OMVs from the Xoo strain BXO43, isolated proteins from the purified OMVs and performed a proteomics study to identify the protein content. We have further investigated the role of Xoo-OMVs in Xoo rice interaction and tried to understand how Xoo-OMVs are perceived by the rice cells. Additionally, our work indicated a crucial role played by the plasmamembrane nanodomains in the perception of Xoo-OMV. We are further investigating the role of membrane dynamics in the perception of biotic stress in plants.

Some of the findings are as follows:

Xoo-OMVs carry several MAMPs and virulence-associated proteins, including several cell-wall-degrading enzymes like cellulase, endoglucanase, esterase, etc., iron-acquisition proteins, and phosphate-acquisition proteins. Xoo-OMVs carry proteins to defend themselves against this ROS response (Figure 1). This finding suggests that Xoo OMVs carry out a dual function of enhancing the virulence and defending the bacteria against plant immune responses and promoting the chance of survival inside the host.

Application of Xoo-OMVs induces a Ca^{2+} signal in the rice and Arabidopsis root cells within a timespan of ten minutes. Interestingly, this early Ca^{2+} signal is necessary for mounting the downstream immune response in rice.

The Xoo-induced Ca^{2+} signal in the rice is responsible for the increase in membrane order and increased nanodomain formation. Subsequently, the Ca^{2+} mediated nanodomain enrichment allows the Xoo-OMVs to get inserted into the rice cell plasma membrane (both in leaves and roots) (Figure 2, 3).

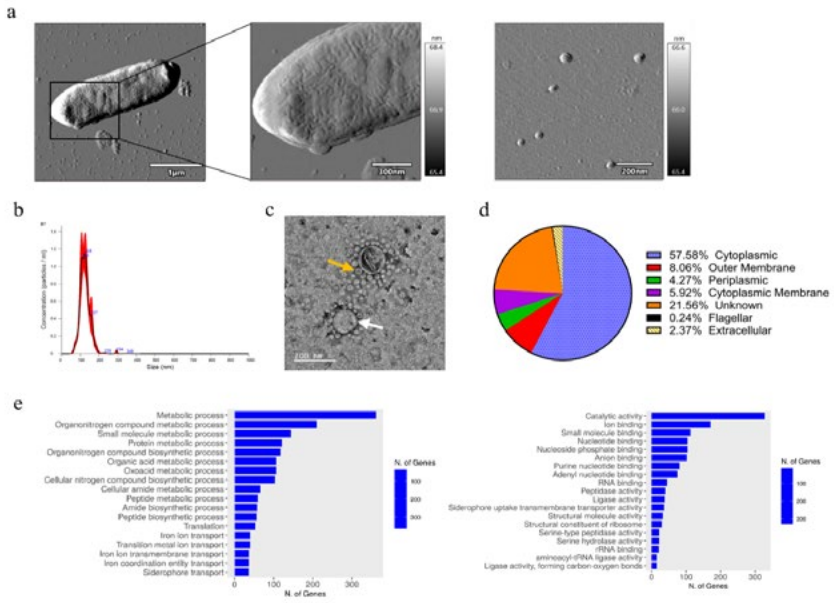


Figure 1: Characterization of Xoo-OMVs and identification of their protein content. a, AFM images show that BXO43 releases OMVs into their surroundings by blebbing. b, NTA exhibit the hydrodynamic size range of the Xoo-OMVs is 125.8 +/- 1.6 nm. c, transmission electron microscopy reveals Xoo-OMVs isolated from the PS media include smaller vesicles (10-60nm), indicated by the yellow arrow, and bigger vesicles (100-150nm), indicated by the white arrow. d, Subcellular localization of 423 proteins identified from Xoo-OMVs. The localizations were designated using PSortB software. e, biological, and molecular functions of the proteins were appointed using ShinyGo software.

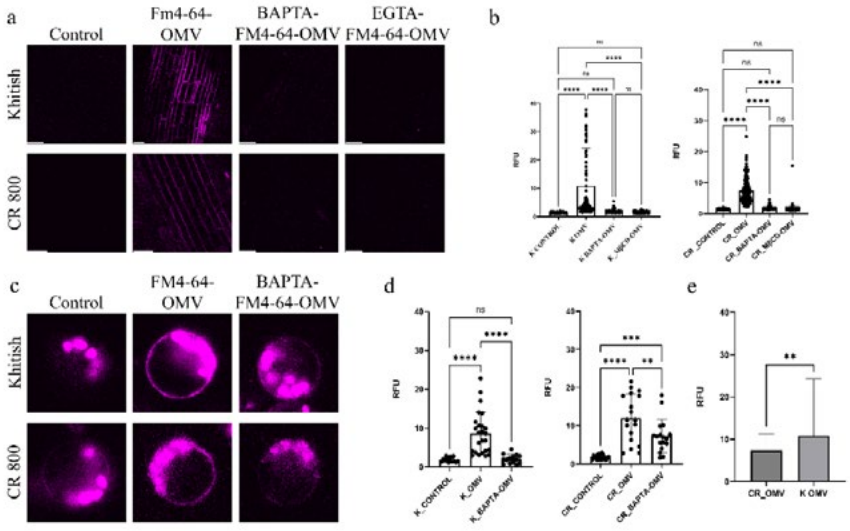


Figure 2: Ca^{2+} and sterol-dependent lipid order increase in rice plasma membrane after incubation in *Xoo*-OMVs. a, Lipid order of rice plasma membrane increases significantly after *Xoo*-OMV exposure. 7-day-old Khitish and CR 800 seedlings were incubated with *Xoo*-OMVs and sterile water (control) for 30min and stained with Di-4-ANEPPDHQ (n ≥6). *Xoo*-OMV treated seedlings of both Khitish and CR 800 show elevation in lipid order of the plasma membrane. Pre-treatment with BAPTA-AM (25 μM) and EGTA (2 mM), respectively, inhibits lipid order increase. b, GP values (-1 to +1) have been calculated using ImageJ software and plotted in a Box-plot using GraphPad Prism software, the corresponding statistical significance have been calculated through one way ANOVA, ($p \leq 0.05$) in Khitish and CR 800 seedlings respectively. c, leaf protoplasts isolated from Khitish and CR 800 show lipid order rise after incubation with *Xoo*-OMVs. BAPTA-AM (25 μM) and MβCD (2 mM) pre-treated protoplasts do not show significant rise in order even after *Xoo*-OMV exposure. d, GP values of protoplast membrane of Khitish and CR 800, respectively, have been represented in a box-plot. The statistical significance has been calculated by one-way ANOVA using GraphPad Prism software (ns, not significant, *P ≤ 0.05; **P ≤ 0.01, ***P ≤ 0.001, ****P ≤ 0.0001).

Future Research Plan

In the future, we would like to understand the mechanism of Xoo-OMV uptake by the rice cells. Study the changes in plasma membrane composition of rice upon Xoo-OMV perception, and ultimately try for OMV-bioengineering for protecting rice against Xoo. Additionally, we will also investigate the role of extracellular vesicles released by rice plants in response to Xoo. Furthermore, we would explore in detail the function of membrane nano-domains and membrane dynamics in rice during Xoo interaction.

Figure 3.

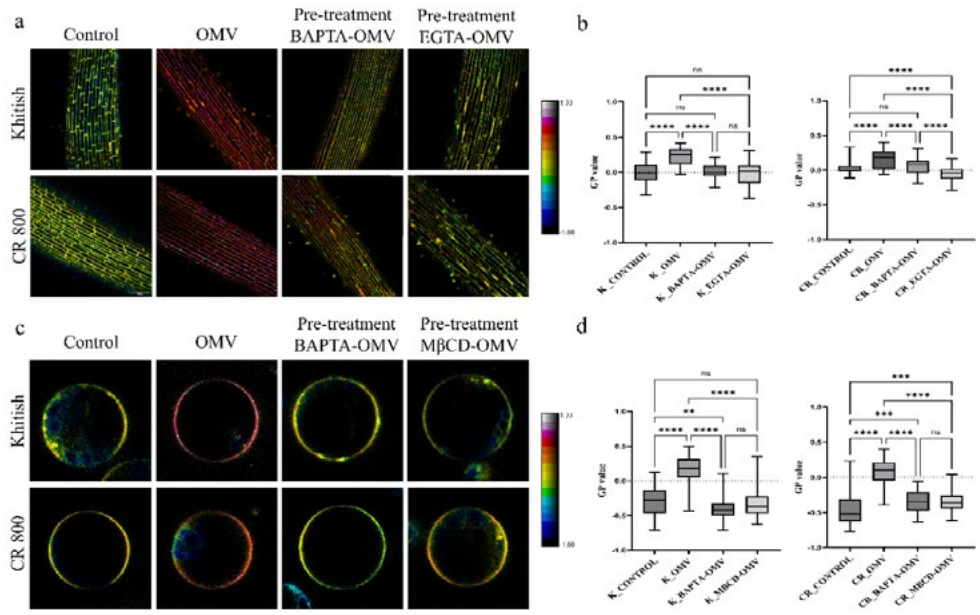


Figure 3: *Xoo*-OMVs get inserted into the plasma membrane of rice. a and c, FM4-64 labelled *Xoo*-OMVs get inserted into the plasma membrane of 7-day-old Khitish and CR 800 roots and leaf protoplasts. FM4-64 added to sterile water does not retain any dye after centrifugation (control) and does not show any considerable fluorescence. Khitish and CR 800 roots pre-treated with BAPTA-AM (25 μM) do not show considerable insertion of FM4-64 labelled *Xoo*-OMVs. Protoplasts isolated from Khitish and CR 800 show significant decrease in *Xoo*-OMV insertion on Ca^{2+}-chelation and sterol-depletion with BAPTA-AM (25 μM) and MβCD (2 mM), respectively. b and d, GraphPad Prism was used to create the histograms and analyse the statistical difference between the samples though one-way ANOVA (n ≥ 7), (ns, not significant, *P ≤ 0.05; **P ≤ 0.01, ***P ≤ 0.001, ****P ≤ 0.0001). e, the relative fluorescence units of Khitish and CR 800 after *Xoo*-OMV insertion have been compared in a histogram.

Extramural / CSIR funding

1. "Investigation of the regulation of plant immunity by sphingolipids in rice", Start-up research Grant, SERB, Department of Science and Technology (DST), 12/12/2022-12/12/2024, 27.7 Lakh, (SRG/2022/00229)

Publications

1. Dutta S, Kothari S, Singh D, Ghosh S, Sarangi N, Behera S, Prajapati S, Sinha P K, Prusty A, Tripathy S. (2024). Novel oceanic cyanobacterium isolated from Bangaram island with profound acid neutralizing ability is proposed as Leptolyngbya iicbica sp. nov. strain LK. *Molecular Phylogenetic Evolution.* (197) 108092

Dr. Smrutisanjita Behera, Scientist

Group Members: Hrimeeka Das, UGC-SRF; Sandeep Barman, UGC-SRF; Ishani Mondal, UGC-SRF; Aasiya Parveen, CSIR-JRF; Ritu Chatterjee, Project JRF

Collaborators: Dr. Sucheta Tripathy, Senior Principal Scientist, CSIR-IICB, Kolkata; Dr. Hitendra Kumar Patel, Senior Principal Scientist, CSIR-CCMB, Hyderabad

ORGANIC AND MEDICINAL CHEMISTRY DIVISION

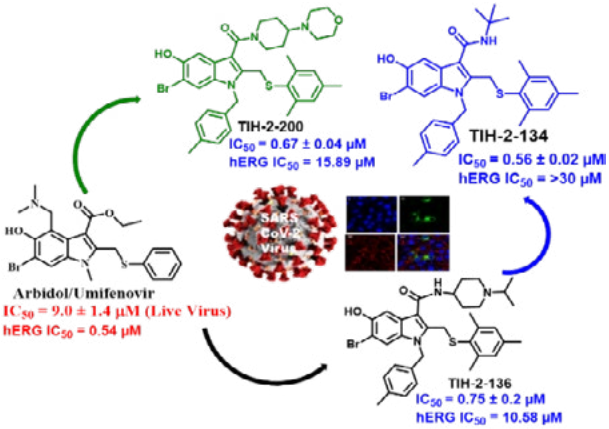
The Organic and Medicinal Chemistry Division of CSIR-Indian Institute of Chemical Biology has very vibrant and encouraging academic ambiance to pursue intense research programs in both basic and applied areas. With Organic & Medicinal chemistry as main theme, the division is continuously striving to excel in other areas such as chemical biology, natural products chemistry, supramolecular chemistry, and applied polymer and material chemistry as well. This has been possible because of the faculty strength of different expertise and talented pool of students who have opted to explore their career in the advancement of research in chemistry and interfacial areas. The division is devoting its strength not only in the advancement of knowledge in basic research but also trying to keep meaningful impact in translation research; the footprints toward these endeavors have been documented through an array of research publications in the journals of international repute and a number of granted national and international patents. It is expected that the symbiotic intra- and inter-institutional research collaborations will further propel the research trajectory contributing in the vision of developed 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

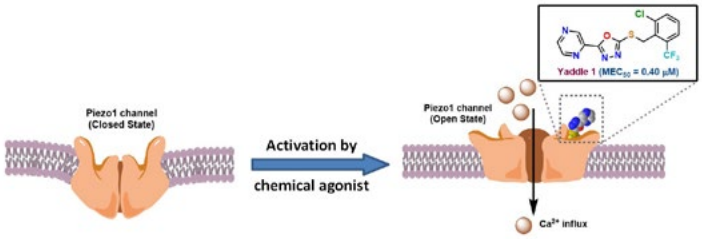


As a part of Antiviral Mission of CSIR, our lab has set up a drug discovery platform on antivirals and created a Pan-CSIR screening facility at CSIR-IICB. Moreover, several drug candidates are being developed as entry-inhibitors against SARS-CoV-2. We have successfully developed the Arbidol (ARB, Umifenovir) derivatives as a potential drug candidate against SARS-CoV-2. ARB is a broad-spectrum antiviral from Russia, has not received approval from the U.S. Food and Drug Administration (FDA) due to a lack of sufficient clinical data and concerns regarding its potential toxicity. The antiviral performance was assessed in VERO E6 cells infected with SARS-CoV-2, with optimization efforts guided by factors like absorption, distribution, metabolism, excretion (ADME), in vivo pharmacokinetics (PK), and hERG toxicity. Mechanistic studies on entry inhibition and immunofluorescence along with invitro ADME, invivo pharmacokinetics data, antiviral potecy, hERG toxicity data confirmed that our potential lead molecules significantly reduced SARS-CoV-2 replication in Vero cells, suggesting strong preclinical potential. The research work is published in *ACS Journal of Medicinal Chemistry (*https://doi.org/10.1021/acs.jmedchem.4c03093*)*

Mechanistic insights into Piezo1 agonist Yaddle1 as a novel adjuvant for T cell activation

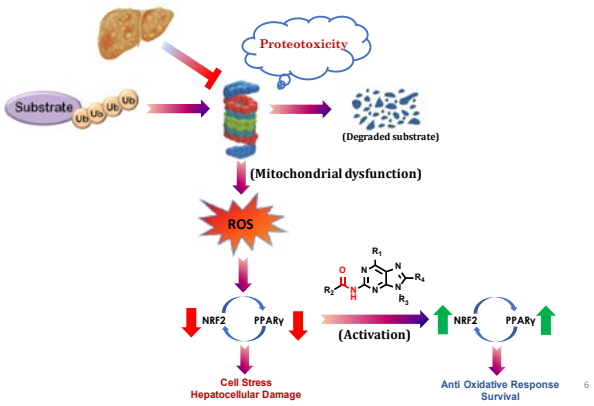
Piezo proteins (Piezo1 and Piezo2) are mechanosensitive, pore-forming cation channels that mediate Na^+ and Ca^{2+} flux across the plasma membrane. Piezo1, broadly expressed in various tissues, plays key roles in immune responses, epithelial homeostasis, and cell differentiation. Its deficiency is associated with disorders such as hereditary xerocytosis, arthrogryposis, and Marden-

Walker syndrome. A high-throughput screen of 3.25 million compounds identified Yoda1 as a potent Piezo1 activator. This study explores the structural determinants of Yoda1 responsible for Piezo1 gating, aiming to develop improved activators. Stepwise chemical modifications led to the discovery of Yaddle1, a trifluoromethyl-substituted agonist (MEC_{50} = 0.40 µM), identified using Piezo1-mCherry transfected HEK293A cells. Yaddle1 stabilizes Piezo1 domains via *tetrel interactions*, acting as an *ambidextrous wedge*, as revealed by in vitro studies and density functional theory calculations. It also induces Ca^{2+} influx in human $CD4^+$ T cells, underscoring its potential as a vaccine adjuvant to boost T cell activation. These findings position Yaddle1 as a promising therapeutic lead. The research work is published in *ACS Journal of Medicinal Chemistry (*https://doi.org/10.1021/acs.jmedchem.4c00322*)*.



Design and development of 'purine' based small molecule modulators for PPARγ in ameliorating Non-Alcoholic Fatty Liver Disease (NAFLD*)*

Non-alcoholic fatty liver disease (NAFLD) encompasses a spectrum of liver conditions ranging from simple steatosis to steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma. Targeting PPARγ modulation offers a promising strategy to treat NAFLD by improving adipocyte differentiation and insulin sensitivity, thereby addressing both metabolic and inflammatory components. PPARγ activation also reduces reactive oxygen species (ROS) and oxidative stress, key contributors to NAFLD progression. Current PPARγ-targeted therapeutics, such as Rosiglitazone and Pioglitazone, feature a thiazolidinedione (TZD) moiety critical for receptor activation. However, TZDs are associated with significant side effects, including weight gain, cardiovascular risks, and edema. To overcome these limitations, our lab is developing a non-TZD-based library of small molecules featuring a purine scaffold as the central core. These compounds are being screened for PPARγ activation in hepatocytes. We have filed a patent based on this research. Filing date: 05/12/2023, 0217NF2023.



Future Research Plans

- *Development of Antiviral agents against COVID-19:* Mechanistic studies on entry inhibition, immunofluorescence, invitro ADME, invivo pharmacokinetics data, antiviral potecy, hERG toxicity data, in vivo efficacy in hemster model also confirmed that our potential lead molecules significantly reduced SARS-CoV-2 replication in Vero cells. These results suggesting for clinical trial against SARS CoV-2 in future.
- *Rational design and discovery of potent PROTAC degraders of ASK1:* Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive liver disease marked by steatosis, inflammation, and fibrosis, with limited therapeutic options. Emerging evidence identifies apoptosis signal-regulating kinase 1 (ASK1) as a key player in MASH pathogenesis, making it a promising target for metabolic and inflammatory liver diseases.
- Our current research explores a novel PROTAC-based strategy to selectively degrade ASK1. We initially developed dASK1 (35), a cereblon-based PROTAC that forms a stable ternary complex with ASK1, enabling efficient degradation via the ubiquitin–proteasome pathway (up to 70% at 100 nM in HepG2 and HEK293A cells). To expand E3 ligase engagement, we designed dASK1-VHL (60), leveraging VHL as the ligase and optimizing the linker using molecular docking and MMGBSA calculations. dASK1-VHL (60) demonstrated favorable ADME profiles, including enhanced solubility, moderate clearance, and improved bioavailability.
- In an MCD diet-induced MASH mouse model, dASK1-VHL (60) effectively reduced ASK1 levels, inhibited p38 MAPK signaling, and decreased hepatic lipid accumulation, confirming its therapeutic potential. These findings underscore the importance of rational PROTAC design, linker optimization, and strategic E3 ligase selection in advancing targeted therapies for metabolic diseases. Moreover, this work lays the foundation for future broader exploration of alternative E3 ligases and linker architectures in the development of next-generation PROTACs for complex inflammatory and metabolic disorders.

Extramural / CSIR Funding

1. Development of PROTACs for Targeted Protein Degradation via Small Molecule–Protein Engineering: A Promising New Approach for Treating NAFLD/NASH. April 2024- March 2026. CSIR- FTT project (FTT070504). Rs 140 lakhs, (PI)

2. Antiviral Mission CSIR: Discovery & Pre-clinical Development of Antivirals for COVID-19 & other diseases. CSIR Mission Mode project. April 2023-March 2025 Rs 247 lakhs. (Nodal)
3. Tuning Lipid Droplets for Antiviral Interventions in Brain. DBT-Neuroscience Specific Call. DBT/PR51484/MED/122/359/2024, 2024-2027, 80 lakhs, (Co-PI)
4. SMASH-ACT: Small Molecule mTOR modulation for Adoptive T cell Therapy (ACT). CSIR – Focused Basic Research (FBR070304). April 2024- March 2026. 70 lakhs, (Co-PI)
5. CSIR-Mission Mode Project on Anti-Microbial Resistance. CSIR MMP075202. Team Member

Publications

1. Goon S, Liu CSC, Dastidar UG, Paul B, Mukherjee S, Sarkar HS, Desai M, Jana R, Pal S, Sreedevi NV, Ganguly D*, Talukdar A*. Exploring the Structural Attributes of Yoda1 for the Development of New-Generation Piezo1 Agonist Yaddle1 as a Vaccine Adjuvant Targeting Optimal T Cell Activation. Journal of Medicinal Chemistry, 2024, 67, 8225−8246. https://doi.org/10.1021/acs.jmedchem.4c00322
2. Hoque I, Singh N, Dastidar UG, Martin AK, Joshi A, Sardana Y, Chawla RS, Das N, Patra B, Devi R, Das S, Das D, Kumar S, Ringe RP, Bokara KK, Thakur KG*, Talukdar A*. Strategic Design and Optimization of Umifenovir Analogues: Balancing Antiviral Efficacy and hERG Toxicity against SARS-CoV-2. Journal of Medicinal Chemistry, 2025, 68, 9371−9406. https://doi.org/10.1021/acs.jmedchem.4c03093.

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. 2-phenyl indole compounds as anti-viral agents, preparation and use thereof. Arindam Talukdar, Binita Patra, Israful Hoque, Nirmal Das, Biswajit Kundu, Krishan Gopal Thakur, Rajesh Ringe, Nittu Singh, Akshay Joshi, Ravneet Singh Chawla, Bokara Kiran Kumar, Alna Kuriyickal Martin, Yogesh Sardana, Renuga Devi, Balamurugan Kanagasabai, Uddipta Ghosh Dastidar, Soupayan Pal, Trisha Ghosh, Dipyaman Ganguly, Jafar Sarif. Application No. 202511008623, Filing date 31/01/2025, 0270NF2024

Invited Lectures

1. Eliciting Agonism-Antagonism in Endosomal Toll-like Receptor Modulators Via convoluted Interplay of chemical subunits. Current Trends In Drug Discovery Research. CSIR-Central Drug Research Institute, Lacknow, Feb 19-22, 2025.
2. Sweet Innovations: How Rasagulla-Making Could Inspire Drug Discovery. CRSI Symposium @ IISER Kolkata. 4th February 2025

Conferences Attended

1. Current Trends in drug discovery techniques and diagnostics: Chemical Biology Approaches, Adichunchanagiri University, BG Nagara, Mandya, India. August 2-3, 2024.
2. Current Trends in Drug Discovery Research, Central Drug Research Institute, Lucknow, India. February 19-22, 2025.
3. CRSI Symposium @ IISER Kolkata. 4th February 2025

Member of Society

Life member, Chemical Biology Society of India.

Dr. Arindam Talukdar, Senior Principal Scientist

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

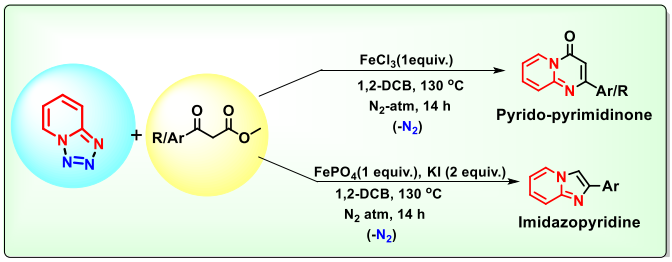
Collaborators: Dr. Partha Chakrabarti, Principal Scientist, Cell Biology & Physiology, CSIR IICB, Kolkata; Dr. Shilpak Chatterjee, Senior Scientist, Cancer Biology & Inflammatory Disorder, CSIR IICB, Kolkata; Prof. Kaustubh Datta, Virginia Commonwealth University, USA; Prof. Artur T. Cordeiro, Brazilian Biosciences National Laboratory (LNBio), Brazil; Prof. Jonathan Baell, Executive Director Discovery Chemistry, Lyterian Therapeutics.

Dr. Biswadip Banerji and his group members

Synthetic Studies Towards Developing New Molecules Having Translational Aspects

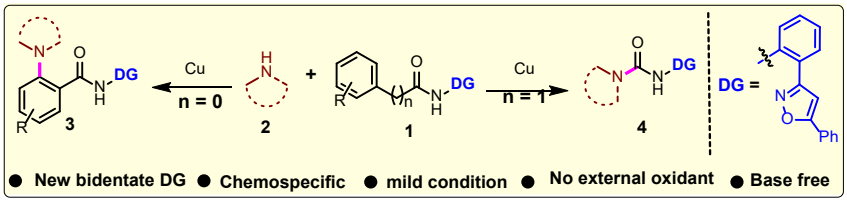
Research Activities

Synthesis of Pyrido-pyrimidinone and Imidazopyridine via Fe(III)-mediated Denitrogenative Annulation Reactions with b-keto ester



We developed an iron(III)-mediated denitrogenative annulation of 1,2,3,4-tetrazole with β-keto esters to produce two classes of nitrogen-containing heterocycles: pyrido-pyrimidinone and imidazopyridine, and the selectivity of product formation was controlled by alkali metal halide salts present in the reaction medium. Mechanistic studies suggested a radical pathway. This single-step reaction yielded diverse N-heterocycles linked to different natural product scaffolds (Chemical Communications 2025, 61, 6312-15).

Directed Amination and Oxidative C(=O)-C Cleavage of Amides Enabling Access to Urea Derivatives via Copper(II)-mediated Dual Reaction of 2-(5-phenylisoxazol-3-yl)aniline

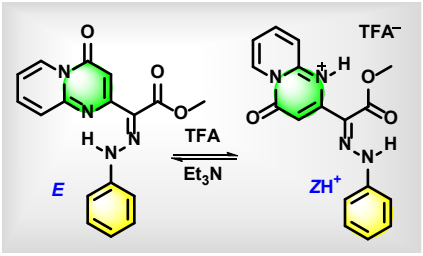


This study explored the dual reactivity of amides fused to 2-(5-phenylisoxazol-3-yl)aniline as a directing group. We reported the chemo-specific cleavage of C(=O)-C bond and C(sp²)-H amination for the formation of urea derivatives. In this protocol, inexpensive copper was used as a catalyst, and O_2 from the air acted as an oxidant, demonstrating broad functional group tolerance for both transformations. Detailed mechanistic studies and DFT calculations were conducted to gain insights into the plausible mechanism of urea derivative formation (Org. Lett. 2024, 26, 41, 8774–8779).

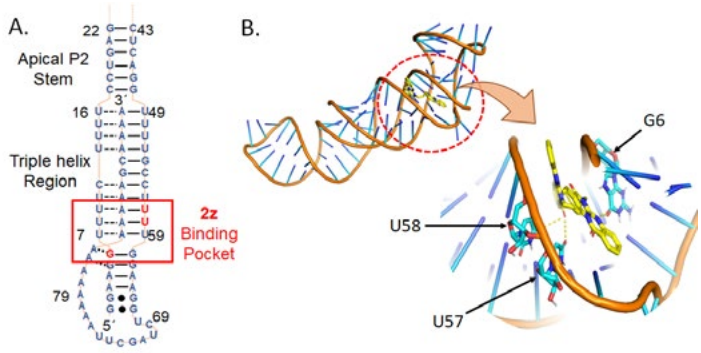
Hydrazone Based pH-Responsive Configurational Molecular Rotary Switches

Pyrido-pyrimidinone derived pH-activated, hydrazone-based molecular switch and its switching mechanism are explored in this research. A new conjugated p electronic framework (enone part in the molecule) was introduced, which allowed the system to undergo hydrazone-azo tautomerization, facilitating *E-Z* isomerization through rotation around the partial C-N single bond. Under

acidic pH, protonation took place selectively on pyrimidinone nitrogen, and that turned the molecule to the corresponding *ZH*⁺ configuration. On the other hand, addition of base (trimethylamine) in the same solution reverted the molecule back to its original *E*-configuration. Extensive proton-NMR, and detailed X-ray crystallography coupled with UV-vis spectroscopy were carried out to establish the switching phenomena. Theoretical DFT calculations leading to free energy diagrams, transition states, and intermediates corroborated the mechanism behind the switching phenomenon (European Journal of Organic Chemistry 2024, 27, 48, 202400981).



Access to N-fused Quinazolino-quinazoline-diones by Metal-free Synthesis as *MALAT1* RNA Triple Helix Intercalator



The development of Chemical scaffolds that target highly conserved MALAT1 RNA has received attention due to its significance in splicing, nuclear organization, and gene expression in disease progression pathways. We synthesized a series of N-fused quinazolino-quinazoline-diones molecules via a PIDA-induced C-N coupling strategy to target MALAT1 RNA. Interestingly, one compound 2z binds to the UUG pocket of MALAT1 RNA triple-helix through intercalation, and also evidenced by molecular docking studies and CD experiments. 2z exhibited cytotoxicity towards MALAT1 RNA overexpressing cancer cells (SKOV-3 = IC50 of 8.0 ± 0.4 μM). These findings demonstrated 2z as a MALAT1 RNA triple-helix intercalator with therapeutic potential, offering an important chemical scaffold to understand MALAT1 activity in disease development pathways (RSC Medicinal Chemistry 2025, 16, 429–434).

Future Research Plans

In the future, my laboratory will focus on designing, synthesizing, and validating PARP Inhibitors to target cancer and biomarkers for cancer. However, designing basic synthetic organic methodology will continue to be our main niche area of research.

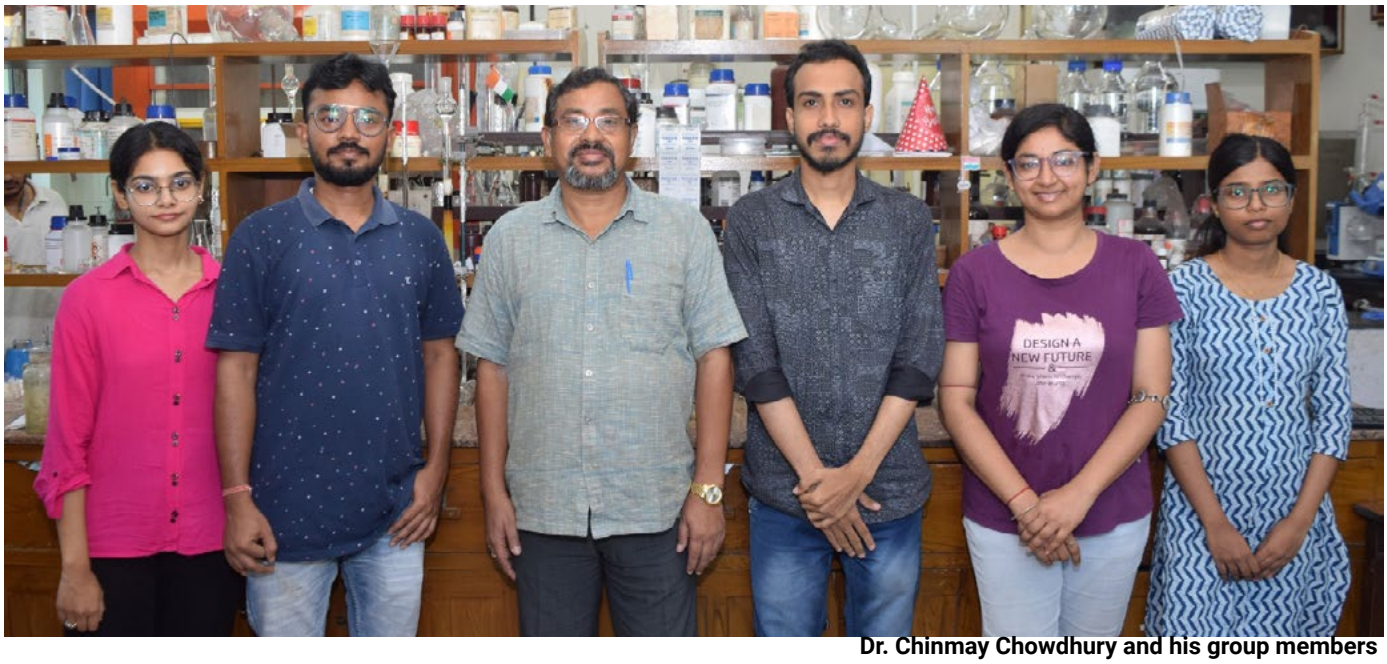
Publications

1. Shee, S.; Khamaru, K.; Banerji, B. Hydrazone Based PH-Responsive Configurational Molecular Rotary Switches Containing a New Conjugated π-Electronic Framework. European Journal of Organic Chemistry 2024, 27, 48, 202400981. (11 September 2024, doi.org/10.1002/ejoc.202400981)
2. Ghosh, S.; Sepay, N.; Banerji, B. Crystal to Hydrogel Transformation in S-Benzyl-L-Cysteine-Containing Cyclic Dipeptides - Nanostructure Elucidation and Applications. Chemistry - A European Journal 2024, 30 (45). (09 June 2024, doi.org/10.1002/chem.202401874)
3. Pathi, V. B.; Das, P.; Guin, A.; Debnath, M.; Banerji, B. Metal-Free Synthesis of N-Fused Quinazolino-Quinazoline-Diones as a MALAT1 RNA Triple Helix Intercalator. RSC Medicinal Chemistry 2025, 16, 429–434. (22 Oct 2024, doi.org/10.1039/D4MD00614C)
4. Manna, A.; Khamaru, K.; Pathi, V. B.; Sett, S.; Ghosh, P.; Banerji, B. Copper(II)-Mediated Dual Reactivity of 2-(5-Phenylisoxazol-3-Yl)Aniline: Directed Amination and Oxidative C(═O)—C Cleavage of Amides Enabling Direct Access to Urea Derivatives. Org. Lett. 2024, 26, 41, 8774–8779. (October 9, 2024, 10.1021/acs.orglett.4c03104)
5. Sk, A.; Banerji, B. Access to Pyrido-Pyrimidinone and Imidazopyridine via Fe(Iii)-Mediated Denitrogenative Annulation of Tetrazolopyridine with β-Keto Ester. Chemical Communications 2025, 61, 6312-15. (25 Mar 2025, doi.org/10.1039/D5CC00258C)

Dr. Biswadip Banerjee, Chief Scientist

Group Members: Subhankar Shee, SRF; Arindam Manna, SRF; Kaushik Seal, SRF; Asikul Sk, SRF; Arpan Adhikary, SRF

Collaborators: Dr. Subhas C. Biswas, Chief Scientist, CSIR-IICB, Kolkata; Dr. K. Chattopadhyaya, Chief Scientist, CSIR-IICB, Kolkata; Dr. Mrinal K. Ghosh, Chief Scientist, CSIR-IICB, Kolkata; Dr. Susanta Kar, Principal Scientist, CSIR-IICB, Kolkata; Dr. Manish C. Debnath, Sr. Scientist, CSIR-IICB, Kolkata; Dr. Nakul.C. Maiti, Sr. Pr. Scientist, CSIR-IICB, Kolkata;



Dr. Chinmay Chowdhury and his group members

Synthesis of Novel Heterocycles of Biological Interests

Research Activities

An Au(I)-catalyzed tandem cyclization of indole/benzofuran based *N*-propargylsulphonamides **3** and **4** led to the formation of dihydro δ-carboline and benzofuro[3,2-*b*]pyridine intermediates which underwent a base (DBU) induced 1,2-elimination (-TsH) resulting in the formation of δcarbolines **1a** and benzofuro[3,2*b*]pyridines **2a**, respectively with 62-97% yields (Figure-1). On the other hand, exposure of substrates **3** and **4** to iodonium monochloride (ICl) and K_2CO_3 in refluxing DCM triggered a tandem iodocyclization followed by 1,2-elimination (-TsH), delivering 3-iodo δcarbolines **1b** and benzofuro[3,2*b*]pyridines **2b**, respectively within 2 h with 44-86% yields (Figure-1). We have proposed plausible reaction mechanisms to explain the formation of products **1a-b** and **2a-b**, respectively. However, the photo-physical study on few selected products revealed their poor emissive property.

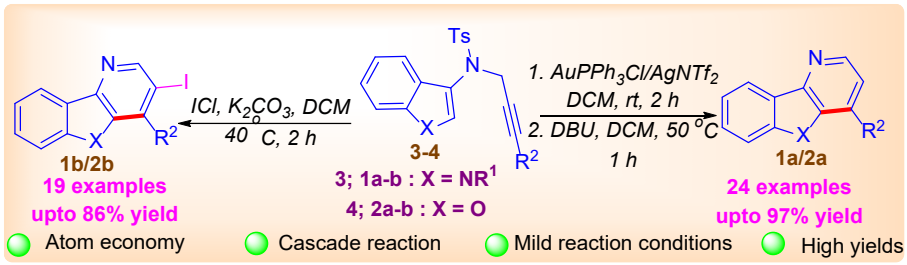


Figure 1: Gold(I)-catalyzed and iodonium monochloride mediated synthesis of δcarbolines and benzofuro[3,2*b*]pyridines

Besides, we also report an elegant method for the construction of fused pyrrole rings via palladium-catalyzed reactions of aryl iodides **10** with *N*-prop-2-ynylated 3-aminobenzofurans/3-aminoindoles **8/9** leading to the general synthesis of benzofuro[3,2-*b*]pyrroles/pyrrolo[3,2-*b*]indoles **1/2** via 3-(arylidene)-2,3-dihydro intermediates (Figure 2). Exposing the intermediates to DDQ delivered benzofuro[3,2-*b*]indoles (BFIs) **5** and indolo[3,2-*b*]indoles (IIs) **6** containing vicinal cyano groups. These transformations constitute a rapid intermolecular assembly through several carbon−carbon bond forming reactions, involving a single electron transfer (SET) process in the crucial steps. Photophysical studies of selected products identified promising candidates for future applications.

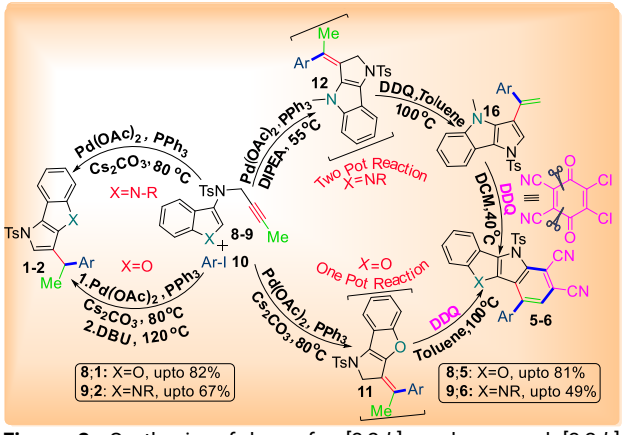


Figure 2: Synthesis of benzofuro[3,2-*b*]pyrroles, pyrrolo[3,2-*b*] indoles, benzofuro[3,2-*b*]indoles and indolo[3,2-*b*]indoles

Future Research Plans

- Palladium-catalyzed herteroannulations of indole/benzofuran based *N*-propargylsulphonamides will be studied for generation of heterocycles of biological interests.
- Synthesis and structure-activity relationship (SARs) studies of novel androdrographolide derivatives will be taken up to elucidate their role for anti-viral efficacies.

Extramural / CSIR Funding

1. Discovery and preclinical development of anti-virals for covid-19 and other diseases. CSIR, 2022-25, 247 lakhs, 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, 2022-2026, 160 lakhs, HCP-40.

Publications

1. Chatterjee, S., Khatun, R., Ali, M., Chowdhury, C. (2024) A Solvent Controlled regioselective synthesis of 2- and 4-substituted a-carbolines under palladium catalysis. *Chem. Commun.,* **60**, 7427–7430.
2. Dutta, D., Hoque, A. A., Paul, B., Park, J. H., Chowdhury, C., Quadir, M., Banerjee, S., Choudhury, A., Laha, S., Sepay, N., Boro, P., Kaipparettu, B. A., Mukherjee, B. (2024) EpCAM-targeted betulinic acid analogue nanotherapy improves therapeutic efcacy and induces anti-tumorigenic immune response in colorectal cancer tumor microenvironment. *Journal of Biomedical Science* 31:81(https:// doi.org/10.1186/ s12929-024-01069-8).

Invited Lectures

1. "Journey of Chemical Science Towards Sustainable Development", Sadhu Ram Chand Murmu University of Jhargram, Jhargram, 20th September, 2025.
2. "Odyssey from Organic to Medicinal Chemistry in Search of New Leads", ICEAC 2025, Agartala, 2nd International Conference on Emerging Areas of Chemistry, 12-14 February 2025.

Conferences Attended

2nd International Conference on Emerging Areas of Chemistry, ICEAC 2025, Agartala. 12-14 February 2025.

Member of Society

Member, Sectional Committee III, Chemical Sciences, West Bengal Academy of Science and Technology (WAST) (2024-2026).

Dr. Chinmay Chowdhury, Chief Scientist

Group Members: Sarat Chatterjee, CSIR-SRF; Raghunath Das, UGC-JRF; Aprajita Mondal, DST-Inspire, JRF; Susmita Pratihar, PA-1

Collaborators: Prof. Biswajit Mukherjee, Department of Pharmaceutical Technology, Jadavpur University, Kolkata.

Dr. Deepak Kumar and his group members

Phytochemical investigation of *Momordica dioica* fruits

Research Activities

Isolation and characterization of compounds from *M. dioica* fruits

The phytochemical investigation of *Momordica dioica* fruits, or Spine gourd, holds significant importance due to its recognized traditional health benefits and growing popularity as a nutritional vegetable. Understanding the composition of these compounds can pave the way for innovative applications in nutrition, dietary supplements, and natural medicine. Additionally, this investigation contributes to the broader knowledge of plant-derived compounds, promoting the exploration of natural products as viable alternatives in disease prevention and treatment. In the present investigation on the chemical characterization of its fruits, we were able to uncover the major secondary metabolites, identified as oleanane saponins (Figure 1).

Future Research Plans

The research efforts are directed towards the development of formulations to improve the limitations of the saponins for their development as nutraceutical or therapeutic candidates.

Extramural / CSIR Funding

1. Phytopharmaceutical development of Sesquiterpene coumarin enriched fraction of Ferula assa-foetida gum against Parkinson's disease. CSIR. 2024-2027. 1.74 Cr. MMP075201
2. Towards discovery and development of novel drugs and pharmaceuticals. Ministry of Earth Science. 2025-2027. 9.76 Cr. GAP490.

Publications

1. Dahat, Y., Ganguly, S., Khan, A., Gajbhiye, R.L., Kumar, D*. (2024) Optimizing ultrasonication-assisted comprehensive extraction of bioactive flavonoids from Pterocarpus santalinus leaves using response surface methodology. *J. Chromatogr. A*. **1738**, 465477. https://doi.org/10.1016/j.chroma.2024.465477 (IF ٣,٨)
2. Dahat, Y., Yatham, P., Kumar, D*. (2025) Fabrication of Saponin-in-Surfactant nano-emulsion for improved in-vitro gastrointestinal bio-accessibility of oleanane glycosides derived from *Momordica dioica* fruits. Manuscript under review.

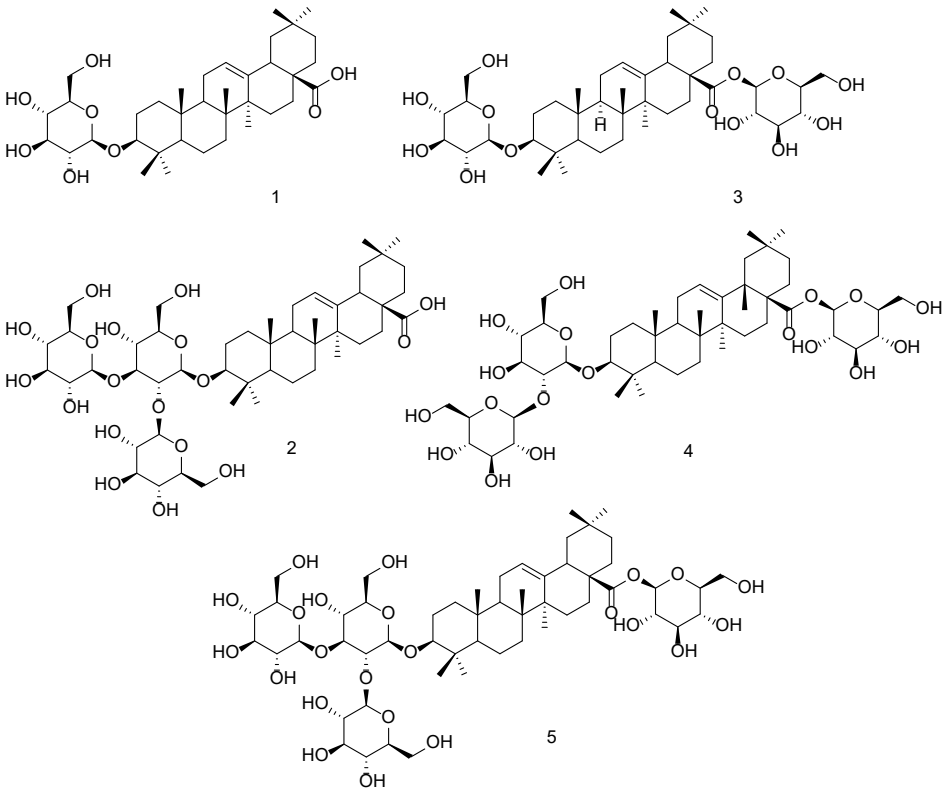


Figure 1: Chemical structures of the identified oleanane glycosides

Patents

1. Composition for treating ovarian cancer and a preparation method thereof. Deepak Kumar, Amit K Srivastava, SS Roy, Shreya Sen Sarma, S Bose, filling date 16/06/2024, IN 202411045945
2. A composition for treating Parkinson's disease. Deepak Kumar, Joy Chakraborty, Priyanka Yatham, Chayan Banerjee, Shreya Sen Sarma. Date of filling 14/05/2024, PCT/IN2024/050529

Conferences Attended

11th Convention, Society for Ethnopharmacology, India [SECON-2024], and conference on the Bioeconomy from Bioresources Promoting Traditional Resources of NER for Viksit Bharat. November 15-16, 2024, Gangtok, Sikkim, India

Dr. Deepak Kumar, Senior Scientist

Group Members: Dr. Bashir A. Lone, Project Scientist-I; Shreya Sen Sarma, DST-WISE, PhD Fellow; Raju Barman, CSIR-Project-JRF; Puja Tripathy, CSIR-SRF; Ravindra Kumar, CSIR-JRF

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

Dr. Indrajit Das and his group members

Electrochemical Generation of Nitrogen-Centered Radicals (NCRs) from Tetrazoles

Research Activities

Nitrogen-centered radicals (NCRs) are highly reactive species that offer exciting possibilities for synthesizing a diverse range of nitrogen-containing compounds. Although the generation of NCRs through visible-light-driven photoredox catalysis and their subsequent synthetic applications have been extensively studied, their potential in electrochemical conditions remains largely unexplored. This gap is primarily due to the lack of general and convenient methods for generating NCRs under these mild conditions. We hypothesized that an electroreductive denitrogenation strategy could be utilized to generate NCRs from tetrazole-containing motifs in a controlled manner. These radicals can then be used in subsequent reactions for synthesizing nitrogen-containing compounds. However, this electrochemical denitrogenation process is challenging due to the inherent stability of the tetrazole moiety.

Tetrazole-containing molecules are versatile intermediates that play a crucial role in synthesizing nitrogen-rich molecules through denitrogenation and denitrogenative annulation reactions. While elegant methods have been developed for these transformations, they often rely on expensive transition metal catalysts and ligands, and

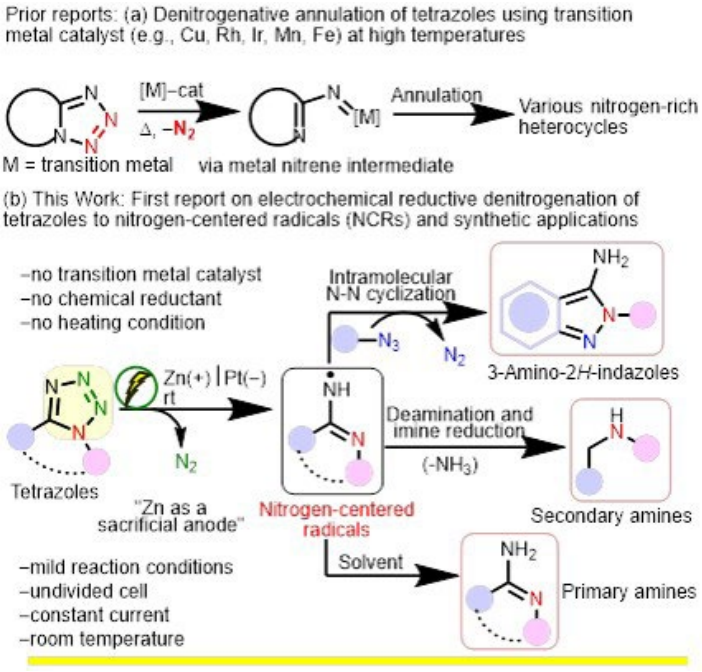


Figure 1. Previous report on (a) Denitrogenative annulation of tetrazoles with a potentially hazardous transition metal catalyst and ligand at high temperatures. (b) This work: First report on electrochemical reductive denitrogenation of tetrazoles to nitrogen-centered radicals (NCRs) and synthetic applications to nitrogen-containing molecules.

typically require high temperatures due to the inert nature of the tetrazole moiety. In 1969, Huisgen and von Fraunberg discovered the first denitrogenative annulation process for tetrazoles using copper powder as a catalyst at 120 °C. In 1976, Wentrup and colleagues reported denitrogenative nitrene-nitrene rearrangement reactions at temperatures over 500 °C through flash vacuum pyrolysis. Despite these advancements, the reliance on transition metals poses a significant challenge to achieving environmentally friendly and sustainable reaction conditions.

Reductive electrosynthesis is a highly sustainable strategy for constructing valuable molecules, often achieved through the oxidation of inexpensive sacrificial metal anodes. In addition to maintaining charge balance during the reductive reaction at the cathode, these metal ions can also prevent the overoxidation of substrates, products, and active intermediates. At times, these metal ions can directly participate as a Lewis acid by interacting with the substrates or by stabilizing the anionic intermediates. Various elegant electroreductive synthetic approaches have been developed using zinc as a sacrificial anode due to its very low oxidation potential. For example, Ackermann and co-workers reported the C–H alkylation of 8-aminoquinoline amides using a sacrificial Zn anode. Additionally, Wang, Guo, and their colleagues developed a C–N bond activation for deaminative reductive coupling of Katritzky salts using a sacrificial Zn anode. The anodic oxidation of aminotetrazoles to isocyanides has been reported by Lam and colleagues. This method involves the elimination of all nitrogen atoms from the tetrazole group by releasing nitrogen gas. However, the denitrogenation of tetrazoles to NCRs under electroreductive conditions remains elusive.

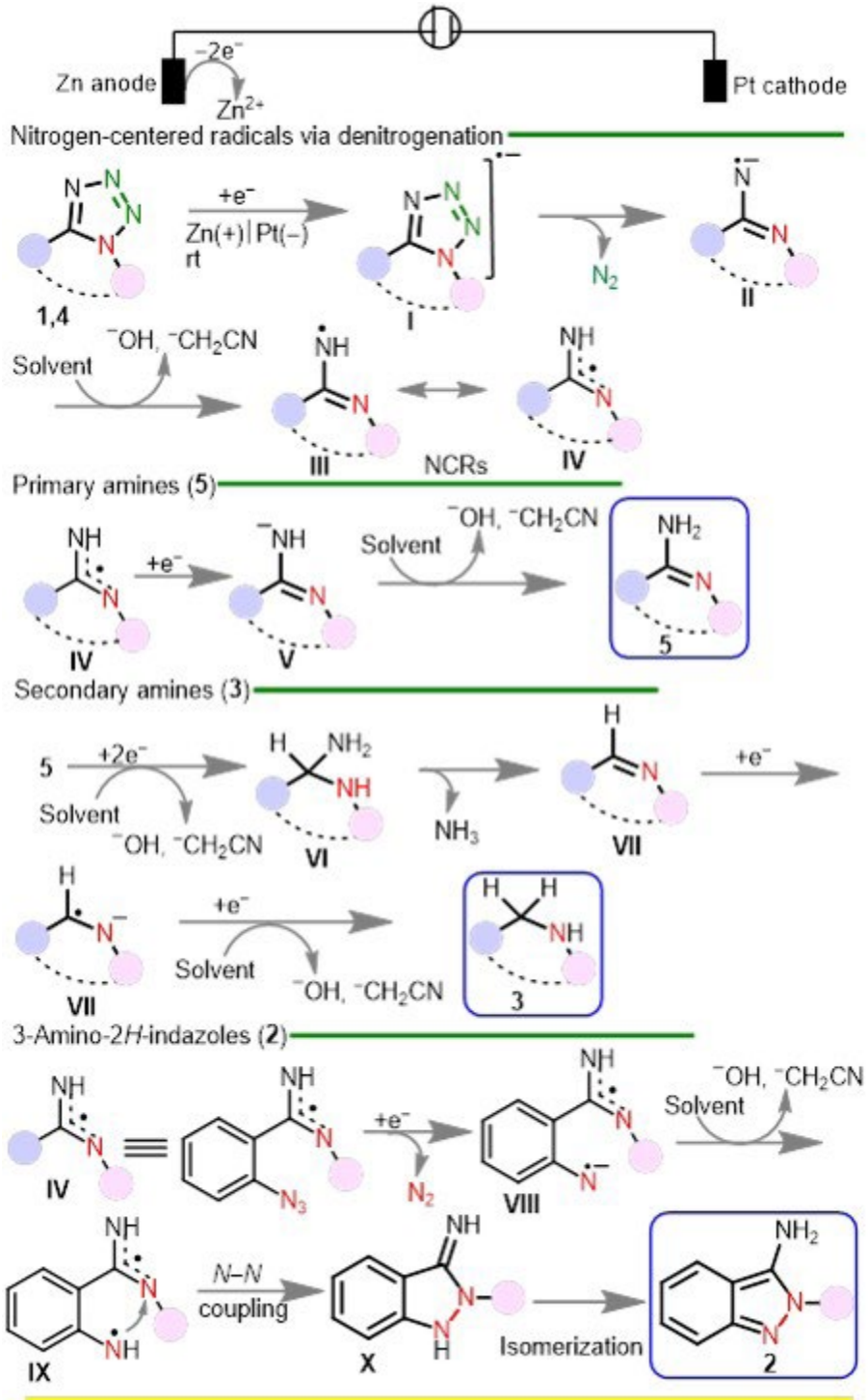


Figure 2. Proposed mechanism for obtaining 3-amino-2*H*-indazoles (**2**), secondary amines (**3**), and primary amines (**5**) from tetrazoles

A possible mechanism is illustrated in Figure 2. Initially, tetrazole (**1**, **4**) may be reduced at the cathode, forming a radical anion intermediate (**I**). This radical anion can then release nitrogen gas (N_2) to generate intermediate **II**. Intermediate **II** can abstract a proton from the solvents (H_2O/CH_3CN), leading to the formation of intermediate **III**. This intermediate can undergo a repetitive sequence of reduction followed by protonation, ultimately yielding the primary amine product (**5**), through an ECEC process. Compound **5** can then undergo a two-electron reduction, producing an imine intermediate (**VII**) while releasing ammonia (NH_3) gas. This imine intermediate can subsequently be converted into the corresponding secondary amine (**3**) through an additional two-electron reduction, followed by proton abstraction from the solvents. In cases where *ortho*-azido tetrazole (**1**) is used as the substrate, a double denitrogenation

may occur through cathodic reduction, affecting both the tetrazole and azide components. This process leads to the formation of intermediate **VIII**. Following protonation by the solvent, intermediate **IX** is generated, which may then undergo N-N cyclization. Ultimately, 3-amino-2*H*-indazole (**2**) is produced through an isomerization process. On the other hand, Zn^{2+} ions are continuously produced at the anode, ensuring charge balance during cathodic reduction. The low oxidation potential of zinc likely prevented the homodimerization or other oxidative degradation of the NCRs or other reactive intermediates at the anode.

To summarize, the denitrogenation of terazoles to generate nitrogen-centered radicals has been reported to occur under mild and sustainable electroreductive conditions at room temperature in an undivided cell. These NCRs serve as key intermediates for the substrate-controlled direct synthesis of 3-amino-2*H*-indazoles, deuterated and non-deuterated unsymmetrical secondary amines, and primary amine-containing N-heterocycles. The electrochemical method is compatible with various functional groups and enables the formation of nitrogen-containing molecules in good yields. It employs a sacrificial zinc anode in a mixed solvent of CH_3CN and a trace amount of H_2O. Although the Zn^{2+} ions produced from the anode may not be essential for the overall transformation, they could facilitate the removal of nitrogen by interacting with the reactants or reactive intermediates. The proposed mechanism is supported by CV studies, control experiments, deuterium labelling experiments, and ESI-HRMS studies. This straightforward electrochemical approach presents a less expensive and non-toxic alternative for the denitrogenation of tetrazoles, which is typically performed in the presence of transition metal catalysts. We are currently expanding the application of these NCRs to synthesize other N-heterocycles.

Future Research Plans

Applications of electrochemically generated nitrogen-centered radicals (NCRs) for the synthesis of various *N*-heterocycles.

Extramural / CSIR Funding

CSIR-Mission Mode Project (MMP): 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 Project coordinator from CSIR-IICB

Publications

1. Biswas, S., Ghosh, S., and Das, I. (2025) A TEMPO–N_3 Complex Enables the Electrochemical C–H Azidation of *N*–Heterocycles through the Cleavage of Alkoxyamines. *ChemSusChem* **18**, e202402139.
2. Malo, S., Santra, S., Saha, J., Ghosh, D., and Das, I. (2024) External photocatalyst-free photocycloaddition between triplet vinylnitrenes with 1,3-biradical character and activated olefins under 420 nm LEDs. *Chem. Commun.* **60**, 12545.
3. Ghosh, S., Biswas, S., and Das, I. (2024) HAT-Mediated Electrochemical C(sp^2)–H Alkoxylation of Pyrido[1,2-*a*]pyrimidin-4-ones with Aliphatic Alcohols. *ChemCatChem* **16**, e202401023.
4. Bankura, A., Ghosh, S., Biswas, and Das, I. (2024) Convergent Paired Electrolysis for [3+2] Cycloaddition of Azidotrimethylsilane with N-Heterocycles. *ChemSusChem* **17**, e202400381.

Patents

1. An Improved Process for Synthesis of Mandipropamid. Indrajit Das, Jayanta Saha, Sumit Biswas, and Subhadeep Ghosh, Indian Patent application number 202411033733 dated 26 April 2024.
2. An Improved Process for Synthesis of Trifloxystrobin. Indrajit Das, Abhijit Bankura, Subhadeep Ghosh, Sumit Biswas, Jayanta Saha, and Kumaresh Das, Indian Patent Application No. 202411075609 dated 03 October 2024.

Dr. Indrajit Das, Senior Principal Scientist

Group Members: Siddhartha Malo, SRF; Sumit Biswas, SRF; Subhadeep Ghosh, SRF; Kumaresh Das, Project Associate-1 (HCP49)

Collaborators: Dr. Abhijit Kumar Das, Senior Professor, Department of School of Mathematical & Computational Sciences, Indian Association for the Cultivation of Science, Kolkata 700032, India; Dr. Debashree Ghosh, Professor, Department of School of Chemical Sciences, Indian Association for the Cultivation of Science, Kolkata 700032, India

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 and 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 in Organic Letters 2024, 26, 9859-9864, Adv. Synth. Catal. 2025, 367, e202401169, and filed for Patents. We have developed the process for the synthesis of an palbociclib and agrochemical mandipropamid.

Aims & Objectives

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, acridane and phenol
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 Zero-Carbon Footprint Intramolecular C(sp3)–H Functionalization to Access pyrroloazepines as Potential Sensor for Nitroaromatics: Patent filed: 202411016683, 2024

A diastereoselective cascade C(sp3)-H functionalization /7-endo cyclization strategy has been developed for the synthesis of pyrroloazepines as a potential sensor of picric acid via iminium intermediate induced by environmentally benign, highly

effective zero carbon footprint electrochemical oxidation of tertiary amines of without involving sacrificial expensive catalysts, and hazardous oxidants and traditional high-temperature techniques. A series of pyrroloazepines were achieved using ortho amino-benzylidene-succinimide derivatives with excellent yield and diastereoselectivity.These synthesized pyrroloazepines demonstrate remarkable efficacy in the nanomolar detection of picric acid (PA) in water, highlighting their potential for advanced environmental sensing applications (Figure 1).

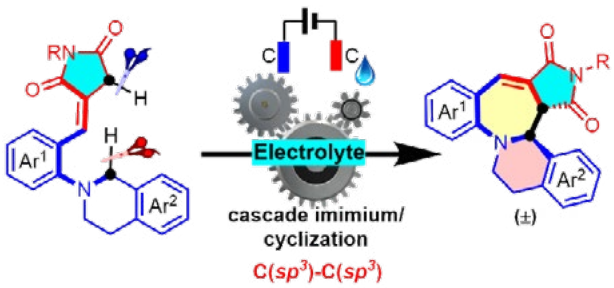
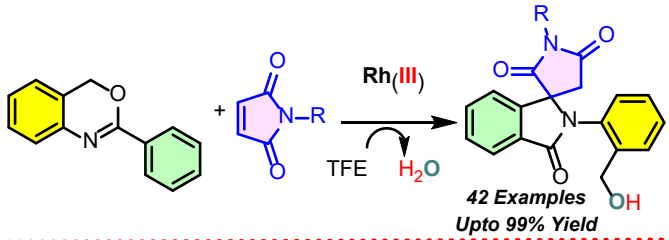


Figure 1: Electrochemical Intramolecular C(sp3)–H Functionalization to Access pyrroloazepines

(b) Synergistic [4+1] Spiro-Annulation and Selective Ring-Opening Strategy towards g-Spirolactams

Recently, a unique and propitious [4 + 1] spiroannulation of 2-aryl-4H-benzo[d][1,3]oxazine with maleimide has been delineated, furnishing diversely embellished γ-spirolactams featuring pendant benzyl alcohol via Rh(III)-catalyzed consecutive ring closing/ ring opening followed by regioselective cleavage of the C4–O bond of 1,3-benzoxazine promoted by an in situ generated water maneuver constructing new C–C, C–N, and C–O bonds at a go. A detailed mechanistic study, including a thorough analysis of the incorporation of an extra oxygen source, has been showcased to make this strategy for structurally orchestrated isoindoline-1-one spiro succinimides and the work has been published in **Org. Lett. 2024, 26, 9859–9864** (Figure 2).



- ♣ *One-pot [4+1] Spiro-Annulation/Ring opening*
- ♣ *No External Oxidant/Nucleophile*
- ♣ *Unleashing 1,3- Benzoxazine as DG*
- ♣ *Formation of C-C ,C-N, C-O Bond & Cleavage of C-O Bond*
- ♣ *One O atom Incorporation & Spiro-Isoindolone scaffolds*
- ♣ *Broad Spectrum of Substrates*

Figure 2: Rh(III)-Catalyzed C-H Bond Activation Reaction for The Synthesis of g-spirolactams

(c) Diastereoselective Intramolecular Spirocyclization via C(sp³)–H Bond Functionalization Towards the Synthesis of 2,7-Diazaspiro[4.5]decane-1,3-diones

We have developed a C(sp³)–H functionalization via intramolecular hydride transfer-initiated cascade annulation reaction for the synthesis of spiro-fused succinimide-containing tetrahydroquinolines induced by iminium intermediates. A series of diastereoselective 2,7-diazaspiro[4.5] decanes-1,3-diones have been achieved using ortho-amino-benzylidene-succinimide using Lewis acid catalysis. This scandium triflate $Sc(OTf)_3$ catalysed, oxidant-free protocol leads to the diastereoselective synthesis of a class of 2,7-diazaspiro[4.5] decanes-1,3-diones derivatives with 48-98% yield in a single step and published in *Adv. Synth. Catal. 2025, 367, e202401169* (Figure 3).).

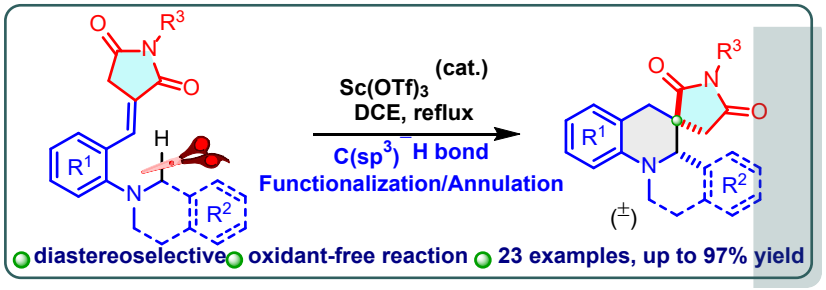


Figure 3: Intramolecular Spirocyclization via C(sp3)–H Bond Functionalization Towards the Synthesis of 2,7-Diazaspiro[4.5]decane-1,3-diones

(d) We are involved in developing the process for the synthesis of palbociclib and the key starting material

for the synthesis of palbociclib in PAN -CSIR Cancer mission (HCP-40). Recently, we have filed the patent for the process for the synthesis of key intermediate of palbociclib using easily available iron catalyst under mild reaction condition. We are actively involved in API mission (HCP-50) to develop a cost-effective process for the synthesis of tenofovir.

(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: 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).

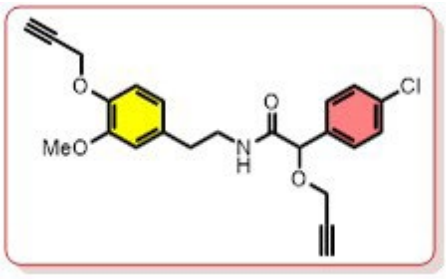


Figure 4: Mandipropamid, an agrochemical

Future Research Plans

- 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.
- 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. (2024) Synergistic [4 + 1] Spiroannulation and Selective Ring-Opening Strategy toward γ-Spirolactams. *Org. Lett. 24,* 9859-9864.
2. Bhowmik, A., Naskar, K., Roy, S., Sahoo, A. and Deb, I. (2025) Diastereoselective Intramolecular Spirocyclization via C(sp3)−H Bond Functionalization Towards the Synthesis of 2,7-Diazaspiro[4.5]decane-1,3-diones. *Adv. Synth. Catal.* 2025, 367, e202401169.
3. Deb, I, Saha, M, and Naskar, K. (2025) Synthesis of 6-acetyl-2-chloro-8-cyclopentyl-5-methylpyrido[2,3-d]pyrimidin-7(8h)-one a key intermediate in the manufacture of palbociclib. Patent filed: 0035NF2025, 2025.
4. Deb, I, Roy, S., Naskar, K., Mondal, I. (2024) A novel dihydrobenzo[b,e]pyrroloazepines hybrids and simple process for the preparation thereof: a potential bioactive heterocyclic scaffolds and bioprobes Patent filed : 0182NF2023, 2025.

Memberships

- Life member of Chemical Biology Society, Kolkata
- 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. Moumita Saha, NPDF; Dr. Anisha Purkait, RA-Project

Dr. Manish Debnath and his group members

Machine Learning-Guided Design of Functional Biomaterials for Tissue Generation and Combating Drug-Resistant Bacteria

Research Activities

Machine Learning-Optimized Nucleoside Hydrogels for 3D tissue generation

Machine learning (ML) is revolutionizing the design of functional biomaterials by enabling data-driven optimization of molecular properties and performance outcomes. In the context of 3D tissue engineering, nucleoside-based hydrogels have gained attention due to their intrinsic ability to self-assemble into supramolecular networks that mimic the extracellular matrix (ECM). These hydrogels, formed through non-covalent interactions such as hydrogen bonding and π–π stacking, offer excellent biocompatibility, tunable mechanics, and reversible gelation behavior. However, identifying nucleoside derivatives with optimal gelation and tissue-supportive properties is experimentally intensive and limited by chemical complexity. To overcome this, ML models trained on physicochemical descriptors, aggregation propensity, and gelation parameters can predict and prioritize promising nucleoside candidates from large virtual libraries. By iteratively coupling prediction with synthesis and validation, ML-guided platforms accelerate the development of next-generation ECM-mimetic hydrogels tailored for specific tissue environments, advancing the field of regenerative medicine and in vitro tissue modeling.

Here, we introduce a machine learning (ML) system to generate novel nucleoside-containing hydrogels for tissue development applications. The ML-predicted combinations integrated nucleosides into a crosslinked polymer matrix to create hydrogels with tunable stiffness, porosity, and bioactivity. A supervised ML model, trained on a dataset of 5,000 hydrogel compositions and their corresponding cellular responses, have been employed to predict optimal nucleoside concentrations and crosslinking densities, maximizing cell viability, proliferation, and differentiation. In vitro studies with an adherent mouse fibroblast cell line demonstrated the formation of ML-optimized 3D tissues through spheroid clustering, metabolic activity, and proliferation compared to non-optimized controls at 28 days These findings underscore the potential of ML-optimized nucleoside-containing hydrogels as advanced potential scaffolds for tissue engineering, regenerative medicine, and drug screening, offering a data-driven approach to biomaterial development.

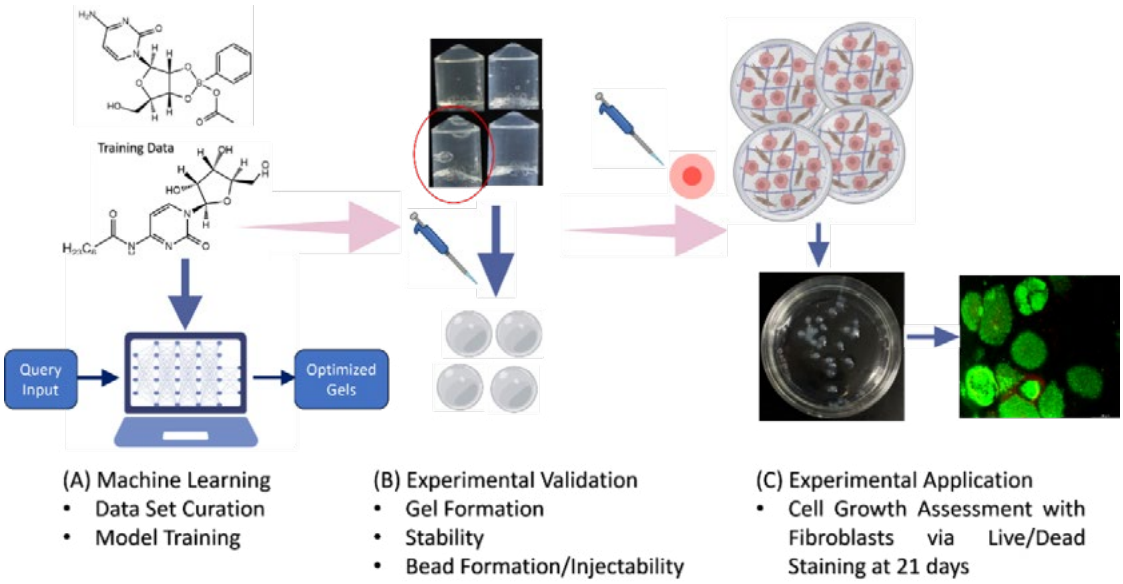


Figure 1: (A) Machine Learning (ML) based optimization is performed using algorithms harvesting literature based training data and wet lab data having over 5,000 datapoints; (B) The ML predicted formulations are validated experimentally for their stability and injectability; (C) Fibroblasts were seeded into ML optimized gel beads and growth assessment through cellular spheroids formation are determined by Live/Dead Staining at 4, 9, 14, 21, and 28 days.

Machine Learning-Guided Design of D-Amino Acid Peptides to Combat Antimicrobial Resistance

The rise of antimicrobial resistance poses a significant threat to public health, with the World Health Organization warning of a post-antibiotic era where common infections can become deadly. As effective treatments dwindle, our research focuses on developing short antimicrobial peptides with D-amino acids, effective against resistant microbes like MRSA. By leveraging Machine Learning, we aim to accelerate the discovery and optimization of these peptides, providing a new arsenal of targeted antimicrobial agents to mitigate the looming crisis of antimicrobial resistance. The key findings of this study include a novel machine learning-based system to screen and identify the extremely short antimicrobial peptides (<8 amino acids) derived from insect host defence peptides. The antibacterial efficiency of these ML-optimized peptides has been tested against a panel of Gram-negative and Gram-positive strains, including multidrug-resistant bacteria in 2D and 3D culture systems. Ultimately, the study successfully obtained Minimum Inhibitory Concentration (MIC) predictions for Melectin-derived short AMPs and validated them through wet-lab experiments, demonstrating the potential of this ML-system for the development of effective antimicrobial therapies.

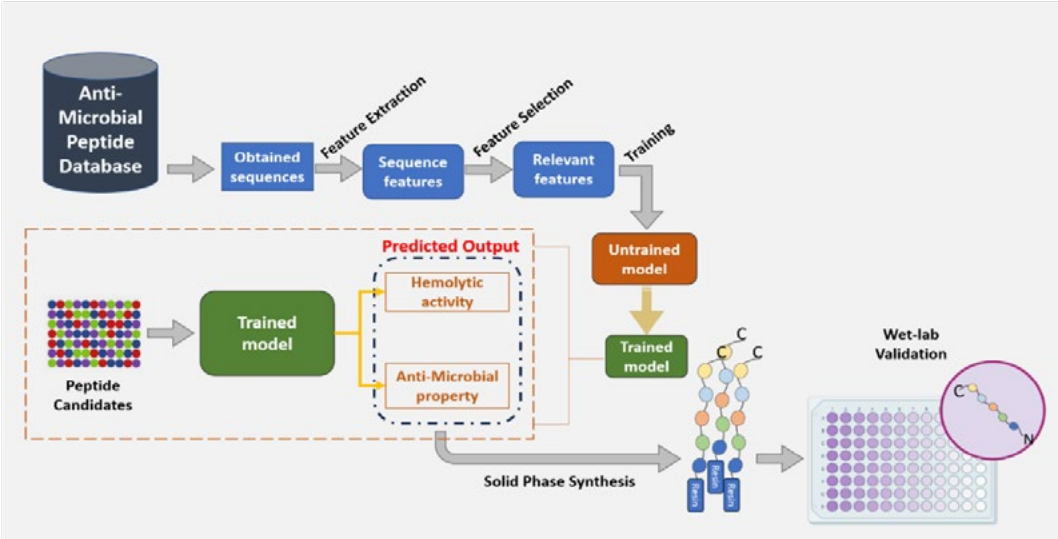


Figure 2: Schematic of framework for designing, synthesizing, and validating short anti-microbial peptides (AMPs) using a machine learning (ML) approach. ML algorithms trained on known AMP datasets to identify key features, followed by synthesis using solid-phase synthesis. Finally, wet-lab validation through MIC testing against bacteria to confirm anti-microbial activity.

Future Research Plans

- Developing nucleoside-carbohydrate conjugates-based biomaterials for skin tissue engineering applications with our improved ML models.
- ML-based systems for Antimicrobial Peptide (AMP) production.

Extramural / CSIR Funding

1. Development of chemically modified aptamers for targeting diseased exosomes (Extramural Funding: DST-ANRF: SRG/2023/001609).
2. Deep Ocean Mission: Towards discovery and development of novel drugs and pharmaceuticals. (MOES: GAP 490)

Publications

1. Das, P.; Das, A.; Debnath, M. (2025). Identification and Classification of Functional Split G-Quadruplexes Using Machine Learning-Guided Activity Screening. *ACS Appl. Bio Mater.* https://doi.org/10.1021/acsabm.5c00215.
2. Pathi, V. B., Das, P., Guin, A., Debnath, M., and Banerji, B. (2025). Metal-free synthesis of N-fused quinazolino-quinazoline-diones as a MALAT1 RNA triple helix intercalator. *RSC Med. Chem.*, **16**, 429-434. https://doi.org/10.1039/D4MD00614C

Book Chapters

Debnath, M., and Deb, P. (2025). Fluorescent carbon nanoparticles: Fundamentals, structure, fluorescent properties and mechanisms, challenges and future perspectives. In *Fluorescent Carbon Nanoparticles* (pp. 41-1). Elsevier.

Dr. Manish Debnath, Scientist

Group Members: Pranotosh Das, UGC-JRF; Souvik Sen, ICMR-JRF; Avimanyu Das, UGC-JRF, Shuvam Mandal, DBT-JRF

Collaborators: Dr. Biswadip Banerji (Chief Scientist), CSIR-IICB, Kolkata; Dr. Sucheta Tripathy (Senior Principal Scientist), CSIR-IICB, Kolkata; Dr. Sourish Ghosh (Senior Scientist), CSIR-IICB, Kolkata, Dr. Raja Roy (Head & Professor), IPGMER Kolkata; Dr. Hirak Jyoti Raj (Professor), IPGMER Kolkata; Dr. Hasina Banu (Assistant Professor), IPGMER Kolkata, Dr. Soumendra Nath Haldar (Head & Associate Professor), School of Tropical Medicine, Kolkata

Dr. Parasuraman Jaisankar and his group members

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

Background

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

A Green Synthetic Approach to Construct C2-Quaternary Indolin-3-Ones at Room Temperature via Regioselective Oxidative Dearomatization of Indoles

Indoles have constantly been an area of interest in the field of organic chemistry and related fields. These ubiquitous structural motifs are the pivotal skeleton in many biologically active natural products and pharmaceuticals. Among them, substituted indoles

constructing C2-quaternary indolines (pseudoindoxyls) have extensively flourished (Figure 1) and have been constantly applied to the synthesis of diverse molecular architecture containing many indole alkaloids and bioactive products such as halichrome A, duocarmycins C1 and B1 and austamide, etc. In addition, isatisine A, an oxindole system having indole 2-substituents, is present in the roots and leaves of Isatis indigotica Fort. Similarly, 2-(1H-indol-3-yl)-2,3'-biindolin-3-one (1) was isolated as the product of indole oxidation by a strain of Claviceps purpurea and has also been characterized from natural (bacterial) sources such as *Vibrio parahaemolyticus* and *Haemophilus influenzae*.

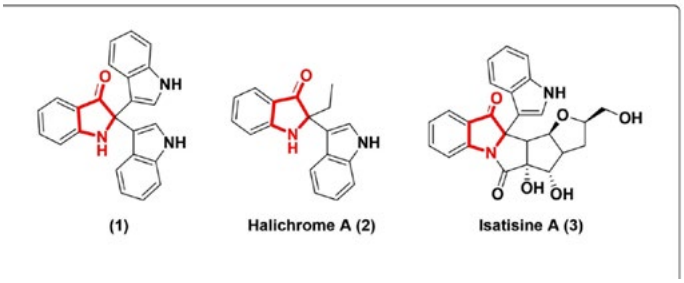
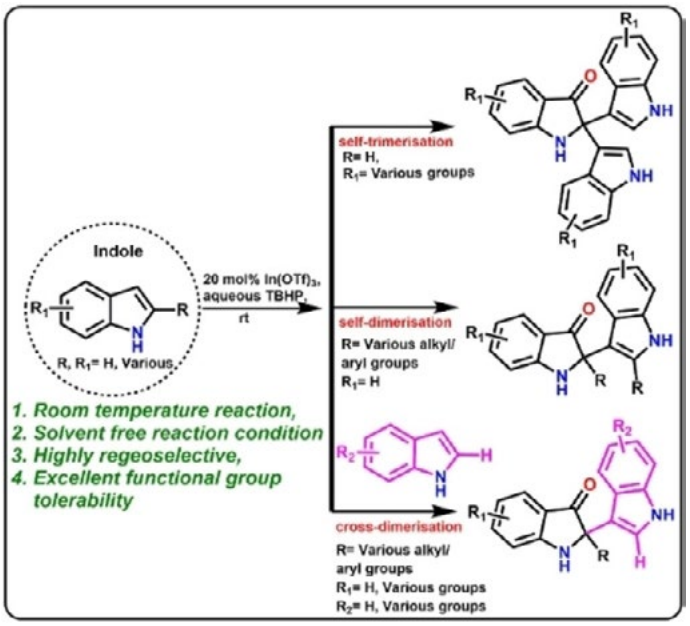


Figure 1: Representative examples of natural products containing C2-quaternary indolin-3-ones.

A new synthetic strategy for the construction of C2-quaternary indole for the formation of Indolin-3-ones has been explored via indium(III) trifluoromethansulphonate catalyst at room temperature with TBHP as a green oxidant in water. This approach for the oxidative dearomatization process allows for the production of the natural product Halichrome A and a broad range of C2-arylated Indolin-3-ones under a milder condition in very good yields. The oxidative self-dimerization and self-trimerization of various indole derivatives have also been achieved under the same conditions as depicted in the Figure 2 and Scheme 1. This result has been published in European Journal of Organic Chemistry.



Scheme 2: General synthetic Approach to Construct C2-Quaternary Indolin-3-Ones at Room Temperature via Regioselective Oxidative Dearomatization of Indoles

Future Research Plans

- Development of high-affinity BET Bromodomain Ligands as activator for exhausted CAR T Cells towards treatment of cancer and SynTEFs for activation of FXN and other genetic 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.

Publications

1. Pinaki Bhattacharjee, Sudip Dey, Salini Kar, Mohammed Rafi, Prasad Sunnapu, Parasuraman Jaisankar*, (2025) A Green Synthetic Approach to Construct C2-Quaternary Indolin-3-Ones at Room Temperature via Regioselective Oxidative Dearomatization of Indoles, *Euro. J. Org. Chemistry*, *28* (2) (https://doi.org/10.1002/ejoc.202401037)
2. Garg, Aakriti; Bhattacharya, Bireswar; Samanta, Uttam; Singha, Subhankar; Ghosh, Dipanjan; bhowmik, Subhendu; Parasuraman Jaisankar*; Gupta, Sreya*, (2025) Photo-Triggered Migration of Indole based Cationic Fluorophore from Mitochondria to Nucleolus in live cells, *SynLett, 36.* (doi number: 10.1055/a-2522-0571)
3. Prabir Kumar Gharai, Juhee Khan, Rathnam Mallesh, Shubham Garg, Sanju Gupta, Parasuraman Jaisankar, and Surajit Ghosh* (2025) Discovery of Carbazole and Theophylline-Based Amyloid Inhibitor for the Promotion of Neuroprotection, *ACS Chemical Neuroscience*, (DOI: 10.1021/acschemneuro.5c00067)

Awards / Honours

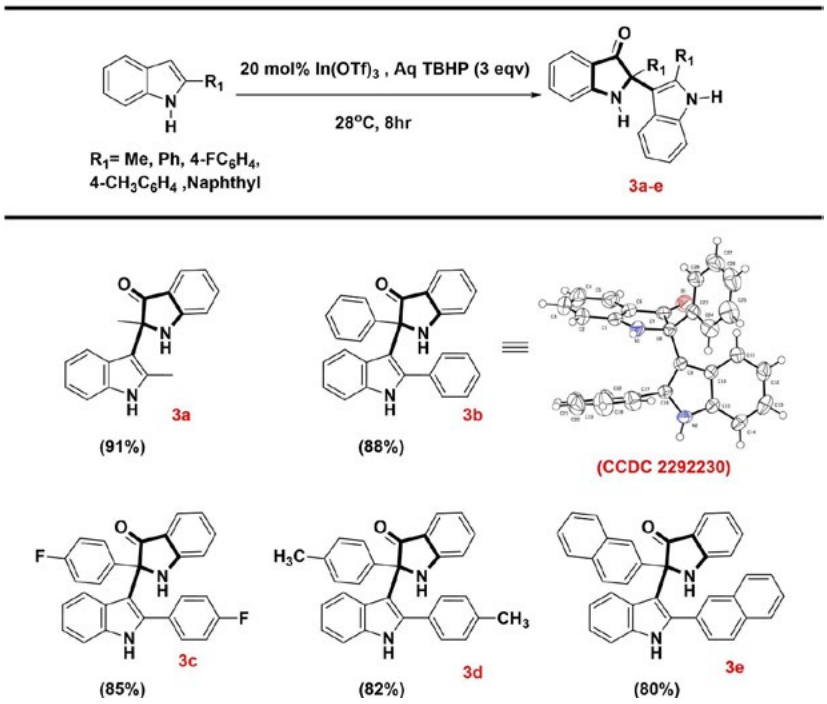
Elected as Global Outreach Contributing Member of American Society for Microbiology, USA, 2025.

Conferences / Events Organized

Skill Development programs of CSIR-IICB, 2024-2025 organized by CSIR-IICB, Kolkata, India.

Invited Talks

1. Development of Small-Molecule Fluorescence Probes for Organelle-Specific Live Cell Imaging Applications, International Conference on Current Trends in Drug Discovery Techniques and Diagnostics: Chemical Biology Approaches, organised by Adichunchanagiri University, BG Nagara, Mandya in association with Chemical Biology Society, 2-3 August 2024.
2. Bioactive Novel Molecules from Natural Product Origins for Drug Discovery in Cancer, Neurodegenerative, and Neglected Infectious Diseases, Conference on Structural Biology and Drug Discovery to commemorate the 102nd birthday of Prof. G. N. Ramachandran, organised by SRM Institute of Science and Technology, Chennai from 8-10 October, 2024.



Scheme 2: Reaction conditions: Indole (0.1 mmol), tert-Butyl hydroperoxide (70 % aqueous solution). H_2O (0.7 mL). (0.3 mmol), $In(OTf)_3$ (0.02 mmol), rt, 8 h. b Isolated yield by flash chromatography.

3. Bioactive Novel Molecules from Andrographis Species and Holarrhena pubescens Bark for Cancer, Neurodegenerative, and Neglected Infectious Diseases, IBSD Conference 2024, 11th Convention Society for Ethnopharmacology, India [SECON 2024], and International Conference on "Bioeconomy from Bioresources: Promoting Traditional Resources of NER for Viksit Bharat" Organized by BRIC-Institute of Bioresources and Sustainable Development (BRIC-IBSD) & Society for Ethnopharmacology, India (SFE, India), during 15-16 November, 2024.
4. Development of Novel Bioactive Small Molecules from Synthetic and Natural Sources for Infectious and Non-Infectious Diseases, "International Conference on Chemistry for Human Development (ICCHD-2025)' at University College of Science and Technology (Razabajar campus of C.U.), organised by Calcutta University, during 4-6, January 2025.
5. Development of Novel Bioactive Small Molecules from Synthetic and Natural Sources for Infectious and Non-communicable Diseases, Commemorating 150th year of the Department of Chemistry International Conference on Innovative Materials: Performance, Advancements, and Comprehensive Transformations (IC-IMPACT2025) organised by Presidency College, Chennai, during 7-8, January, 2025
6. Sustainable Innovations in Green Chemistry and Biocatalysis for a Greener Future, International Convention on "Research Trends in Sustainability Development, Science and Technology, organised by SPSU University, Udaipur, during 19-20, March 2025.

Conference/Training attended

Refresher Training Course for GLP Inspectors, organised by National GLP Monitoring Authority (NGCMA)-DST, New Delhi, during 13-14, January, 2025.

Dr. Parasuraman Jaisankar, Chief Scientist

Group Members: Vivek K. Gupta, ICMR-SRF; Nipun Abhinav, SRF, NIPER; Narendar Goel, SRF, NIPER; Aakriti Garg, SRF, NIPER; Sudip Dey, DST Inspire SRF; Mohammed Rafi, Project Fellow; Bedabrata Ray, DST Inspire JRF

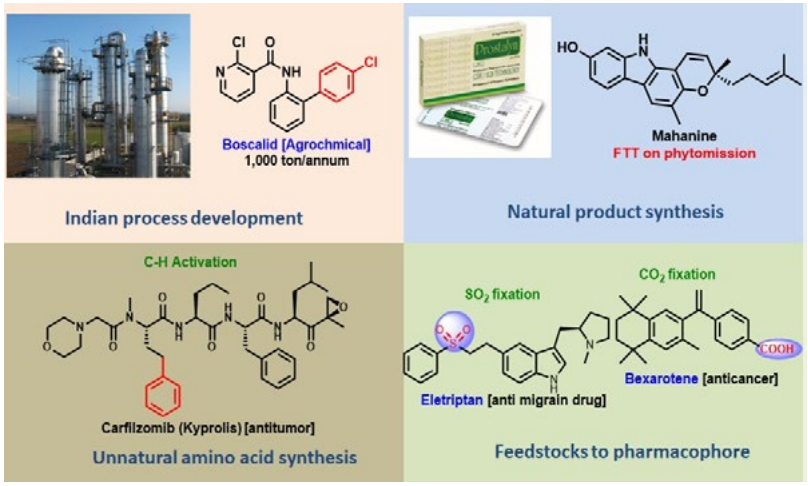
Collaborators: Prof. Surajit Ghosh, IIT-Jodhpur; Dr. Mabali Rajan, CSIR-IICB; Dr. Ramalingam Natarajan, CSIR-IICB, Dr. H. K. Majumdar, CSIR-IICB, Dr. Sreya Gupta, NIPER-Kolkata

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. 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. Varalaxmi, K.; Pradhan, K.; Begam, H. M.; Polley, A., Kumar, D.; Jana, R. (2024) Transition-metal-free iterative two-fold reductive coupling and 1,3-borotropic shift to form 1,4-skipped dienes, *Org. Biomol. Chem*. **22**, 8596-8601.
2. Das, S.; Banerjee, A.; Das, P.; Jana, R. (2024) Visible-Light Organophotoredox-Catalyzed Phosphonoalkylation of Alkenes via Deaminative Three-Component Radical–Radical Coupling, *Synlett*, **35**, 2471–2476. (Invited Special Issue on 75th Birthday of Professor B. C. Ranu.)
3. Mondal, S.; Nandi, S.; Das, S.; Jana, R. (2024) A chemoselective hydroxycarbonylation and ^{13}C-labeling of aryl diazonium salts using formic acid as the C-1 source, *Chem. Commun*., **60**, 13758-13761.
4. Das, S.; Rahaman, Sk. A.; Pradhan, K.; Jana, R* (2024) Organophotoredox-Catalyzed Synthesis of Unnatural α/β Amino Acids and Peptides via Deaminative Three-Component Coupling, *Org. Lett*. **26**, 5955-5960.
5. Jana, R*, Pradhan, K. (2024) Shining light on the nitro group: distinct reactivity and selectivity, *ChemCommun*, **60**, 8806-8823. (Invited Review)
6. Mondal, S.; Jana, R* (2024) Green light-mediated dual eosin Y/PdII-catalyzed C(sp^2)–H arylation of N–H unprotected 2-arylquinazolinones, *Org. Biomol. Chem*., **22**, 5540-5545.

Invited Lectures

1. Development of Visible Light-Mediated Sustainable Cross-coupling Reactions, Indian Photobiology Society, UEM, Calcutta, 31st Jan-1st Feb, 2025.
2. Molecular Diversity through Casacde C-H Activation, ICCHD-2025, University of Calcutta, 5th January, 2025.
3. Molecular Diversity through Casacde C-H Activation, Emerging Trends in Chemical Sciences University of Calcutta, 9th Feb, 2024.
4. Molecular Diversity through Casacde C-H Activation, IITKGP, Emerging Trends in Chemical Sciences, 7-9th March, 2024.
5. Molecular Diversity through Casacde C-H Activation, IACS, International Conference on Catalysis, 11-13th March, 2024.

Conferences Attended

1. 32nd CRSI National Symposium in Chemistry, BITS, Pilani, 01-04 February, 2024.
2. 33rd CRSI National Symposium in Chemistry, Dr. Reddy's Laboratories, Hyderabad, 04-6th July, 2024

Member of Society

1. American Chemical Society
2. Indian Chemical Society (ICS)
3. Chemical Research Society of India (CRSI)

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; Subhamoy Chakraborty, CSIR-JRF, Amit Banerjee, HCP-49- Project Associate I

Dr. R. Natarajan and his group members

Development of synthetic supramolecular receptors

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. Our research is focused on the design, synthesis, and application of novel supramolecular structures, particularly organic and metal-organic cages, and metal-organic frameworks from organic cages. These studies are at the forefront of supramolecular chemistry and the development of functional materials for various applications, including sensing, recognition, transport, and catalysis.

Metal–Organic Cage Receptors for Encapsulation and Sensing of Bile Acids:

Bile acids are steroidal molecules derived from cholesterol that aid in digestion and regulate metabolic and signalling pathways. The primary bile acids (cholic acid and chenodeoxycholic acid) and secondary bile acids (deoxycholic, ursodeoxycholic, and lithocholic acids) act as emulsifiers, with about 95% recycled back to the liver and the remainder excreted—making them useful disease biomarkers. Removing excess bile acids can lower cholesterol by prompting the body to convert it into new bile acids, but current sequestrant drugs (ammonium-functionalized polymers) require high doses, lack specificity, and cause side effects. Synthetic supramolecular receptors offer a more targeted way to bind and remove bile acids therapeutically, and, when paired with indicator dyes, can also detect changes in bile acid levels. Presently, bile acid analysis depends largely on mass spectrometry.

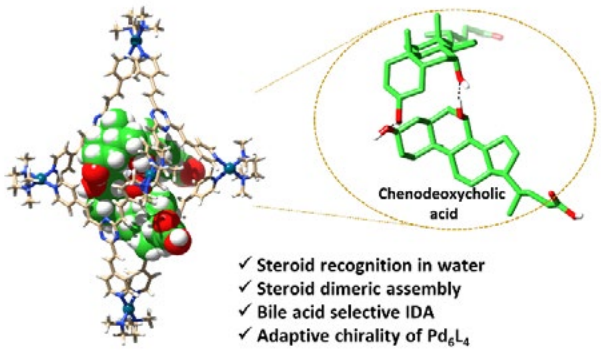


Figure 1: Pd6L4-metal-organic cage for the recognition and sensing of bile acids

We developed a C_2-symmetric metal-organic cage $[Pd_6\mathbf{L2}_4]^{12+}$, an expanded version of the Fujita cage $[Pd_6\mathbf{L1}_4]^{12+}$, built with a conformationally flexible ligand **L2**, accessed through coordination-driven self-assembly. We examined both cages for steroid recognition in water: both have certain shared characteristics and distinctive features. $[Pd_6\mathbf{L1}_4]^{12+}$ binds hydrophobic bile acids and

other steroids by forming 1:1 complex. In contrast, the expanded $[Pd_6\mathbf{L2}_4]^{12+}$ cage exhibits affinity for amphiphilic bile acids and selective steroids to encapsulate them as dimers, promoted by cooperative inter-guest hydrogen bonding (Figure 1). $[Pd_6\mathbf{L2}_4]^{12+}$ has a five times stronger solubility enhancement ability for cholic acid compared to $[Pd_6\mathbf{L1}_4]^{12+}$. Further, the expanded $[Pd_6\mathbf{L2}_4]^{12+}$ cage can selectively sense bile acids in nanomolar detection limits through indicator displacement assay by employing sulforhodamine 101 (SR 101). The results reported provide valuable strategy to access supramolecular receptors through coordination-driven self-assembly for encapsulation of steroids as dimers and sensing of selective bile acids in water.

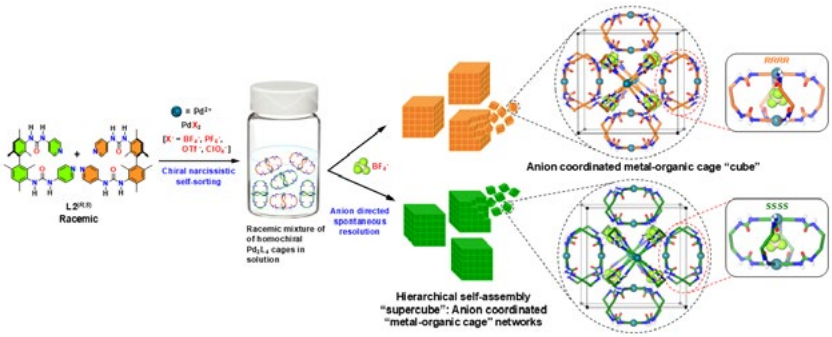


Figure 2: Hierarchical self-assembly of metal-organic cages

Hierarchical self-assembly in metal-organic cage receptors

The ability to collectively program chiral recognition and the hierarchical self-assembly of molecular and supramolecular building blocks into complex higher-order superstructures is a significant goal in supramolecular chemistry to develop functional materials. Metal-organic cages are excellent model systems to examine chiral self-sorting and build hierarchical self-assembly. While aiming to develop novel synthetic recepotrs based on metal-organic cages, we identified about how limiting the conformational flexibility and incorporating hydrogen bonding functional groups in the ligands can influence chiral self-sorting and hierarchical self-assembly of metal-organic cages into metal-organic cage frameworks. BF_4^- anion directed high-fidelity chiral narcissistic self-sorting with **L2** followed by spontaneous resolution of enantiopure crystals in the solid state. In the solid state, the $Pd_2\mathbf{L2}_4$ cages undergo hierarchical self-assembly into hexameric cube of metal-organic cages and subsequent organization of the face-sharing cubes into super-cube mediated by anion coordination of BF_4^- with urea through hydrogen bonding interactions (Figure 2). Overall, this study opens up a new approach in developing hierarchical self-assembly of metal-organic cages through hydrogen bonding anion-coordination with appropriately functionalized ligands in metal-organic cages.

A Metal–"Organic Cage" Framework for Efficient Polycyclic Aromatic Hydrocarbon Removal from Water

PAHs (polycyclic aromatic hydrocarbons) are persistent, hydrophobic pollutants containing fused aromatic rings (e.g., naphthalene, pyrene, benz[a]pyrene) that enter air and water through activities like combustion and smoking. Even at microgram-per-liter levels, they resist standard water treatments and, if ingested, transform into carcinogenic metabolites that damage DNA and promote cancer. Existing adsorbents do not capture them effectively Organic molecular cages—especially cyclophanes and other structures with cofacial aromatic planes—can tightly bind PAHs in solution, and incorporating these cages into crystalline metal–organic frameworks (MOFs) offers a way to translate solution-phase complexation into solid-phase scavenging.

We developed a metal-"organic cage" framework, **MOF-CC-1**, for the effective scavenging of PAHs from water. **MOF-**

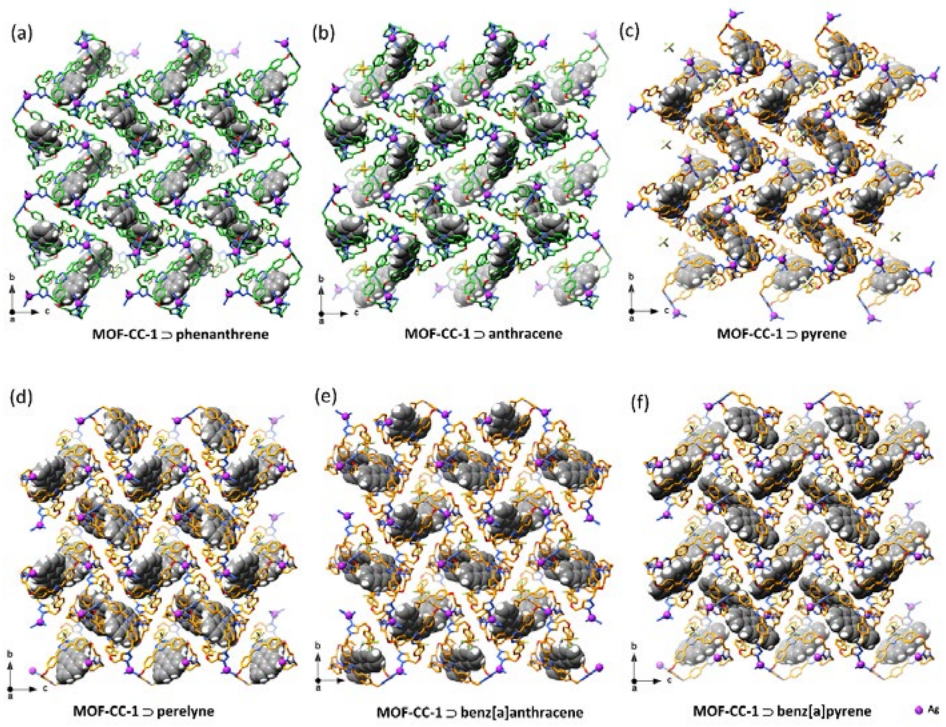


Figure 3. Polycyclic aromatic hydrocarbons encapsulated in MOF-CC-1

CC-1 uniquely encapsulates diverse PAH molecules within the cavities of CC-1, as confirmed by single-crystal X-ray diffraction, marking it as the first metal-"organic cage" framework with structural evidence of guest inclusion inside the organic cage linker. Further, **MOF-CC-1** exhibits soft porosity, remaining non-porous to N_2 gas when compressed but expanding to encapsulate PAHs in solution. Moreover, **MOF-CC-1** exhibits exceptional efficacy in scavenging ppb levels of PAHs from water. This work represents a significant advancement in utilizing organic cages as ligands towards MOF construction, paving the way for tailored adsorbents for PAH removal, addressing a critical need for selective and efficient materials in environmental remediation.

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) development of novel lead molecules against specific targets

Publications

1. Paul, B.; Natarajan, R. Metal–Organic Cage Receptors for Encapsulation and Sensing of Bile Acids. *Inorg. Chem.* 2024, *63*, 8449–8461.
2. Ghorai, S.; Natarajan, R. Chiral Self-Sorting, Spontaneous Resolution, and Hierarchical Self-Assembly in Metal–Organic Cages. *Small* 2024, *20*, 2400842.
3. Paul, B.; Ghorai, S.; Samanta, J.; Natarajan, R. Encage the Carcinogens: A Metal–"Organic Cage" Framework for Efficient Polycyclic Aromatic Hydrocarbon Removal from Water. *Small* 2025, *21*, 2408482.

Invited Lectures

1. International Conference on Modern Trends in Inorganic Chemistry (MTIC), 21st Edition, IIT-Kharagpur, 14-17 December, 2024
2. 2nd International Conference on Emerging Areas of Chemistry (ICEAC 2025), Tripura University, 12-14 February 2025

Dr. R. Natarajan, Senior Principal Scientist

Group Members: Bhaswati Paul, SRF; Suvajit Pal, JRF; Subhajit Dutta, JRF; Parna Bhattacharya, PA; Akash Adhikari, PA; Ipsita Ganguly, PA

Dr. Rashmi Gaur and her group members

Extraction, isolation of bioactive phytomolecules from Indian Medicinal Plants and their synthetic modification 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. Plant *Myena spinosa* belongs to the family Rubiaceae. Boiled extract of fruits: cure diabetes by Meitei/ Meitei-pangal communities in Thoubal district, Manipur, India. Seed paste with water also used as abortifacient by the rural people in Tinsukia district, Assam. Dried leaf powder of the plant with turmeric rhizome (3:1) made into paste and used in the removal of intestinal worm by Oraons.

- DCM extract of the *Myena spinosa* fruit showed good anticancer activity (ovarian cancer) with IC_{50}= 42.8µg/ml.
- Oleanolic acid, betulinic acid and trans-cinnamic acid were isolated from the DCM extract and identified by NMR data along with several other phenolics.
- GCMS analysis of various extract detected 42 molecules in the fruit.
- Chemical transformation of isolated phytomolecules for enhancing the potential biological activities and their SAR studies.
- Molecular docking 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.
- Deep Ocean Mission: Towards discovery and development of novel drugs and pharmaceuticals.

Publications

1. Gaur R*, Jyoti, Khan S, Cheema H.S., Khan F, Darokar M.P., Bhakuni R.S. (2024) Synthesis, molecular modelling studies of artemisinin-chalcone derivatives and their antimalarial activity evaluation. Natural Product Research, https://doi.org/10.1080/14786419.2024.2375784,. (*Correspondind Author)

Invited Lectures

Nanodrugs based on Natural Products for Cancer Theranostics, International Conference on Nanochemistry and Theragnostics (ICNT-2024). 29-30 July, 2024.

Member of Society

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

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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. Debasis Nayak, 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 small molecules

Research Activities

Structural information of nucleic acids with small molecule or ligands can be useful for designing DNA/RNA targeting therapeutics. Our group was the first to show that a benzyl switches in a nitroquinoxaline small molecule provide important insights about molecular architecture which control specific DNA binding modes and is useful in designing functionally important monomeric quinoxaline DNA binders. Previous work from our laboratory shows that the DNA superstructure formation by mono-quinoxaline derivatives is highly entropically favored and predominantly driven by hydrophobic interactions. We are utilizing this strategy to target bacterial DNA to develop antibacterial compounds. Furthermore, some of the designed quinoxalines amines were shown to cleave abasic sites in DNA and potentiate the therapeutic ability of known anticancer drugs in colon cancer cells.

Work done

In our recent work we have shown that DNA abasic sites can act as a rational therapeutic target can be targeted by small molecules. Temozolomide (TMZ) is widely employed as a frontline agent in chemotherapeutic regimens for various malignancies; however, its clinical efficacy is markedly compromised by resistance, particularly in mismatch repair (MMR)-deficient cancers. Our findings underscore the critical yet underappreciated role of the base excision repair (BER) pathway in mediating resistance. Our study demonstrates a dose-dependent increase in DNA abasic (AP) site accumulation following TMZ treatment in both MMR-proficient and -deficient cancer cells, identifying AP sites as critical molecular targets to potentiate TMZ cytotoxicity. We have synthesized amino-quinoxaline derivatives (RA-1) featuring a hydrophobic scaffold that selectively binds AP sites through base stacking interactions, preferentially opposite adenine residues. RA-1 induces efficient cleavage of TMZ-generated AP sites at low micromolar concentrations via Schiff-base chemistry in vitro. Notably, the combinatorial treatment of TMZ with RA-1 synergistically enhances cytotoxicity, irrespective of MMR status. Mechanistically, RA-1-mediated AP site cleavage disrupts BER progression, resulting in DNA double-strand breaks. This damage activates the ATM-Chk2 and ATR-Chk1 signaling cascades, induces S-phase arrest, and culminates in apoptotic cell death. Our findings underscore the therapeutic potential of targeting DNA abasic sites to overcome TMZ resistance, providing a strategic framework to improve treatment outcomes in cancers irrespective of MMR status.

We have also developed a synthetic method for fused quinoxaline 1,5-disubstituted-[1,4]-diazepine hybrids which doesnot involve any metal ions under mild conditions. This involves a domino intermolecular SNAr followed by an internal nucleophile triggered intramolecular SNAr pathway. Utilizing this strategy, we can introduce of a broad variety of functionalities at the N-1 position of

fused diazepine moiety by employing suitable diamine tails to design structurally diverse scaffolds. The DNA binding properties of representative quinoxaline diazepine hybrids were studied using UV–vis absorbance and EtBr displacement assay and were found to be governed by the functionalities at the N-1 position. We envision that our work will offer newer methodologies for the construction of fused quinoxaline 1,5-disubstituted-[1,4]-diazepine class of molecules.

Future Research Plans

We are synthesizing the quinoxaline-diazepine hybrids to target DNA abasic sites in cancer cells. Our laboratory is also involved in the development of small molecules targeting the bacterial DNA and topoisomerases which can be used as antibacterials. We are also targeting the RNA of Hepatitis C Virus and SARS COV2 with small molecules.

Extramural / CSIR Funding

1. Project Title: "Targeting RNA driven processes: Novel Chemical Biology Approaches to Identify New Classes of RNA Modulators" CSIR; (2020-2025), 450 lakh, MLP-139.
2. Project Title: "Non-alcoholic Fatty Liver Disease (NAFLD): Novel Pathogenetic mechanism and therapeutic development. CSIR, (2020-2025), 499 lakh, MLP-138.
3. Mission Mode Project on Antimicrobial Resistance in collaboration with other CSIR institutes. Title: A comprehensive approach to address Antimicrobial Resistance (AMR), CSIR (2024-2027), 495 lakh MMP075202.

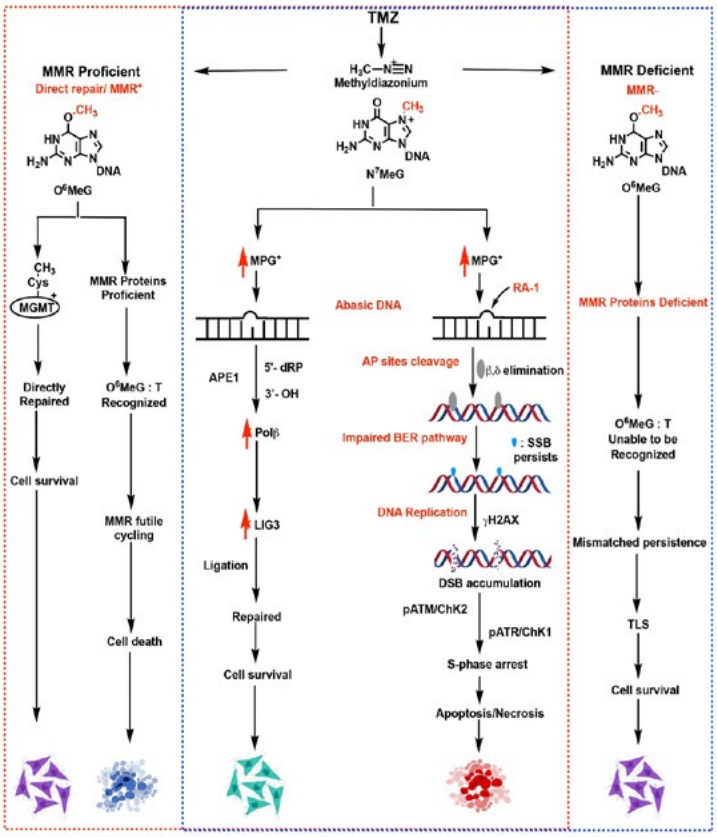


Figure1: Proposed Model for the synergistic enhancement of TMZ response with RA-1 via BER pathway-mediated cleavage of abasic sites. (adapted from *NAR Cancer*, 2024, zcae034)

Publications

1. Bora, A., Pal, R., Mandi, C. S., Dutta, S*. (2024) DNA abasic sites act as rational therapeutic targets to synergize temozolomide response in both MMR-proficient and deficient cancer, *NAR Cancer*, Volume 6, Issue 3, zcae034, https://doi.org/10.1093/narcan/zcae034.
2. Majhi, B., Bora, A., Palit, S., Dev, S., Majumdar, P., Dutta, S*. (2024) "Metal-free internal nucleophile-triggered domino route for synthesis of fused quinoxaline [1,4]-diazepine hybrids and the evaluation of their DNA binding properties", *Bioorganic Chemistry*, Volume 151, 107694, ISSN 0045-2068, https://doi.org/10.1016/j.bioorg.2024.107694.
3. Saha, R., Pal, R., Ganguly, B., Majhi, B., 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. doi: 10.1016/j.ejmech.2024.116377.

Patents

An antiviral compound and process for preparation thereof. Subhadeep Palit, Bhim Majhi, Rimita Saha, Sanjay Dutta. Application number 202411087083 dated 11-11-2024, 0183NF2024/IN)

Dr. Sanjay Dutta, Senior Principal Scientist

Group Members: Achyut Bora, CSIR-NET, SRF, PhD completed; Rimita Saha, DBT-NET, SRF, PhD completed; Bhim Majhi, CSIR-NET, SRF, PhD completed; Aymen Parwez, CSIR-NET, SRF; Mayank Gardia, DST-Inspire, SRF; Bhaskar Gangopadhyay, UGC-NET, SRF; Biswadip Chakraborty, DST-Inspire, JRF; Niloy Biswas, UGC-NET, JRF; Rounak Patra, UGC-NET, JRF; Sulekha Chaudhury, CSIR-NET, JRF; Dr. Abhi Das, Women Scientist

Collaborators: Dr. H. H Krishnan (CSIR-CCMB), Dr. Mandar Deshmukh (CSIR-CCMB)

Group members of Prof. Vibha Tandon

Deciphering Clinical Heterogeneity in Oral Squamous Cell Carcinoma using Patient-Derived Single Cell Spheroids and Multiple Approaches to Combat Antimicrobial Resistance Against ESKAPE Pathogens

Research Activities

The laboratory's research is primarily based on: elucidating the molecular and cellular heterogeneity of oral squamous cell carcinoma (OSCC) using patient-derived xenograft (PDX) models and three-dimensional (3D) spheroid cultures, and, addressing the mechanisms of antimicrobial resistance.

OSCC is the most prevalent aggressive malignancy within head and neck squamous cell carcinoma (HNSCC), with a striking disease burden within India. The elevated rates of tobacco consumption, in conjunction with socioeconomic factors, contributes to both high disease prevalence and a 50% low survival rates, primarily due to resistance to therapy. Therapeutic resistance is largely driven by pronounced intra- and inter-tumoral heterogeneity, as revealed by both bulk and single-cell molecular profiling.

Cancer stem cells (CSCs) are pivotal in mediating OSCC heterogeneity, chemo-resistance, metastatic capacity, and recurrence. These CSCs, which can remain quiescent or develop drug-resistant and metastatic phenotypes, interact dynamically with the tumour microenvironment, resulting in persistent disease following standard chemotherapy and radiotherapy. Patient-derived xenograft models established in immune-deficient mice and 3D spheroid and organoid cultures derived from patient tumours or cell lines drastically mimic in vivo tumour heterogeneous genetic alterations, clonal evolution, and cell–cell interactions, enabling high-resolution functional studies of OSCC heterogeneity and therapy resistance. Integrative use of scRNA-seq allows us to dissect lineage-specific drug sensitivities and adaptive responses.

Staphylococcus aureus is a major cause of infections in humans and animals, ranging from minor skin infections to severe, life-threatening diseases. A major challenge in controlling this pathogen is Antimicrobial Resistance (AMR) which can be achieved by studying the genetic basis of resistance that will further support global efforts to combat the growing threat of antimicrobial resistance (AMR).

This scientific report thus underscores the laboratory's research of unravelling the tumour microenvironment of OSCC and inform the next generation of targeted, personalized therapies for this highly lethal malignancy besides studying antimicrobial resistance.

Aims and objectives of our research are as follows:

- To investigate and functionally characterize the heterogeneity of cancer stem cell (CSC) subpopulations in OSCC
- To use patient-derived xenograft and 3D single-cell spheroid models to study their role in tumorigenesis, therapeutic resistance, and disease recurrence
- To develop therapeutic agent against multidrug resistant bacteria

Our research areas are as follows:

Identification and characterization of cancer stem cell heterogeneity in head and neck cancer patients and their response to chemotherapy and radiation

Head and Neck Squamous Cell Carcinoma (HNSCC) is a highly aggressive malignancy characterized by frequent recurrence, metastasis, and resistance to standard therapies. Emerging evidence suggests that a small subset of tumor cells known as **cancer stem cells (CSCs)** plays a pivotal role in driving tumor initiation, therapeutic resistance, and disease relapse.

This investigation focuses on the systematic identification and characterization of **CSC heterogeneity** within HNSCC and explores strategies to enhance treatment response. In this context, **Prochlorperazine (PCZ)**, an FDA-approved phenothiazine antipsychotic, was evaluated for its potential to act as a **radiosensitizer** by targeting **KRAS signaling** pathways. In KRAS-mutant HNSCC cell lines, PCZ selectively reduced cell viability in a **dose-dependent manner**, exhibiting greater cytotoxicity in cancer cells compared to normal oral fibroblasts. When combined with radiation, PCZ significantly enhanced radiosensitivity, inducing **G2/M cell cycle arrest** and **apoptosis**, while markedly suppressing **cell proliferation and migration**. The observed **lower IC_{50} values** in KRAS-variant cancer cells highlight its selective efficacy. Collectively, these findings underscore PCZ's potential as a **targeted adjuvant to radiotherapy**, capable of overcoming radio-resistance in KRAS-mutant HNSCC. This work contributes to a broader understanding of CSC heterogeneity and identifies PCZ as a promising therapeutic candidate to improve clinical outcomes in aggressive and treatment-resistant head and neck cancers.

Functional Characterisation of patient-derived single cell spheroids from OSCC to decipher clinical heterogeneity

This study focuses on establishing and characterizing a **patient-derived single-cell spheroid model** from **Indian patients diagnosed with Oral Squamous Cell Carcinoma (OSCC)** and **oral epithelial dysplasias** such as **leukoplakia and erythroplakia**. These 3D spheroid cultures were developed to closely recapitulate the structural, cellular, and molecular heterogeneity of primary tumours. The **characterization of these spheroids** involved comprehensive analyses of **morphology, growth kinetics, and viability**, along with the evaluation of **key functional traits** including **cell proliferation, apoptosis, invasion, and migration**. Advanced techniques such as **live-cell imaging, immunohistochemistry (IHC), and histological analysis** were employed to assess spatial organization, cellular composition, and differentiation patterns within the spheroids. These in vitro findings were further corroborated *in vivo* using **patient-derived xenograft (PDX)** models to confirm the tumorigenic potential of the spheroid-derived cells.

Based on this, we further explored the molecular mechanisms underlying tumour progression and therapeutic response, focusing specifically on the **miR-3170–VAV2 regulatory axis**. Through comprehensive *in silico* analysis of TCGA-derived small RNA and RNA sequencing datasets, along with transcriptomic profiling of oral cancer patient samples, **miR-3170** was identified as a novel and significantly downregulated microRNA in OSCC. Target prediction using TargetScan, miRTarBase, and miRDB identified **VAV2**, a guanine nucleotide exchange factor, as a potential downstream effector. Validation by **qRT-PCR** in patient tissues and OSCC cell lines (HSC-3, SAS) confirmed **downregulation of miR-3170** accompanied by **upregulation of VAV2**. Functional luciferase reporter assays with wild-type and mutant 3'UTR constructs established **direct binding between miR-3170 and VAV2**, while gain-of-function studies using stable miR-3170 overexpressing cell lines demonstrated reduced proliferation and migration with increased apoptosis. These results were further supported by xenograft models, which exhibited suppressed tumour growth upon miR-3170 overexpression. In the ongoing phase, OSCC spheroids are being treated with therapeutic molecules, including miR-3170 mimics and VAV2 modulators, to delineate the mechanistic role of the miR-3170–VAV2 axis within a 3D tumor context. This system allows dynamic monitoring of treatment responses through live imaging, morphometric analysis, and molecular profiling. Rescue experiments using stable VAV2-overexpressing cell lines will further clarify the downstream pathways involved in cytoskeletal dynamics and cell motility. Collectively, this integrated approach — combining patient-derived 3D spheroids, PDX validation, and molecular targeting — aims to establish miR-3170 as a potential biomarker and therapeutic target in OSCC, offering new avenues for precision-based treatment strategies in head and neck cancer.

A Comprehensive Approach to Address Antimicrobial Resistance

This study investigates *Staphylococcus aureus*, a major pathogen increasingly exhibiting multidrug and extensively drug resistance (MDR/XDR) to antibiotics such as ciprofloxacin, vancomycin, methicillin, and linezolid. Recognized by WHO as a high-priority AMR pathogen, *S. aureus* employs diverse mechanisms—mutations in antibiotic targets, drug-modifying enzymes, and stress-induced DNA repair—to survive antibiotic pressure. A genome-wide association study (GWAS) of ~1,000 clinical isolates identified the DNA repair gene RecN as a potential contributor to resistance. Candidate mutations in RecN are being validated experimentally to determine their impact on bacterial survival under antibiotic stress. Complementary assays, including MIC determination, time-kill kinetics, resistant mutant isolation, and mutation frequency analysis, will comprehensively assess the role of RecN in mediating antimicrobial resistance. The findings aim to reveal how DNA repair mechanisms drive AMR and guide the development of next-generation antibacterial strategies.

Future Research Plans

- To validate PCZ in in vivo models (xenograft/animal studies) and conduct mechanistic studies to define KRAS–PCZ interaction and downstream signalling pathways, explore synergistic combinations with other standard treatments (cisplatin, immunotherapy) and investigate PCZ's role as a predictive biomarker-driven therapy in KRAS variant patients and eventual development of PCZ as a cost-effective adjuvant to radiotherapy. Besides, delineating the mechanistic role of the miR-3170–VAV2 axis in OSCC, particularly in pathways governing cytoskeletal dynamics and cell motility. In addition, we aim to explore the therapeutic potential of targeting miR-3170 through the use of miRNA mimics or inhibitors, alone or in combination with standard chemotherapeutics, in preclinical models.
- We also aim to identify novel mutations in DNA repair genes that directly contribute to AMR. These mutations could serve as powerful biomarkers for predicting resistance, improving diagnosis, and guiding personalized treatment strategies. They also have potential to become new drug targets, offering innovative approaches to reduce AMR in *S. aureus*.

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. Maurya, V.; Singh, R.; Kutmutia, S.; Chaudhary, B.; Bhattacharjee, S.; Tandon, V. (2025) Adaptive laboratory-evolved MRSA with PPEF manifests cross-susceptibility to oxacillin and hypersensitivity to ciprofloxacin. *Microbiol Spectr*, **13**, e02974-24
2. Pandey, J.; Malik, Md. Z.; Ritis K. Shyanti, R. K.; Parashar, P.; Kujur, P. K.; Mishra, D.; Tailor, D.; Lee, J. M.; Kataria, T.; Gupta, D.; Verma, H.; Yadav, A.; Kateriya, S.; Malhotra, S. V.; Tandon, V.; Chaturvedi, R.; Singh, R. P. (2025) Uncovering Functional Divergence and Cellular Clusters with Specific Gene Signatures in HNSCC Clonal Spheroids, *Cell Communication and Signaling*, (Accepted).

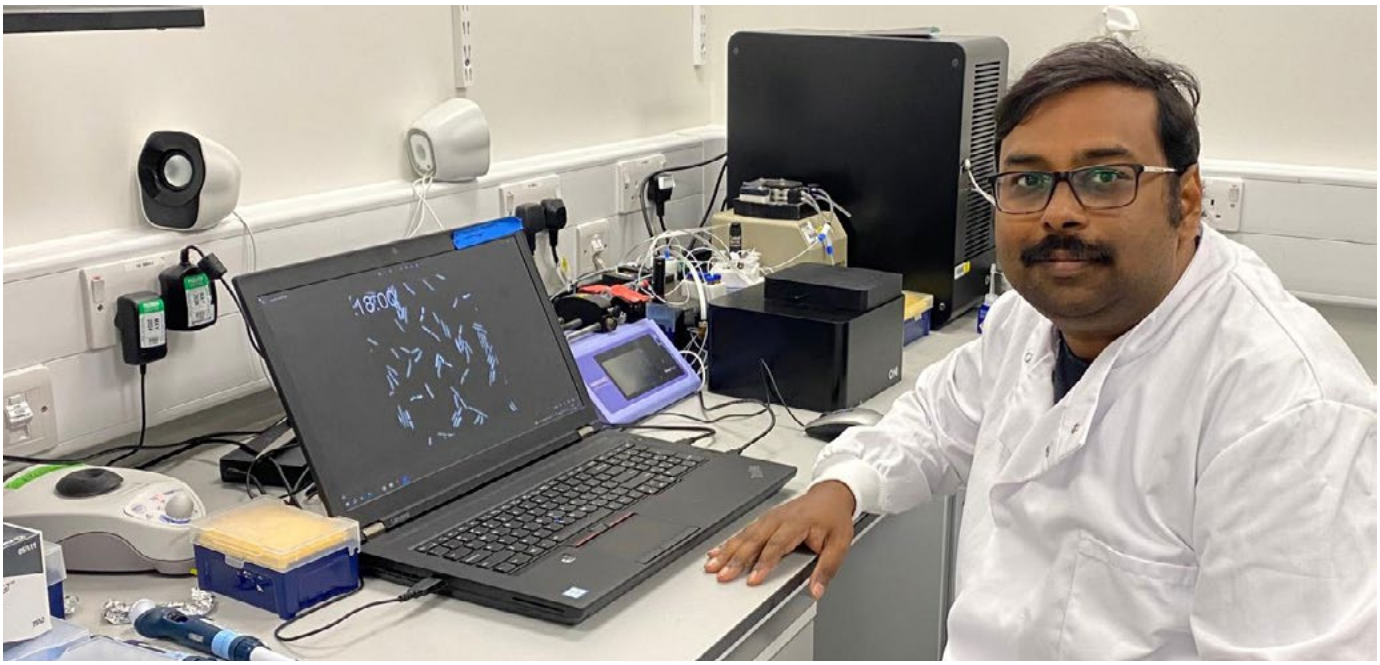
Prof. Vibha Tandon, Director, CSIR-IICB, Kolkata

Group Members: Dr. Pamelika Das, Nasrin Ara, Tanisha Ghosh, Shreya Ghosh

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, Dr. Swaradendu Ghosh, Saroj Gupta Cancer Centre and Research Institute, India and Prof. Sujata Mohanty, DBT-Centre of Excellence for Stem Cell Research, All India Institute of Medical Sciences, India.

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

The Structural Biology and Bioinformatics Division comprises 12 faculty members and a DBT/Wellcome Trust India Alliance Intermediate Fellow engaged in various disease-oriented research projects. The primary aim of this research is to understand the key molecular causes of diseases. At the molecular level, the interactions between various proteins and protein complexes are crucial for regulating our biological functions. Any abnormalities in these processes may lead to diseases. Basic research in structural biology is conducted to elucidate these causes of abnormalities and to develop prevention methods. Our division focuses on cutting-edge research in neurodegenerative diseases such as Alzheimer's and Parkinson's, metabolic disorders like diabetic retinopathy and NAFLD/NASH, as well as severe parasitic diseases like kala-azar, caused by Leishmania donovani and malaria, caused by Plasmodium falciparum. We also study the highly infectious disease tuberculosis, which is due to Mycobacterium tuberculosis. In addition, researchers are investigating fundamental aspects of prokaryotic and eukaryotic gene regulation and their roles in various diseases. Moreover, our division addresses pressing global health concerns highlighted by the World Health Organization (WHO), such as Antimicrobial Resistance (AMR) and the recent outbreak caused by the SARS-CoV-2 virus. Two proteins, alpha-synuclein, and tau, are of particular interest in the study of neurodegenerative diseases. Prokaryotic ribosomes are also a focus of intense research related to tuberculosis and malaria. Our faculty utilizes various advanced biophysical techniques, including Raman Spectroscopy, Fluorescence Correlation Spectroscopy (FCS), Nuclear Magnetic Resonance (NMR), Circular Dichroism (CD), and Isothermal Titration Calorimetry (ITC), to analyze biological macromolecules and their complexes in solution. Those interested in obtaining atomic resolution structures employ single-crystal X-ray diffraction and cryo-electron microscopy (Cryo-EM) techniques. In bioinformatics, our research encompasses genome sequencing, genome analysis, and multi-omics data analysis to identify new molecules that could serve as disease markers or contribute to drug development.



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.

Site specific labelling of NusG: Initially, we prepared constructs for expressing a single cysteine mutant of NusG for site specific fluorescent probe labelling, purified the modified NusG protein (NusG-156C), labelled it with Cy3B or Alexa647 to obtain NusG-Cy3B or NusG-A647, and performed biophysical measurements to establish both labelled NusG derivatives could bind to RNA polymerase (RNAP) core enzyme, 30S, 50S and 70S subunits of the ribosome. Further we performed a luciferase activity assay to confirm these NusG derivatives were functional in a coupled transcription-translation reaction in-vitro.

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) 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. Our results indicate that although NusG does not influence the kinetics of transcription initiation, it actively displaces s^{70} from early transcription elongation complexes – a phenomenon likely to have massive consequences in bacterial gene expression as this directly influences s^{70} dependent pausing throughout the gene.

Lifetime of NusG bound to a TEC *in-vitro*: To investigate the lifetime of a bound NusG to a TEC we performed single molecule measurements on a TIRF microscope. We could detect transient binding events and estimate the on- and off-rates of NusG binding (Fig. 3) in absence and presence of a ribosome. The presence of a ribosome in our assays led to an increase in the bound lifetime

of NusG (~0.7 s) compared to that in absence of a ribosome (~0.4 s) – indicating additional favourable contacts being made by NusG to a TEC in presence of a ribosome. More interestingly both lifetimes were relatively short, considering in 1 second the RNAP transcribes ~40 nt on an average.

Lifetime of NusG bound to a TEC *in-vivo*: To assess the TEC bound lifetimes of NusG in-vivo we optimised the following workflow: (i) We developed an optimised protocol for internalisation of fluorescent probe labelled proteins in live E. Coli and delivered few copies of NusG-Cy3B into E. Coli cells; (ii) We performed single particle tracking experiments under HILO illumination on a widefield microscope using cells containing NusG-Cy3B molecules; (iii) Developed an analysis pipeline and used it to track and separate TEC bound molecules, and from these tracks extracted the TEC bound lifetimes. Results of our experiments show the presence of two TEC bound states with lifetimes of ~0.6 s and ~1.4 s. Again, these lifetimes are comparable to ones obtained from in-vitro experiments and were short compared to the time taken for transcribing the average gene.

Single molecule FRET experiments studying NusG conformational dynamics: We have purified a double Cysteine labelled NusG derivative (Cysteines at positions 104 and 156) and labelled it with Cy3B and Alexa 647 maleimide to prepare the NusG FRET construct, DL-NusG. In a first experiment we immobilised DL-NusG to glass slides and imaged them on a TIRF microscope. Results show FRET efficiency vs time-trajectories characteristic of three subpopulations: a low FRET, a middle FRET, and a high FRET species with transitions between these states indicating NusG in solution can undergo rapid conformational fluctuations.

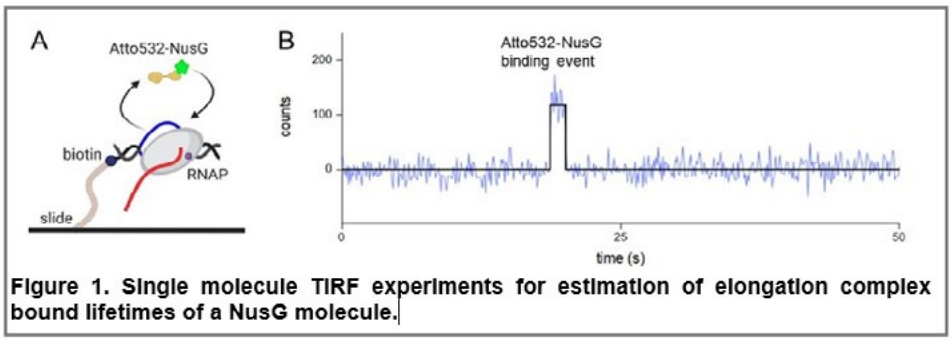


Figure 1. Single molecule TIRF experiments for estimation of elongation complex bound lifetimes of a NusG molecule.

Figure 1: Single molecule TIRF experiments for estimation of elongation complex bound lifetimes of a NusG molecule.

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.

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.

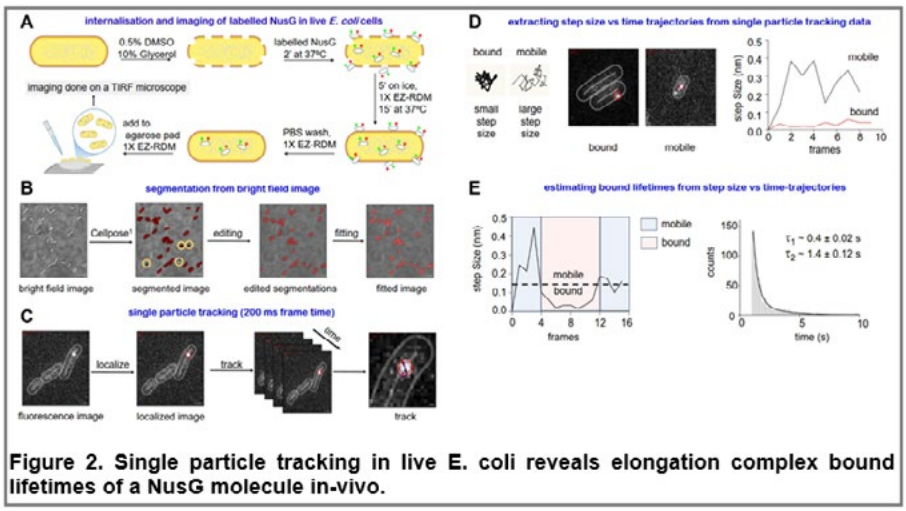


Figure 2. Single particle tracking in live E. coli reveals elongation complex bound lifetimes of a NusG molecule in-vivo.

Figure 2: Single particle tracking in live E. coli reveals elongation complex bound lifetimes of a NusG molecule in-vivo.
Schematic description of an optimised protocol developed for developing fluorescent probe labelled proteins in live E. Coli.
Workflow describing segmentation of E. Coli cells from image obtained on a widefield microscope using brightfield illumination.
Localisation and tracking of spots obtained from movies recorded using highly inclined and laminated optical sheet illumination using a 532 nm laser on a widefield microscope.
Classification of genomic DNA bound and mobile molecules from single particle tracks using step size. E. Extraction and estimation of bound lifetimes from step-size vs time trajectories.

Future Research Plans

From April 2025 onward, this project will investigate the interaction of NusG with in-vitro reconstituted transcription-elongation complexes (TECs) and transcription-translation complexes (TTCs) using single-molecule TIRF microscopy to measure binding kinetics and elucidate its role in transcription elongation and coupling. A double fluorescent probe-labeled RfaH derivative (DL-RfaH) will be prepared for FRET experiments, followed by smFRET studies with labeled NusG and RfaH to analyze conformational dynamics within active TTCs. A pipeline for single-particle tracking FRET (spt-FRET) in live *E. coli* will be developed, enabling live-cell tracking of NusG and RfaH using optimized electroporation and smFRET to study transcription-translation coupling in bacteria. Both in-vitro and in vivo experiments will continue, alongside method refinement, data analysis, and manuscript preparation, with a final emphasis on publishing all remaining results by December 2027.

Extramural / CSIR Funding

Single molecule studies of transcription-translation coupling in bacteria. DBT/Wellcome Trust India Alliance 2023-2027, INR 3.58 crores (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

1. Optic Within Life Sciences (OWLS-17), IIT-Bombay, Mumbai, Nov 18-21, 2024.
2. Transcription Assembly meeting, Bose Institute, Kolkata, Mar 19-21, 2025.

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

Interplay Between Glycosphingolipid Accumulation and Protein Aggregation in the Pathogenesis of Lysosomal Storage-Linked Neurodegeneration

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 one year, we are working on the structural investigation of sphingolipid accumulation association with Globoid cell leukodystrophy (GLD), or Krabbe disease, is a rare autosomal recessive lysosomal storage disorder caused by loss-of-function mutations in the galactosylceramidase (GALC) gene. Deficiency of GALC leads to the lysosomal accumulation of galactosylceramide (GalCer) and galactosylsphingosine (GalSph, psychosine), neurotoxic sphingolipids that severely impair oligodendrocyte and Schwann cell function, culminating in widespread demyelination and rapid neurodegeneration. The classical infantile form manifests within the first six months of life and is typically fatal by two years of age.

In this study, GalCer and GalSph were discovered to self-assemble into supramolecular fibrillar structures resembling proteinaceous amyloids, as demonstrated using biophysical and spectroscopic analyses including amyloid-specific dye binding, fluorescence microscopy, FTIR, XRD, and small-angle X-ray scattering (SAXS). Under TEM, these lipid exhibited fibrillary structure with distinct features, GalCer fibrils displayed twisted filament whereas the GalSph fibrils showed straight filament (Figure 1). The distinct fibrillary morphologies of the two lipids may lie in their chemical structure, GalCer contains a double chained lipidic unit with an unsaturation which possibly the reason of its twisted fibrillary morphology. In case of GalSph, there is a single chained lipid moiety help it to form straight-fibrillar structure.

These lipid-derived fibrils displayed marked cytotoxicity toward neuronal (SH-SY5Y) and oligodendroglial cell lines. Furthermore, GALC inhibition in cultured cells recapitulated the intracellular accumulation of these fibrils, supporting their pathological relevance

to GLD. Importantly, small-molecule amyloid inhibitors effectively disrupted the in vitro formation of GalCer and GalSph fibrils and significantly reduced their associated cytotoxicity in neuronal cells. Collectively, these findings uncover a previously unrecognized lipid amyloid-like aggregation mechanism contributing to GLD pathogenesis and highlight GalCer and GalSph fibrillization as a novel biophysical basis for lysosomal dysfunction and neurotoxicity. The study further suggests that anti-amyloid small molecules may represent a promising therapeutic strategy for this devastating orphan neurodegenerative disorder.

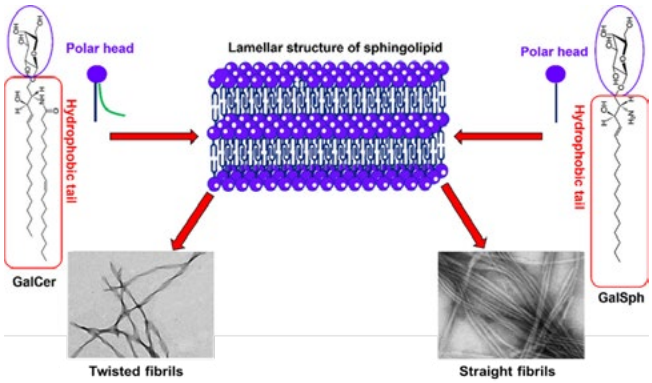


Figure 1: A schematic diagram representing a possible mechanism of GalCer/GalSph fibril formation.

In addition, we are working on identifying different putative sites of PTMs available on tau proteins and designed short tau derived model peptides to understand the role of site specific PTMs on tau aggregation and its toxicity 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 few peptide-based inhibitors that effectively binds with those domains and plausibly inhibit the amyloid formation and slow down the disease progression. Our designed peptide molecules are mainly of two types, one type is linear peptides, comprise of either coded or non-coded amino acids with a beta-breaker unit to inhibit protein aggregation. Another type is cyclic peptides, which presumably have higher proteolytic stability than their linear variants and may show high efficiency to inhibit the aggregation of amyloidogenic proteins.

So far, we have synthesized tau derived peptides and its phosphorylated analogs. We are standardizing the condition for the peptides aggregation using Thioflavin T assay and CD spectroscopy. Once, conditions are optimized, we will perform a series of biophysical assay including ThT, Turbidity assay, TEM, FTIR, and cell-based assays including MTT, LDH leakage assay, apoptosis assay to understand the impact of PTM on aggregation and toxicity.

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) accumulates in lysosome and are associated with lysosomal storage disorders. In addition, to investigate how those lipid accumulates 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 small molecule-, and peptide-based therapeutic molecules to target protein aggregation associated with neurodegenerative diseases.

Extramural / CSIR Funding:

Received Rs. 15L for consumables and Rs. 5L for non-consumables, from CSIR-IICB (under OLP project).

Publication

Kumar, S., Nikelshparg, E., Pilátová, J., Paul, A., Kumar, V., Koren, G., Beck, R., Jensen, H. H., and Segal, D. (2025) Sphingolipids Accumulated in Globoid Cell Leukodystrophy Self-assemble in vitro into Cytotoxic Fibrils that can be Mitigated by Small Molecule Inhibitors. ACS Nano (under revision)

Member of Society

Lifetime Member of Chemical Biology Society (India) (2024-onwards).

Dr. Ashim Paul, Senior Scientist

Group Members: Sangramjit Biswas, UGC-JRF; Md. Aminur Islam, CSIR-JRF; Rima Mondal, CSIR-JRF

Collaborators: Dr. Subhas C. Biswas, Chief Scientist, CSIR-IICB, Kolkata; Dr. Saikat Majumder, Senior Scientist, CSIR-IICB, Kolkata; Dr. Shilpak Chatterjee, Principal Scientist, CSIR-IICB, Kolkata; Prof. Daniel Segal, Emeritus Professor, Tel-Aviv University, Israel; Prof. Mattan Hurevich, Hebrew University of Jerusalem, Israel.

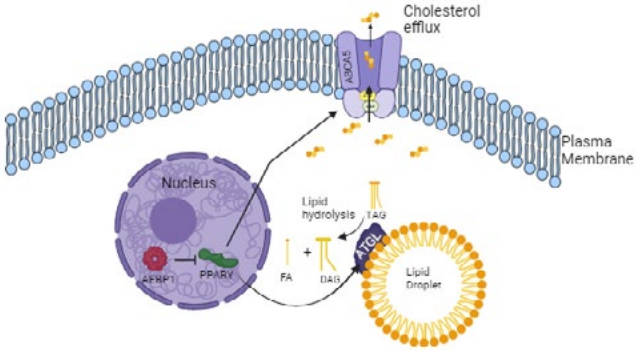
Dr. Dhabaleswar Patra and his group members

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

Background

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.



Deciphering Cardivascular & Neuro diseases: The interplay of ABCA5, AEBP1 & ATGL in maintaing lipid homeostasis.

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, PNPLA7, 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.

Expression and purification of different domains of PNPLA7.

Research activities

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 (Figure3A, 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(Figure.4).

Purification and Expression of ATGL:DNA was purified and transformed in various bacterial strains and induced with 0.2mM of IPTG for protein expression. To confirm the expression western blot was performed using specific antibody (Figure 5a). Being a lipid interacting protein, purifying ATGL is a tedious task especially solubilizing it. Thus, various soluble tags like Glutathione-S-Transferase (GST) and Small Ubiquitin-related Modifier (SUMO) tags were used targeting the protein to get in soluble fraction. Finally, the SUMO tag was successfully used to purify the protein (Figure 5b).

We have cloned, overexpressed and purified CGI-58, the activator of PNPLA2 (Figure.6). Negative staining TEM has been done for preliminary structural characterization (Figure.7)

We have successfully cloned, overexpressed and purified the Nucleotide binding domain 1 (NBD1) of PNPLA7 (Figure.8).

Future Research Plans

- Structural and Functional analysis of ABCA5, ATGL and PNPLA7.
- Testing and identifying small molecule interventions against these proteins.
- As a long-term plan, structural analysis of all the members of PNPLAs.

Extramural Funds

ANRF-IRG and Deep Ocean Mission Discovery and development of novel drugs and pharmaceuticals.

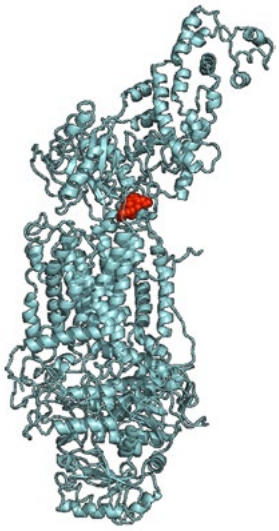


Figure.1A: Docking of ABCA5 with Cholesterol

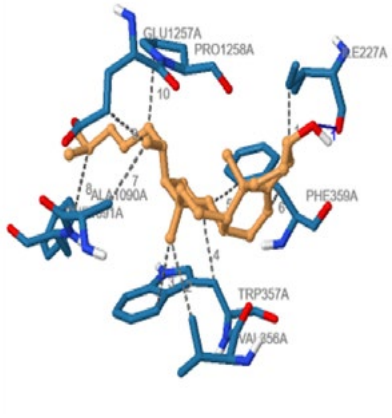


Figure.1B: Interacting residues of ABCA5 with Cholesterol

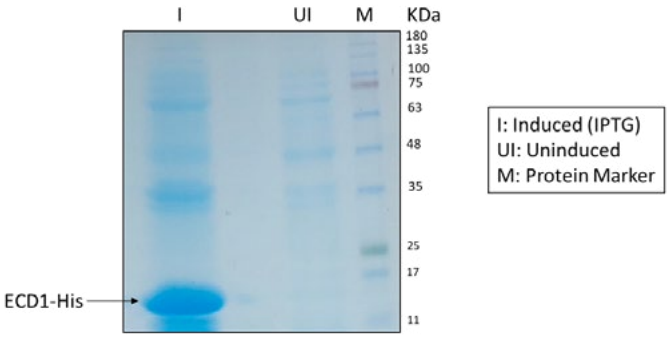
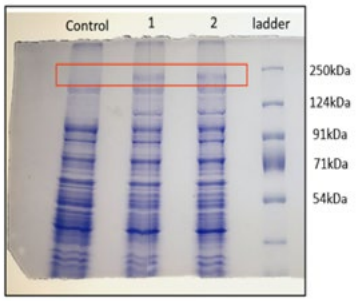


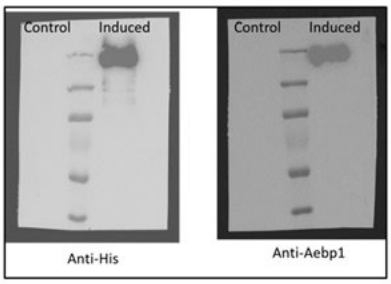
Fig: Expression of Extracellular Domain 1 (ECD1) of ABCA5 (pET28a)

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



Coomassie stained gel showing the expression of Full length Aebp1

Figure 3A: Expression of AEBP1 full length



Western blot showing the expression of Full length Aebp1

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

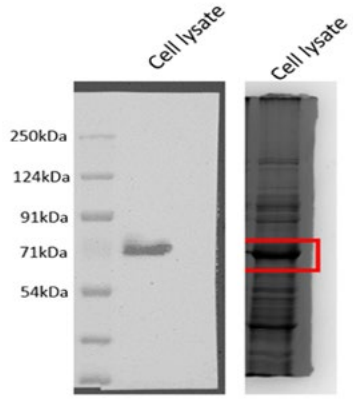


Figure 3C: Expression of AEBP1 structured region

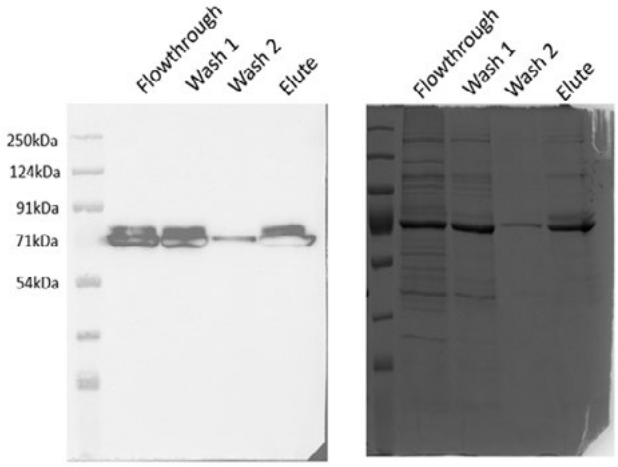


Figure.3D: Purification of AEBP1 structured region

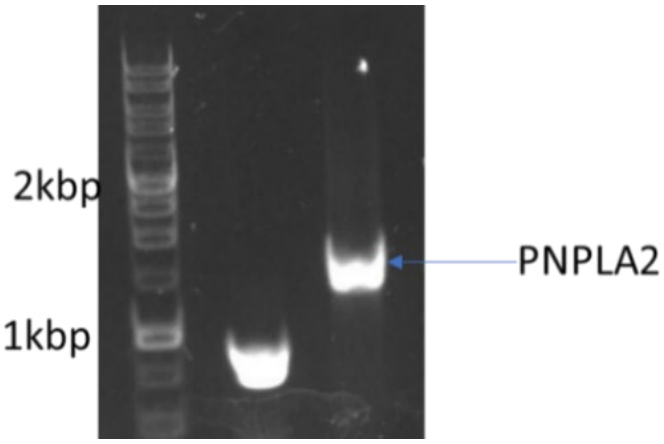


Figure.4: Cloning of PNPLA2

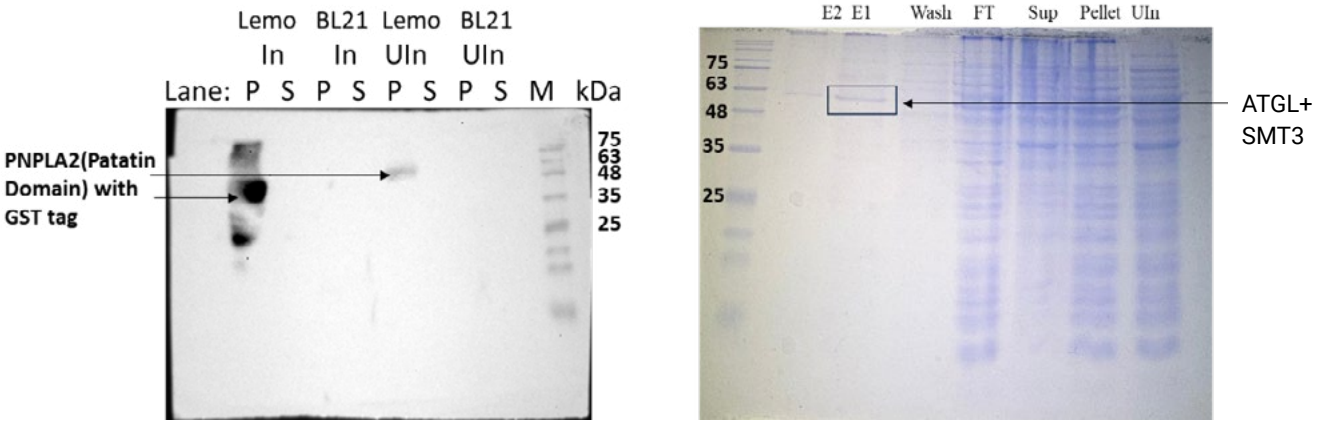


Figure.5(a): Western Blot of PNPLA2 using specific antibody (b) Purification of patatin-like domain with SMT3 tag using affinity chromatography

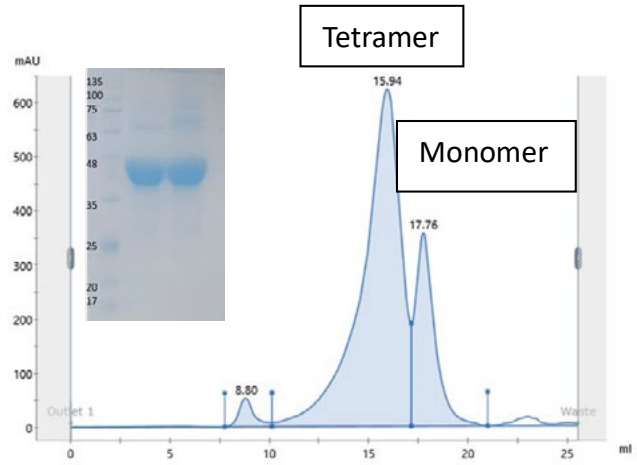


Figure.6: Size exclusion chromatogram of CGI-58 using Hiload Superose 6 Increase 10/300 column.

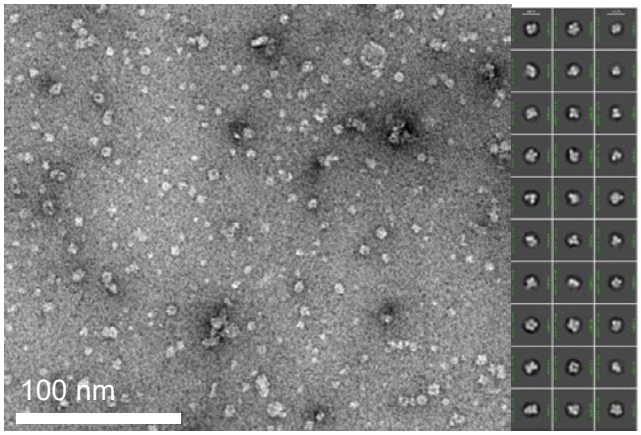


Figure.7: Negative staining TEM and 2D class average of purified CGI-58.

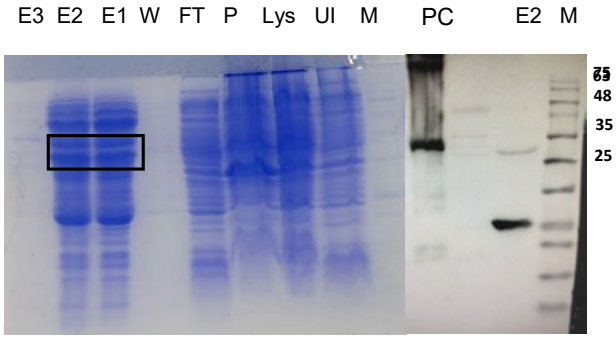


Figure.8: Purification of NBD1 of PNPLA7 in BL21 DE3 pLysS cells. Western blot using anti His antibody confirming purification of NBD1 domain.

Publications

Madasu PK, Maity A, Patra D, Chandran T. Betacoronaviral lectins: Identification through a genomic search-A structural and evolutionary biology perspective. *Journal of Carbohydrate Chemistry* 2023 Nov 30. doi: 10.1080/07328303.2023.2285970.

Dr. Dhabaleswar Patra, Senior Scientist

Group Members: Bhaskar Bhattacharya (UGC-JRF), Ela Lepcha (UGC-JRF), Soumyajit Nandy (CSIR-JRF); Teasha Biswas (DBT-JRF); Dr. Sayan Chakraborty (Project Associate)

Dr. G. Senthil Kumar and his group members

Unveiling the Oncogenic Role of UNC5D in Retinoblastoma as a Novel Therapeutic Target via PI3K/AKT Pathway Modulation

Research Activities

Retinoblastoma (Rb) is the most common pediatric intraocular malignancy, primarily caused by biallelic mutations in the ***RB1*** tumor suppressor gene. Despite significant advances in diagnosis and treatment, challenges such as tumor recurrence, metastasis, and resistance to therapy continue to limit long-term outcomes. Therefore, identifying novel molecular targets is essential to improve therapeutic strategies and patient prognosis.

Our previous observation and emerging evidence highlight the role of dependence receptors, particularly UNC5D, in cancer progression. Unlike its pro-apoptotic function in other cancers, We observed that UNC5D is significantly overexpressed in Rb cell lines (Y79 and Weri Rb1) compared to normal retinal cells (hTERT-RPE), indicating a potential context-dependent oncogenic role. Functional studies using shRNA-mediated UNC5D knockdown demonstrated reduced proliferation, migration, invasion, and colony formation in vitro, along with increased apoptosis. In vivo, xenograft models further confirmed UNC5D's tumor-promoting role, with knockdown resulting in significantly reduced tumor volume and weight.

Further, Molecular mechanistic studies revealed that UNC5D modulates the PI3K/AKT signaling pathway, a key regulator of cell survival and proliferation. Knockdown of UNC5D led to reduced levels of phosphorylated PI3K and AKT, suggesting its involvement in pathway activation. Additionally, a strong positive correlation and binding affinity between UNC5D and its ligand Netrin-1 (NTN1) were observed, indicating to a possible ligand-dependent mechanism in Rb pathogenesis. Further investigation into the UNC5D–NTN1 axis may uncover new therapeutic opportunities for targeting aggressive and treatment-resistant retinoblastoma.

Future Research Plans

Future research will focus on elucidating the role of the NTN1/UNC5D axis in modulating the PI3K/AKT pathway and apoptosis in retinoblastoma, aiming to uncover its precise molecular mechanism. Therapeutic strategies will include exploring small-molecule inhibitors or gene therapy approaches targeting UNC5D or its downstream effectors such as PI3K/AKT. To establish clinical relevance,

UNC5D expression levels will be validated in retinoblastoma patient samples to assess their prognostic value and correlation with disease progression. Additionally, combination therapy approaches will be investigated to determine whether UNC5D inhibition enhances the efficacy of existing chemotherapeutics and overcomes drug resistance. Finally, extended in vivo studies will evaluate the long-term therapeutic potential and safety of UNC5D-targeted interventions, with the ultimate goal of developing novel, effective treatment strategies for retinoblastoma.

Extramural / CSIR 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 funded by ICMR, Govt of India, 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 funded by ICMR, Govt of India, 2023 –2026, 40 Lakhs (5/4/6/30/OPH/2021-NCD-II)

Publications

1. Ahamad, K. MM., Ganguly, A., Barman, S., Das, C., Ganesan, SK. (2025) Unveiling ferroptosis genes and inhibitors in diabetic retinopathy through single-cell analysis and docking simulations. *Biochem Biophys Rep.* 41:101932
2. Mandal, T., Shukla, D., Khan, MMA., Ganesan, SK., Srivastava, AK. (2024) The EXO1/Polη/Polι axis as a promising target for miR-3163-mediated attenuation of cancer stem-like cells in non-small cell lung carcinoma. *Br J Cancer*. 131:1668-1682
3. Shukla, D., Mishra, S., Mandal, T., Charan, M., Verma, AK., Khan, MMA., Chatterjee, N., Dixit, AK., Ganesan, SK., Ganju, RK., Srivastava, AK. (2025) MicroRNA-379-5p attenuates cancer stem cells and reduces cisplatin resistance in ovarian cancer by regulating RAD18/Polη axis. *Cell Death Dis*. 16:140

Dr. G. Senthil Kumar, Senior scientist

Group Members: Nidhi Kumari, CSIR-SRF; Aditi Karmakar, UGC-SRF; Chirasmita Das, DBT-JRF; Shubhrajit Barman, DBT-JRF; 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. Amit Kumar Srivastava, Senior Scientist, Cancer Biology & Inflammatory Disorder Division, CSIR-IICB, Kolkata.

Dr. Jayati Sengupta and her group members

Cryo-electron microscopy for structural elucidations of mycobacterial ribosomal complexes to understand the functional mechanisms

Research Activities

Anti-associator role of methionine aminopeptidase type 1c on the 30S ribosomal subunit in mycobacteria

Methionine aminopeptidase (MetAP), a metalloprotease, is an essential co-translational nascent chain processing enzyme that cleaves the initiator methionine from the nascent polypeptide chains by binding near the peptide exit tunnel on the 70S ribosome. *E. coli* expresses a single subclass of type1 MetAP whereas *Mycobacterium smegmatis* (Msm) contains two subclasses i.e. MetAP1a and MetAP1c differentiated by the presence of a 40 amino acid N-terminal extension in the later. Even though both the proteins are enzymatically active with some variation in substrate preference, the exact reason for maintaining the two subclasses in mycobacteria remained elusive. To obtain a better understanding of the MetAP's interaction with the ribosomal subunits, we analysed the *in-vitro* and *in-vivo* binding of both the proteins and observed a unique 30S subunit affinity of MetAP1c. A 5Å cryo-EM map of Msm MetAP1c-30S subunit complex pinpointed the binding of MetAP1c on the inter-subunit face of the 30S subunit facilitated by the interaction of N-terminal extension with ribosomal proteins S13 and S19. Further analysis of the 16S rRNA structure revealed major alterations near the beak region and helix 44 which has the potential to make the 30S subunit unfit for association with 50S subunit. Several biochemical, N-terminal deletion and swapping assays confirmed a moonlighting anti-association property of Msm MetAP1c which is mediated by the interaction of the N-terminus with the 30S ribosomal subunit.

Future Research Plans

Our lab is among the pioneers in India to adopt 3D cryo-electron microscopy (cryo-EM) for studying biological molecules. Our research centers on the translational machinery of pathogenic bacteria, with a focus on discovering previously unknown ribosome-associated factors involved in stress-response mechanisms. Using high-resolution 3D cryo-EM, we aim to characterize these ribosome-factor interactions in detail. Ultimately, our goal is to uncover species-specific mechanisms that can serve as potential drug targets.

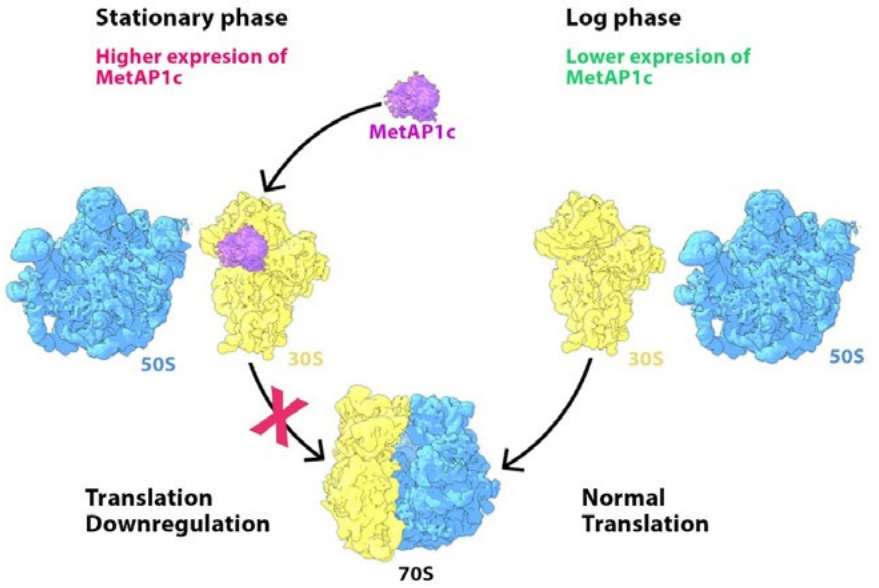


Figure 1: Schematic representation of the mechanism of MsmMetAP1c-mediated anti-association. During the stationary growth phase, the level of MsmMetAP1c is heightened, potentially leading to increased binding to the 30S subunit. However, this increased binding of MsmMetAP1c to the 30S subunit disrupts the formation of active 70S ribosomes by inhibiting its association with the 50S subunit, ultimately resulting in a reduced rate of translation. During the log phase of growth, the low level of MsmMetAP1c results in reduced binding to the 30S subunit. Consequently, this facilitates the smooth association of the 50S subunit with the 30S subunit, forming an active 70S ribosome essential for maintaining translation rates.

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

Srinivasan, K., Banerjee, A., Sengupta, J. (2024) Cryo-EM structures reveal a molecular mechanism underlying HflX-mediated erythromycin resistance in mycobacteria. *Structure* 32:1443-1453.e4

Invited Lectures

1. EMBO workshop (CEM3DIP-2024), at IISc, Bangalore
2. Invited lecture at 12th RNA Meeting, IIT, Guwahati, 2024

Dr. Jayati Sengupta, Chief Scientist

Group Members: Ankit Dhur, UGC-SRF; Aneek Banerjee, DBT-SRF; Krishnamoorthi Srinivasan, CSIR-SRF; Priya Baid, CSIR-SRF

Dr. Krishnananda Chattopadhyay and his group members

Using 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

Summary of progress made in last one year

Developing small-molecule modulators of Alpha-synuclein phase separation (with Biswadip Banerji)

The phenomenon of liquid–liquid phase separation (LLPS) involving biological polymers such as proteins and nucleic acids has gained significant importance in the formation of membraneless organelles. By concentrating biomolecules (proteins and nucleic acids) at particular cellular locations to perform diverse intracellular functions, these liquid condensates play a critical role. The phase separation and droplet formation of alpha synuclein (aSyn) have been suggested to play a crucial role in the pathology of Parkinson's Disease (PD). As a part of this work package, we synthesised a series of novel zwitterionic compounds, which modulated alpha synuclein phase separation and subsequent formation of fibrillary aggregates in a concentration dependent manner. A binding vs phase separation hypothesis has been developed understand the data using a series of molecules of varying hydrophobicity.

Investigating the Stability, Flexibility, and Phase Separation Properties of H46R and H80R Disease Mutants of SOD1: Insights into ALS Pathogenesis

Human Cu, Zn superoxide dismutase (SOD1) is the primary enzyme in the cellular antioxidant defense system. Mutations in SOD1 are associated with amyotrophic lateral sclerosis (ALS), where protein misfolding and aggregation contribute to the disease pathology. Recently, SOD1 mutants have been shown to undergo phase separation, forming protein-rich droplets that can serve as precursors to the fibrillar aggregates, the pathological hallmarks of ALS. In this study, we investigated two ALS-associated SOD1 mutants, H46R and H80R, and compared them to the wild-type (WT) and Apo forms to elucidate the relationship between phase separation and SOD1's biophysical properties. Using a battery of computational studies, chemical denaturation, and in vitro condensate formation assays, we explored how these mutants influence protein phase separation propensity. Our findings demonstrate that altered secondary structures, stability, and inherent disorder in these mutants directly impact their phase separation behaviors. This study provides new insights into the role of phase separation in ALS pathogenesis and its potential as a therapeutic target.

Crowder induced conformational fluctuations modulate the phase separation

This study investigates how molecular crowding, specifically the size and shape of crowders like Dextran and Ficoll, modulates the conformational states and phase separation behavior of Sup35NM. Using fluorescence correlation spectroscopy and molecular dynamics simulations, we observed that Dextran, depending on its molecular weight, induces both compaction and expansion of IDPs, driving phase separation at certain thresholds. Notably, rod-like Dextran crowders promote phase separation, while spherical Ficoll does not, highlighting the impact of crowder geometry on IDP behavior. Computational modelling further revealed that the crowder shape influences conformational ensemble by modulating intra- and inter-domain interactions. These findings elucidate the role of crowding agents in IDP phase behavior, suggesting that cellular crowding may regulate IDP functionality through conformational control.

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 cellular environment. In addition, we have been planning to use patient samples

Extramural / CSIR Funding

1. Developing KMP-11 as a possible target to block host invasion by leishmania donovani; ICMR, 2023-26, 54.2 lakhs, (6/9-7(295)/2022-ECD-II).
2. Mutation-aggregation profiling of ALS patients of West Bengal; WBDSTBT, 2023-26 65.8 lakhs, (STBT-11012(99)/12/2023-ST SEC).

Publications

1. Bera, B., Jana, P., Mandal, S., Kundu, S., Das, A., Chattopadhyay, K., Mondal, TK. (2024) Fabrication of thiosemicarbazone-based Pd(ii) complexes: structural elucidations, catalytic activity towards Suzuki–Miyaura coupling reaction and antitumor activity against TNBC cells; *Dalton Transaction.* 53, 11914-11927
2. Sannigrahi, A., Ghosh, S., Pradhan, S., Jana, P., Jawed, JJ., Majumdar, S., Roy, S., Karmakar, S., Mukherjee, B., Chattopadhyay, K. (2024) Leishmania protein KMP-11 modulates cholesterol transport and membrane fluidity to facilitate host cell invasion; *EMBO Reports.* 25, 5561-5598
3. Mishra, S., Sannigrahi, A., Ruidas, S., Chatterjee, S., Roy, K., Misra, D., Maity, BK., Paul, R., Ghosh, CK., Saha, KD., Bhaumik, A., Chattopadhyay, K. (2024) Conformational switch of a peptide provides a novel strategy to design peptide loaded porous organic polymer for Pyroptosis pathway mediated cancer therapy. *Small*. 20, 2402953-70
4. Roy, R., Sanyal, D., Roychowdhury, S., Chattopadhyay, K. (2024) Studies of Protein Phase Separation Using Leishmania Kinetoplastid Membrane Protein-11; *J Phys Chem B.* 129, 114-124
5. Das, S., Jain, R., Banerjee, KK., Chattopadhyay, K., Karmakar, S. (2024) Cholesterol-driven modulation of membrane-membrane interactions by an antimicrobial peptide, NK-2, in phospholipid vesicles; *Biochemical and Biophysical Research Communications*. 741, 151021-25
6. Chatterjee, S., Mohanta, A., De, A., Mukherjee, A., Hazra, A., Chattopadhyay, K., Samanta, A. (2024) Evaluation of gum odina/carbopol composite mucoadhesive hydrogel on pharmaceutical performance: *Focusing on potential periodontal treatment*. 288, 138708
7. Kaur, J., Jain, R., Roychowdhury, S., Roy, R., Chattopadhyay, K., Roy, I. (2025) Influence of Magnesium Ions and Crowding Agents on Structure and Stability of RNA Aptamers; *Biochemistry*. 64, 1233-1243
8. Mandal, S., Jana, P., Naskar, R., Halder, A., Bera, B., Chattopadhyay, K., Mondal, TK. (2025) An Investigation into Substitution-Kinetics, Biomolecular Responses and Multimodal Anticancer Potential of a Dihalide Pd (II) Complex; *Chemistry–An Asian Journal*. 20, e202401832-46

Book Chapters

Bidisha Das, Joy Chakraborty, Krishnananda Chattopadhyay (2025) Emerging Techniques in Cellular and Biomolecular Research; (Springer Nature Singapore); Biochemical and Biophysical Methods in Molecular and Cellular Biology; pages 1-28

Invited Lectures

1. Conformational fluctuations of proteins: from test tubes to neurodegenerative diseases. IIT-Bombay; FCS XV and OWLS 17; Nov 16-18, 2024
2. Protein conformation, dynamics and aggregation: from test tubes to human diseases, Saha Institute of Nuclear Physics; Kolkata Biophysics Meet; Apr 02, 2024
3. Conformation fluctuations of proteins: Biophysics to the disease biology of neuro-degeneration; Utkal University; Emerging Trends and Prospects in Biotechnology; Sep 27-28, 2024
4. Conformational Fluctuations of Proteins: from the test tubes to neuro-degenerative diseases; Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, New Delhi; Drug Discovery 2025: Emerging Trends and Future Prospects; Feb 24-26, 2024
5. Invited Speaker, CSIR-Foundation Day, CSIR-Imtech, Oct 28, 2024

Conferences Attended

1. Conformational fluctuations of proteins: from test tubes to neurodegenerative diseases. IIT-Bombay; FCS XV and OWLS 17; Nov 16-18, 2024
2. Protein conformation, dynamics and aggregation: from test tubes to human diseases, Saha Institute of Nuclear Physics; Kolkata Biophysics Meet; Apr 02, 2024
3. Conformation fluctuations of proteins: Biophysics to the disease biology of neuro-degeneration; Utkal University; Emerging Trends and Prospects in Biotechnology; Sep 27-28, 2024

Member of Society

1. Fellow of National Academy of Sciences, India (NASI)
2. Fellow of Indian Academy of Sciences (IASc)
3. Fellow of West Bengal Academy of Science and Technology
4. Member of American Chemical Society (award)
5. Fellow of Royal Society of Chemistry
6. Member of Indian Biophysical Society
7. Member of Indian Society of Chemical Biology
8. Member of Indian Photobiology Society
9. Member of Indian Fluorescence Society
10. Member of International Parkinson's and Movement Disorder Society

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Dr. Krishnananda Chattopadhyay, Chief Scientist

Group Members: Ayantika Sarkar, JRF; Sampa Mondal, JRF; Pratip Mukherjee, SRF; Ahana Banerjee, SRF; Rajdip Roy, SRF; Souradip Paul, SRF; Rajeev Jain, SRF; Pulak Jana, SRF; Tathagata Acharya, Project Student; Ashmita Mukherjee, Project Student

Collaborators: Professor Jeetain Mittal, Texas A & M University College of Engineering, USA; Professor Budhaditya Mukherjee, IIT-Kharagpur, India; Professor Sanat Karmakar, Department of Physics, Jadavpur University, India; Profesor Timir Tripathy, North Eastern Hill University, India

Dr. Nakul Chandra Maiti and his group members

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

Research Activities

Protein misfolding of intrinsically disordered proteins (IDPs) or structured proteins—often initiates amyloid fibril formation. This process is a hallmark of several conformation-related human diseases, such as Alzheimer's, Parkinsons and other major neurological disorders. Among the IDPs, amyloid beta (Aβ) and α-synuclein are central to these neurodegenerative disorders. In parallel, the structural dynamics of functional enzymes such as insulin and viral proteases which are implicated in human pathologies also demand intensive research. To investigate these complex protein systems, biophysical techniques such as biological Raman spectroscopy, fluorescence spectroscopy, and molecular dynamics (MD) simulations are proving invaluable. These methods allow for detailed examination of protein aggregation, phase transitions in protein solutions, and the intricate structure-function relationships of key biomolecules. Raman spectroscopy was discovered nearly a century ago at the Indian Association for the Cultivation of Science, however, after about a century gap, my laboratory made an indigenous biological Raman spectroscopy facility at CSIR-IICB. Our goal is to harness this tool, alongside complementary methods, to deepen our understanding of protein structure and function, with a primary focus on understanding the mechanisms of neurodegenerative diseases.

A major focus of the laboratory is the use of Raman spectroscopy to develop a novel quantitative method for characterizing the conformational states of amyloid proteins and aggregates. These are critically implicated in the pathogenesis of neurodegenerative diseases such as Parkinson's, Alzheimer's, and related disorders. This approach can differentiate of structurally distinct oligomeric entities, providing new insights into their roles in disease progression. This advancement holds great promise for the development of early diagnostic tools. In parallel, my group has explored nanotechnology-based interventions to combat amyloid-related pathologies. He developed nanoparticles capable of inhibiting the formation of toxic amyloid aggregates. This promising strategy paves the way for nanoparticle-based therapeutics in treating amyloid-associated neurodegenerative disorder, a field of growing clinical importance. Additionally, we have invented a new class of fluorescent silver nanodots that demonstrate remarkable optical properties. These nanodots exhibit tunable fluorescence, high stability, and excellent biocompatibility, making them ideal candidates for a wide range of applications, including bioimaging, sensing, and nano-electronics.

The role of protein oligomers in the associated disease states, we are now studying different types of protein oligomers under Raman microscope. In addition, we are actively involved in developing methods that could aid in the structural detection of proteins linked to dieses by Raman spectroscopy. Small molecule binding plays a key role in conformational stability and thus modulating the underlying molecular mechanics that govern the protein misfolding and aggregation. Our current investigation established that coomassie brilliant blue G-250 (CBBG) binding impaired the in-situ fibrillation of the hormonal insulin. (ii) I extended my work to investigates the inhibition of amyloid

formation using nanoparticles. (III) Further investigation was on phase separation of proteins. Phase-separated protein accumulation through the formation of several aggregate species and they are linked to the pathology of several human diseases. We detailed Raman signature and structural intricacy of bovine insulin in its various forms of aggregates produced in situ at an elevated temperature (60 °C). The amide I band in the Raman spectrum of the protein in its native-like conformation indicated the presence of a high content of α-helical structure as prepared freshly in acidic pH. The disorder content also was predominately present in both the monomeric and oligomeric states and was confirmed by the presence houlder amide I maker band at ~1680 cm^{-1}. The protein, however, maintained most of its helical conformation in the oligomeric phase. Tyrosine phenoxy moieties in the protein entered in more hydrophobic environment in its journey of fibril formation. It was also noticed that oligomeric bovine insulin maintained the conformation of the disulfide bonds. In the fibrillar state, the disulfide linkages became more strained and preferred to maintain a single conformation state. (IV) Furthermore, we have invented a new class of fluorescent silver nanodots, which exhibit exceptional optical properties and hold vast potential in the fields of bioimaging, sensing, and nano-electronics. Their tunable fluorescence, stability, and biocompatibility make them excellent candidates for next-generation applications in nanotechnology, including targeted drug delivery, diagnostic imaging, and the development of nano-scale electronic devices.

Future Research Plans

This research have the potential to guide the development of targeted therapeutic strategies and early diagnostic tools, making this contribution highly significant to both basic science and public health. In parallel, my group has explored innovative approaches to inhibit amyloid formation using engineered nanoparticles. These nanomaterials not only prevent the formation of toxic aggregates but can also reverse existing fibril structures under certain conditions. This line of investigation opens up promising avenues for the development of nanoparticle-based therapeutics for amyloid-related diseases, a field with growing clinical relevance. Focus is now to develop better Raman substrate to increase the Raman signal by making nano platform. My vision is to expand these research directions through integrated, translational efforts that bridge fundamental science with real-world applications for healthcare and advanced materials.

Publications

1. Dolui, S., Roy, R., Paul, U., Kundu, S., Pandit, E., Ratha, B.N., Pariary, R., Saha, A., Bhunia, A., Maiti, NC. (2024) Raman Spectroscopic Insights of Phase Separated Insulin Aggregates. *ACS Physical Chemistry Au*. 4, 268–280 (cover page article)
2. Saha, D., Pramanik, A., Freville, A., Siddiqui, A. Z., Uttam, P., Banerjee, C., Nag, S., Debsharma, S., Pramanik, S., Mazumder, S., Maiti, NC., Datta, S., Christiaan, VO., Bandyopadhyay, B. (2024) Structure–function analysis of nucleotide housekeeping protein HAM1 from human malaria parasite Plasmodium falciparum. *The FEBS J.* 291, 4349-4371

Conferences Attended

1. Invited Speaker, on the Raman Spectroscopy in Medicine and Biology, inter-college quiz competition, organized by R. K. Mission Residential College Narendrapur, Kol-103, W.B. India. April 29, 2024.
2. Invited as a resource person in two-day workshop on Raman Spectroscopy from August 26 – 27, 2024, organized by Goa University funded from Department of Science and Technology (DST), Government of India.
3. Invited Speaker in Mini-Symposium on Photobiology inclusive Physics, Chemistry, Biology, Medicine, Pharmacy, Environment and Engineering & Technology, organized by Department of Chemistry, Jadavpur university, held on 3rd September 2024.
4. Invited speaker on 38th annual meeting of society for neurochemistry (INDIA) and international conference on innovations and future perspectives in neurochemistry, September 2024, organized by department of biochemistry, Panjab University, Chandigarh (INDIA).
5. Attened 16th Annual Meeting of Proteomics Society, India, from November 21-23, 2024, and International Conference titled “Integrated Omics Approaches for Decoding Biological Research”, organized by CSIR-National Chemical Laboratory (CSIR-NCL), Pune, INDIA.
6. Attend as a Chairman for a session in the 5th Flow Chemistry and Natural Products Synthesis Symposium, November 2024, organized by NIPER Kolkata at IIT Kharagpur Research Park Auditorium, AA3, Newtown, Kolkata,
7. Invited chairperson in one day international seminar on “Emerging Trends in Innovation: Towards Convergence of Theoretical Sustainability and Interdisciplinarity”, organized by “VISION”, in collaboration with Department of Chemistry, Maharaja Manindra Chandra College on January 7, 2025.

Dr. Nakul Chandra Maiti, Senior Principal Scientist

Group Members: Banadipa Nanda, SRF; Rajdip Misra, SRF; Shubham Kundu. SRF; Anupam Maity, SRF; Mrinmay Bhunia, JRF

Collaborators: Dr. Achinta Kumar Saha, Professor, University of Calcutta, Kolkata; Dr. Anirban Bhunia, Professor, Bose Institute, Kolkata; Dr. Biswadip Banerji, 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

Our research is a unique and rare amalgamation of biology, chemistry, mathematics, data science, and AI-ML based interpretations to understand the alterations of biomolecular interplays in systemic diseases like cancer and host-pathogen interactions in infectious diseases (e.g., malaria, leishmaniasis). Our group aims to identify and subsequently analyze important bio-molecular interactions involving proteins, DNA and other macro-molecules through integration of large scale “omics” data via a) developing network biology, mathematical modelling, machine learning, and graph theoretical algorithms, b) in-depth analysis of molecular interaction patterns using state-of-the-art molecular modeling, docking and dynamics strategies, and c) subsequently validating the identified biomarkers using experimental techniques.

Our group has contributed significantly in identification of novel diagnostics and prognostic markers in cancer and leishmaniasis. Our expertise in omics data interpretation, biomolecular structure analysis, macroscopic and microscopic image processing has successfully complemented research of numerous academicians and clinicians within India and abroad leading to several publications. Beyond fundamental research, our group also develops various computational tools, techniques and web servers, which are freely available to users and are extremely beneficial to the global scientific community. Notably, the development of image processing and AI-based software for analyzing brain MRI and CT scans provides early diagnostic tools for Alzheimer’s disease and hemorrhagic stroke; two significant contributions to the translational arm of biomedical science.

Through continued innovation, collaboration, and mentorship, we aim to further harness computational biology and experimental science to bridge gaps in translational biomedical research and make meaningful contributions to human health. 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.

Aims and Objectives

- Detection of Alzheimer's disease using brain magnetic resonance image (MRI) processing and machine learning techniques.
- 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.
- Development of tools and techniques for protein-ligand docking and novel machine learning-based method to evaluate protein-ligand docking results.

Work Achieved

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), eXtreme Gradient Boosting (XGBoost), K-Nearest Neighbor (KNN), and Artificial Neural Network (ANN) classifiers to predict AD or Mild Cognitive Impairment (MCI). Exhaustive benchmarking on ADNI data reveals high prediction accuracies for different AD severity levels. CCADD empowers clinicians and researchers for AD detection. This server is available at: http://www.hpppi.iicb.res.in/add. Figure 1 provides a snapshot of the CCADD web server.

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

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. Comparison analysis 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.

Future Research Plans

- 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.
- 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. Understanding the impact of ER^{UPR} on mitochondrial integrity mediated by a mitochondrial protein, PDK4.
- 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. Chaudhuri, A., Das , S., Chakrabarti, S. (2024) Mutational and evolutionary dynamics of non-structural and spike proteins from variants of concern (VOC) of SARS-CoV-2 in India. *The International Journal of Biological Macromolecules (IJBM).* 282:137154.

2. Kamal, I.M., Das, A., Datta, S., Paul, K., Chakrabarti, S., Chakrabarti, S., Bhattacharjee, P. (2024) A Novel spice-antioxidant-based nano-vehicle as a putative green alternative of synthetic AChE inhibitor drugs. *J Biomol Struct Dyn.* 42:8813-8830.
3. Lu, H., Twan, W.K., Ikawa, Y., Khare, V., Mukherjee, I., Schou, K.B., Chua, K.X., Aqasha, A., Chakrabarti, S., Hamada, H., Roy, S. (2024) Localization and function of key axonemal microtubule inner proteins and dynein docking complex members reveal extensive diversity among vertebrate motile cilia. *Development.* 151:dev202737.
4. Borar, P., Biswas, T., Chaudhuri, A., Huxford, T., Chakrabarti, S., Ghosh, G., Polley, S. (2024) Dual-specific autophosphorylation of kinase IKK2 enables phosphorylation of substrate IκBα through a phosphoenzyme intermediate. *eLife*. 13:RP98009.
5. Gayen, A., Mukherjee, A., Kumar, K., Majumder, S., Chakrabarti, S., Mukherjee, C. (2024) The mRNA-capping enzyme localizes to stress granules in the cytoplasm and maintains cap homeostasis of target mRNAs. *J Cell Sci*. 137:jcs261578.
6. Panigrahi, P., Das, S., Chakrabarti, S. (2024) CCADD: An online webserver for Alzheimer's disease detection from brain MRI. *Comput Biol Med*. 177:108622.

Patents

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, PCT (PCT/IN2024/050632) published on 12/12/2024.

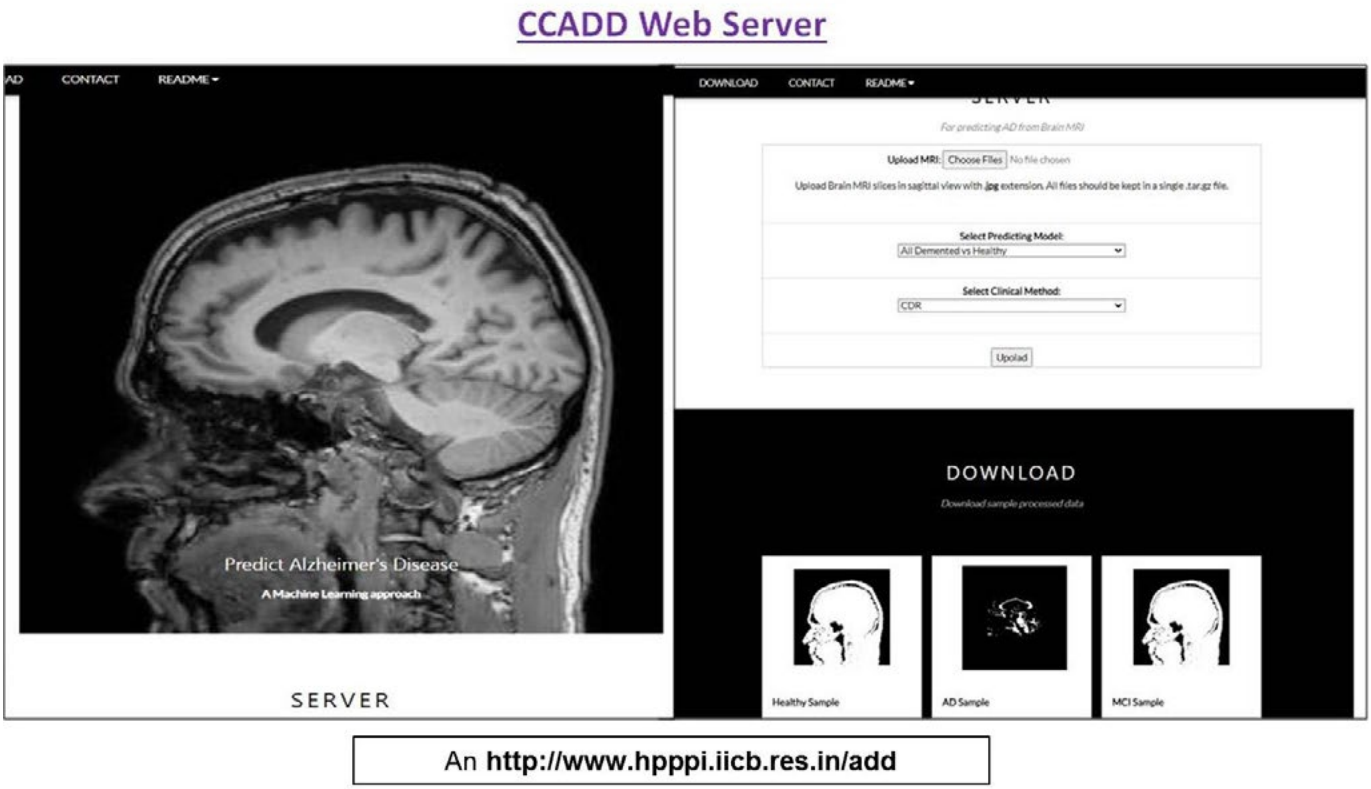


Figure 1: Snapshot of the CCADD web server. Combination of structural MRI (sMRI) and functional MRI (fMRI) derived image analysis may provide unique ability to capture the dynamic state of change in the degenerating brain. Hence, to capture the overall structural and functional anomalies of brain tissues 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 2) can aid clinical diagnostics of AD and AD like symptoms in an efficient manner. We published a Patent Cooperation Treaty (PCT) at World Intellectual Property Organization (WIPO) for developing an Alzheimer's disease (AD) detection system. This is the first ever patent and device for detection of AD from CSIR-IICB.

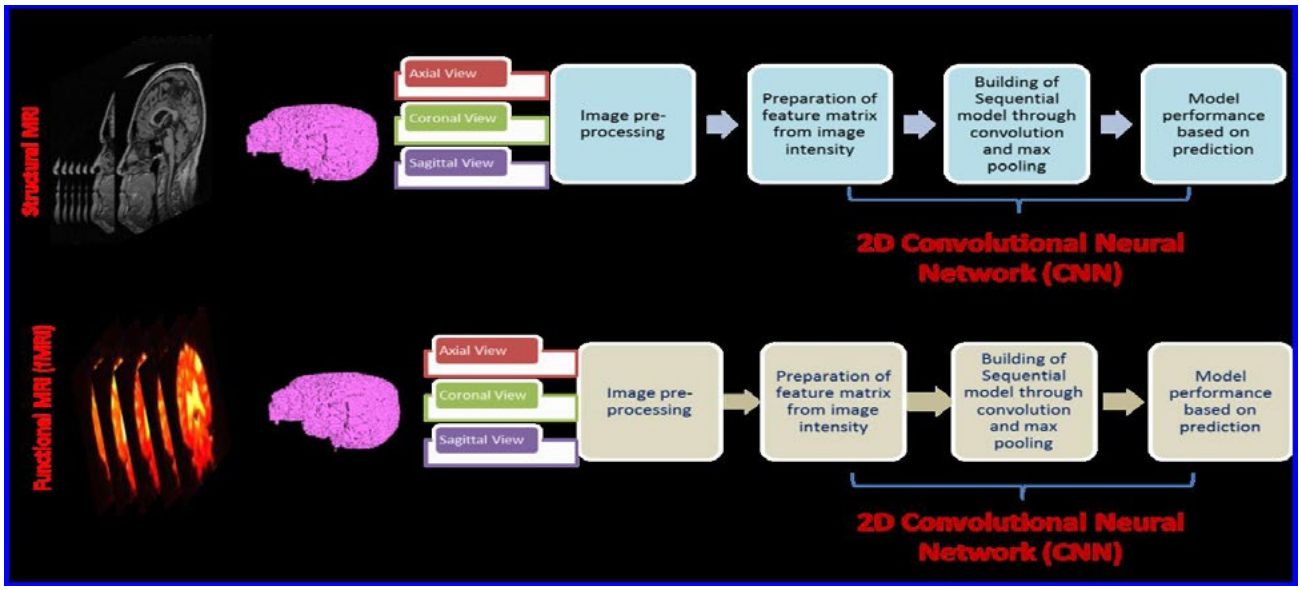
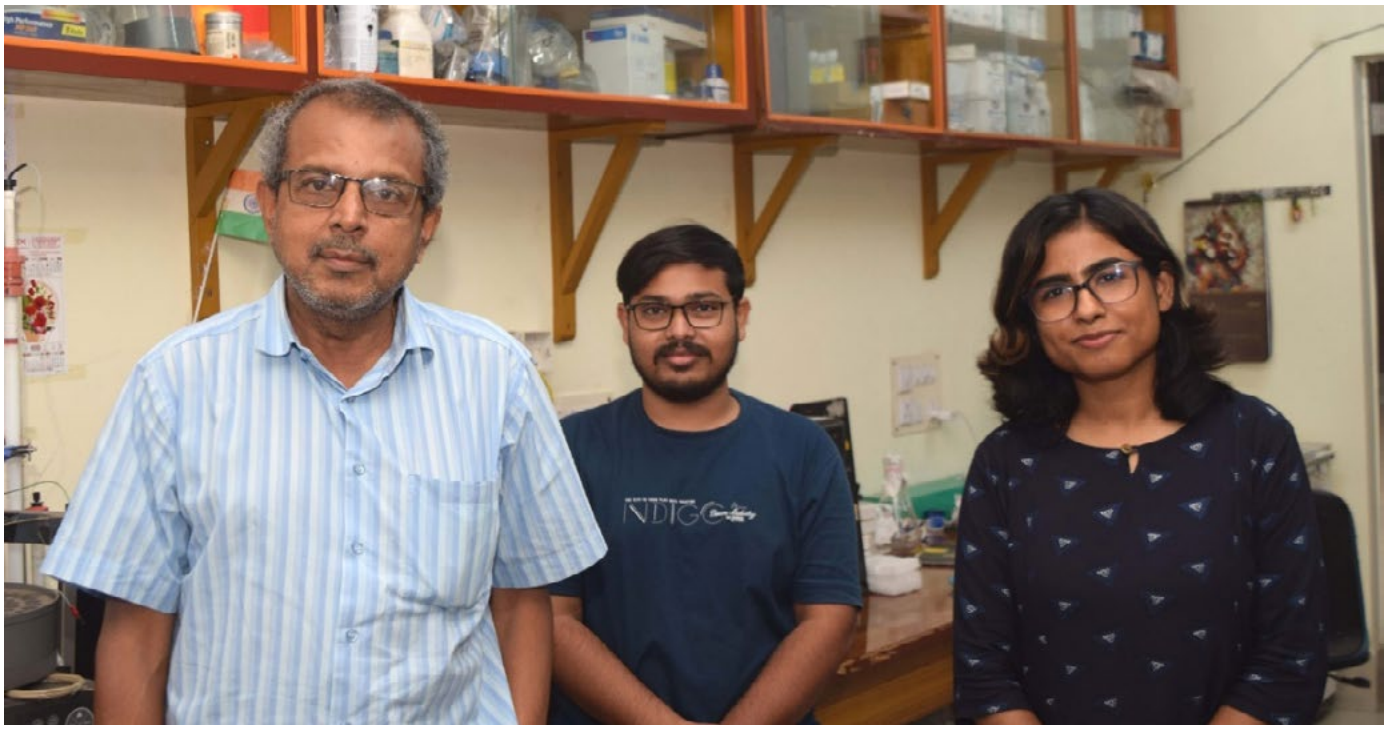


Figure 2: Overview of the protocol and the prototype of the detection system for Alzheimer's disease using brain structural and/or functional magnetic resonance image processing and machine learning techniques.

Dr. Saikat Chakrabarti, Senior Principal Scienctist

Group Members: Liana Mukherjee, JRF; Dibyendu Naskar, JRF; Raktim Chowdhury, SRF; Sangita Bose, SRF; Izaz Monir Kamal, SRF; Priyanka Panigrahi, SRF; Anindita Choudhury, SRF; Sarpita Bose, SRF; Priyanka Mallick, SRF; Subhangshu Das, Research Associate; Dr. Parna Kanodia, Research Associate; Dr. Ankur Chaudhuri, Research Associate

Collaborators: Dr. Sudipto Roy, IMCB, Singapore; Dr. Smarajit Polley, Bose Institute, Kolkata; Dr. Chandrama Mukherjee, Presidency University, Kolkata



Dr. Saumen Datta and his group members

Implication of Molecular Constraints Facilitating the Functional Evolution of *Pseudomonas aeruginosa* KPR2 into a Versatile α-Keto-Acid Reductase

Research Activities

***Pseudomonas aeruginosa*, an opportunistic pathogen found ubiquitously in nature, exhibits remarkable metabolic capacity and a wide range of attributes for environmental adaptability.**

As a significant causative agent of cystic fibrosis, *P. aeruginosa* demonstrates a preference for altered phenotypes, supported by diverse metabolic requirements, when transitioning from its natural environment to a host system. Notably, this organism boasts a large genome size, surpassing that of other prokaryotes, and showcases high genomic diversity and complexity. Long-studied genome evolution and adaptation of bacterial populations provide evidence related to the importance of their genomic diversity and dynamics. Dynamics implicates the fundamental processes by which microbes gain or lose functions that are deeply responsible for their evolution. They also contribute to the adaptability of microorganisms to various environmental niches. Through gene duplication and divergence, many enzymes have changed over time. Bacterial genes have also gone through different paths because of horizontal gene transfer (HGT) and other changes.

Aims and Objectives

Our recent research uncovered a novel aspect of the evolution of the vitamin B5 production pathway. We found that the genes responsible for this pathway are subject to dynamic evolutionary selection, leading to the acquisition of multiple copies of these genes by several bacterial species or their dependence on alternative sources of this crucial nutrient. One of the well-studied metabolic pathways is pantothenate synthesis, which we have examined in terms of its genomic, structural, and functional contexts. One of the genes involved in this pathway, panE, is reported to be duplicated in around 20% of bacterial species. The gene codes for the enzyme 2-dehydropantoate reductase or ketopantoate reductase (KPR; EC 1.1.1.169), which takes part in the second step of the pantothenate synthesis pathway. Interestingly, in the *P.aeruginosa* genome, two reported genes for this conversion step

are reported according to the KEGG database (https://www.genome.jp/entry/pae:PA1752+pae:PA4397). Functional and structural perspective studies of the first panE gene or PaKPR1 established its efficiency as a canonical KPR in the organism; however, nothing much is known about the second copy of the panE, i.e., PaKPR2. These KPRs in *P. aeruginosa* did not cluster together, so it is evident that the duplicate copies of KPRs do not follow the traditional 16 s rRNA-based phylogenetic tree. From previously reported phylogenetic analysis, it is understood that panE1 and *Azotobacter chroococcum* KPR have a greater nucleotide sequence similarity than *P. aeruginosa* KPR2 (PaKPR2). In this context, our study focused on the current status of the second copy of *P. aeruginosa* KPR in the context of its structural divergence and functional diversification. These results strongly enlighten the reasons behind the protein's newly attained functional versatility. Detailed structural evidence underscoring the protein's current functional form as a new versatile keto-acid reductase also opens up a perspective for its usage as a potent biocatalyst in green chemistry.

Work Achieved

Native Structures of KPR 2 of *P. aeruginosa* Revealed the Possible Reason Behind the Inactivity of the Protein toward the Ketopantoate.

Interestingly, the dimeric xenologous KPR of *P. aeruginosa*, denoted as PaKPR2/PanE2 in this study, is inactive as analyzed in an initial activity assay in the presence of NADPH and the substrate KPL. These observations make it a popular choice, in general, to identify this gene as a pseudoenzyme for the pantothenate pathway. Because an enzyme and pseudoenzyme pair typically have relatively little pairwise sequence similarity, despite their high structural similarity. In addition, pseudoenzymes share the same superfamily and tertiary structures as true enzymes. However, they lack catalytic residues or have steric disruption at the catalytic site entrance, rendering them catalytically inert. However, paKPR2 has conserved active site residues. We have established that from the MSA of the PaKPR2 sequence with the sequences of all the previously reported KPR structures. The KPL to pantoate conversion process is primarily facilitated by two lysine residues (*E. coli* K72 and K176) that are entirely conserved, as well as four conserved acidic residues (*E. coli* E210, E240, D248, and E256) that could serve as generic acid/base groups. To investigate the probable cause behind the inactivity in the context of structural divergence, we wanted to find the structural differences in the specific PaKPR2 protein. To shed light on the conserved and diversified facets of the protein's catalytic mechanism, the divergences in the native structural features of the protein were first identified. We crystallized it and solved the structures with two different native 3D structures (Figure 1). These structures were deposited in the PDB as 8IWG and 8IWQ (resolution: 2.15 and 2.19 A). It was noted that the secondary structure components, like helix and β sheets, are more or less similar as compared to previously reported KPR homologues in PaKPR2. However, the tertiary structure was dimeric, where C-terminal domains of two monomers joined end to end to make the dimeric interface of the protein (highlighted region in Figure 1A). As we focus on more intricate analysis for each monomeric unit, the tertiary structure seems a bit squeezed between the two well-constructed domains. Our crystal structures also observed that the solvent accessibility of the area has been changed to make the active site of the protein more confined. The characteristic hinge region is missing, too. Comparative analysis with other reported KPR structures for this hinge region is analysed. Changes in the residue interaction networks of that area converted the conserved cleft like active side, into a two-sided pocket, one for the cofactor entry and another for the substrate entry. It was found that this protein's domain movement and cleft closure are very different from other KPR native structures and which in turn lead to the inactivilty of KPR2 toward ketopantoate.

Molecular Interaction Properties of PaKPR2 with Several Ligands Suggest That Its Active Site May be Functional against Substrates Other than Ketopantoate.

A characteristic molecular cleft present in all the homologue KPRs converts to the active site of the protein in a ternary complex. However, we observed that this site is partially closed in PaKPR2, and it becomes a two-way pocket. In our next step of analysis, we consider doing interaction analysis with a few α-keto-acid substrates and cofactors in ITC to check whether, with altered conformation, the protein is still capable of accepting those closely related molecules. For cofactor interaction, we decided to go with NADPH, NADH, and coenzymeA because previously these cofactors have been reported to bind with other homologue KPRs in different organisms. In addition to that, we selected our α-keto-acid substrates to be structurally close to KPL, having a keto group at the C2 carbon (α position) and an extended aliphatic or aromatic chain. Substrates tested in ITC analysis are KPL, 3-methyl-2-ketopentanoate/KIL, α-keto-isocaproate (KIC), KCA, phenylglyoxylate (PGA), 2-furylglyoxylic acid (FGA), 2-thiopheneglyoxylic acid (TGA), indole glyoxylate (IGA), and indole pyruvate (IPA). All these molecules, except FGA, TGA can be found in different biological metabolic systems or pathways. Substrates tested in ITC analysis are KPL, 3-methyl-2-ketopentanoate/KIL, α-keto isocaproate (KIC), KCA, phenylglyoxylate (PGA), 2-furylglyoxylic acid (FGA), 2-thiopheneglyoxylic acid (TGA), indole glyoxylate (IGA), and indole pyruvate (IPA). All these molecules, except FGA, TGA can be found in different biological metabolic systems or pathways.

An interesting finding with ITC is that, despite being unable to bind its canonical substrate, KPL, the protein finds it suitable to bind a few other substrates with moderate to high affinity. KIL, KIC, KCA, PGA, FGA, and TGA_all these substrates were observed to show the exothermic nature of the binding isotherm (Figure 2), with all their Δ*H* values being negative with different *K*d values in μM (NADPH - 7.68±0.5; NADH - 98±12.0; 3-methyl-2-ketopentanoate - 15.41±3.7; 2-ketoisocaproate - 3.048±0.02; 2-ketocaproate - 13.85±1.20; phenyl glyoxylate - 3.525±0.31; 2-thiophenyl glyoxylate - 1.344±0.11; 2-furyl glyoxylate - 0.392±0.05). The data implies that the structurally closest KPL substrate, KIL, is showing the lowest affinity. But substrates with a more planar, 3-dimensional structure can have a higher affinity for the binding site. Substrate with bulky aromatic group in PGA also showed good interaction, which suggests the available space is not so squeezed to be fully closed. Interestingly, the substrates TGA and FGA that contain five carbon rings with sulfur and oxygen atoms in the extended region showed the best *K*d values (1.392 and 0.392 *μ*M). It implies that the charged atoms (sulfur and oxygen) of the ring are getting stabilized through positive interaction at the binding site. A high negative enthalpic value also justifies this claim. ITC results indicate that all these substrates can at least have an interaction site within the protein with varying degrees of attraction due to the limited molecular space.

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

1. Surin, S., Singh, R., Kaur, M., Basu, Choudhury., G, Sen., H, Dureja., C, Datta., S, Raychaudhuri S. (2024) Identification of critical amino acids in the DNA binding domain of LuxO: Lessons from a constitutive active LuxO. *PLoS One*. 19:e0310444

2. Saha, D., Pramanik, A., Freville, A., Siddiqui, A.A., Pal, U., Banerjee, C., Nag, S., Debsharma, S., Pramanik, S., Mazumder, S., Maiti, NC., Datta, S., Ooij, C and Bandyopadhyay, U. (2024) Structure-function analysis of nucleotide housekeeping protein HAM1 from human malaria parasite Plasmodium falciparum. *The FEBS Journal*. 291, 4349–4371.

3. Basu Choudhury, G and Datta, S. (2024) Implication of Molecular Constraints Facilitating the Functional Evolution of *Pseudomonas aeruginosa* KPR2 into a Versatile α-Keto-Acid Reductase. *Biochemistry*. 63 (14):1808-1823.

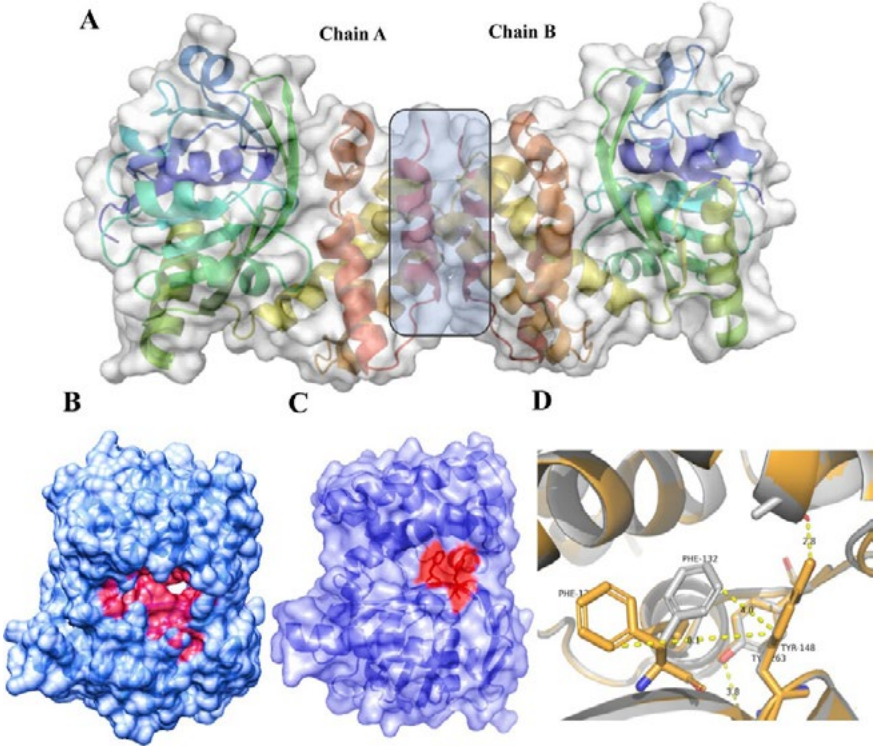


Figure 1: Native structure of PaKPR2. (A) Dimeric KPR with interface region highlighted with blue color box. (B) PDB: 8IWQ native structure of PaKPR2 with open gate conformation. (C) PDB: 8IWG native structure of PaKPR2 with closed gate conformation (gate residues F132 and Y148 shown in red). (D) Two native structures superimposed to evaluate the change of orientation of F132 responsible for dynamic molecular gate.

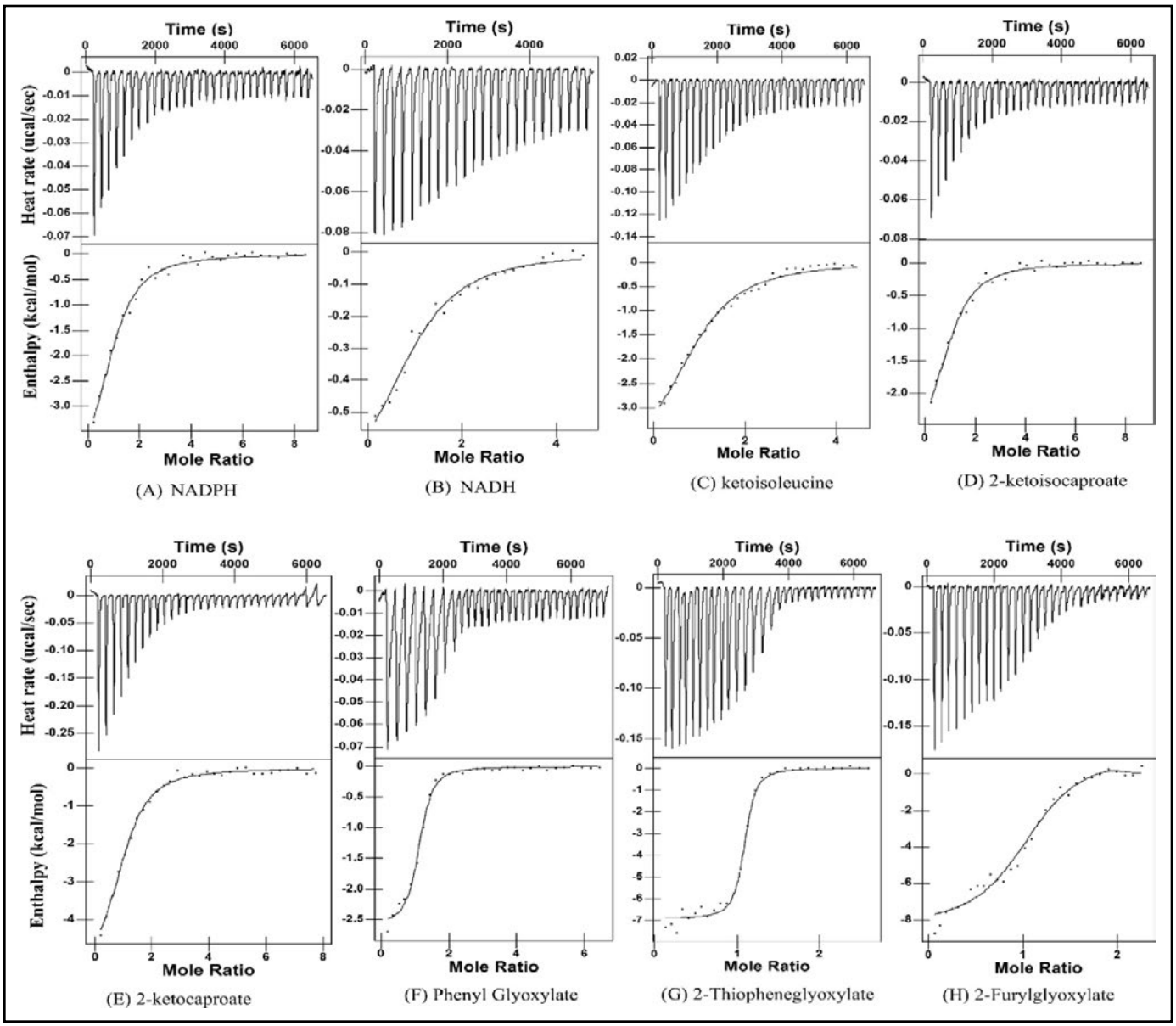


Figure 2: Representative ITC isotherms for the binding of PaKPR2 to the different ligands (A) NADPH, (B) NADH, (C) ketoisoleucine, (D) 2-ketoisocaproate, (E) 2-ketocaproate, (F) phenyl glyoxylic acid, (G) 2 -thiopheneglyoxylate, and (H) 2-furylglyoxylate. The lower panels show a change in molar heat expressed as a function of the molar ratio of protein to ligand. In the upper panels, raw ITC data is expressed as a change in thermal power with respect to time throughout titration. The solid lines in the lower panels show the fit of data to an independent-site binding model using the integrated NanoAnalyze software.

Dr. Saumen Datta, Chief Scientist

Group Members: Debayan Saha, UGC-JRF; Gourab Basu Choudhury, DBT-SRF; Bidisha Chakraborty, UGC-SRF

Collaborators: Saumya Ray Chaudhuri, PhD, CSIR-Institute of Microbial Technology

Dr. Siddhartha Roy and his group members

Metformin as an Epigenetic Modulator: Inhibition of CARM1-Mediated Histone Methylation to Regulate Gluconeogenesis

Research Activities

In our laboratory, research has been focused on uncovering the molecular mechanism by which metformin, a widely used antidiabetic drug, functions as an epigenetic modulator through the inhibition of CARM1-mediated histone methylation. The research demonstrates that metformin structurally mimics asymmetrically dimethylated arginine (ADMA), the product of CARM1, and competitively binds to its substrate-binding site, thereby reducing histone H3 methylation at arginine residues H3R17me2a and H3R26me2a (Figure 1).

Using biochemical and biophysical assays, we showed that metformin binds to CARM1 with low micromolar affinity (Kd = 6.6 μM), inhibiting its methyltransferase activity in a dose-dependent manner. Molecular docking studies confirmed that metformin occupies the same binding pocket as histone H3R17, further supporting its role as a competitive inhibitor. Mutational analysis of key residues (Glu-266, Glu-257, Tyr-153, and His-414) in CARM1 abolished metformin binding, validating the specificity of this interaction.

In cellular and animal models, metformin treatment significantly reduced H3R17me2a and H3R26me2a levels without altering CARM1 expression or its recruitment to gluconeogenic gene promoters. This epigenetic modulation led to the downregulation of key gluconeogenic enzymes (G6Pase, FBPase, and PCK1), which are critical for glucose production in the liver. Chromatin immunoprecipitation (ChIP) assays revealed diminished H3R17me2a marks at the promoters of these genes, linking metformin's epigenetic effects to transcriptional suppression.

Metformin's specificity for type I PRMTs (e.g., CARM1 and PRMT1) over type II PRMTs (e.g., PRMT5) was highlighted, as it selectively reduced asymmetric dimethylation while leaving symmetric dimethylation unaffected. Additionally, metformin reversed CARM1-induced glycolytic suppression in hepatic cells, as evidenced by increased extracellular acidification rates (ECAR) and reduced glucose production. These findings provide a mechanistic explanation for metformin's antihyperglycemic effects beyond its classical AMPK-dependent pathway (Figure 2).

The study bridges gaps in understanding how metformin influences chromatin dynamics and gene expression, offering new therapeutic insights for metabolic disorders. It also suggests potential applications in cancer, given CARM1's role in tumor progression.

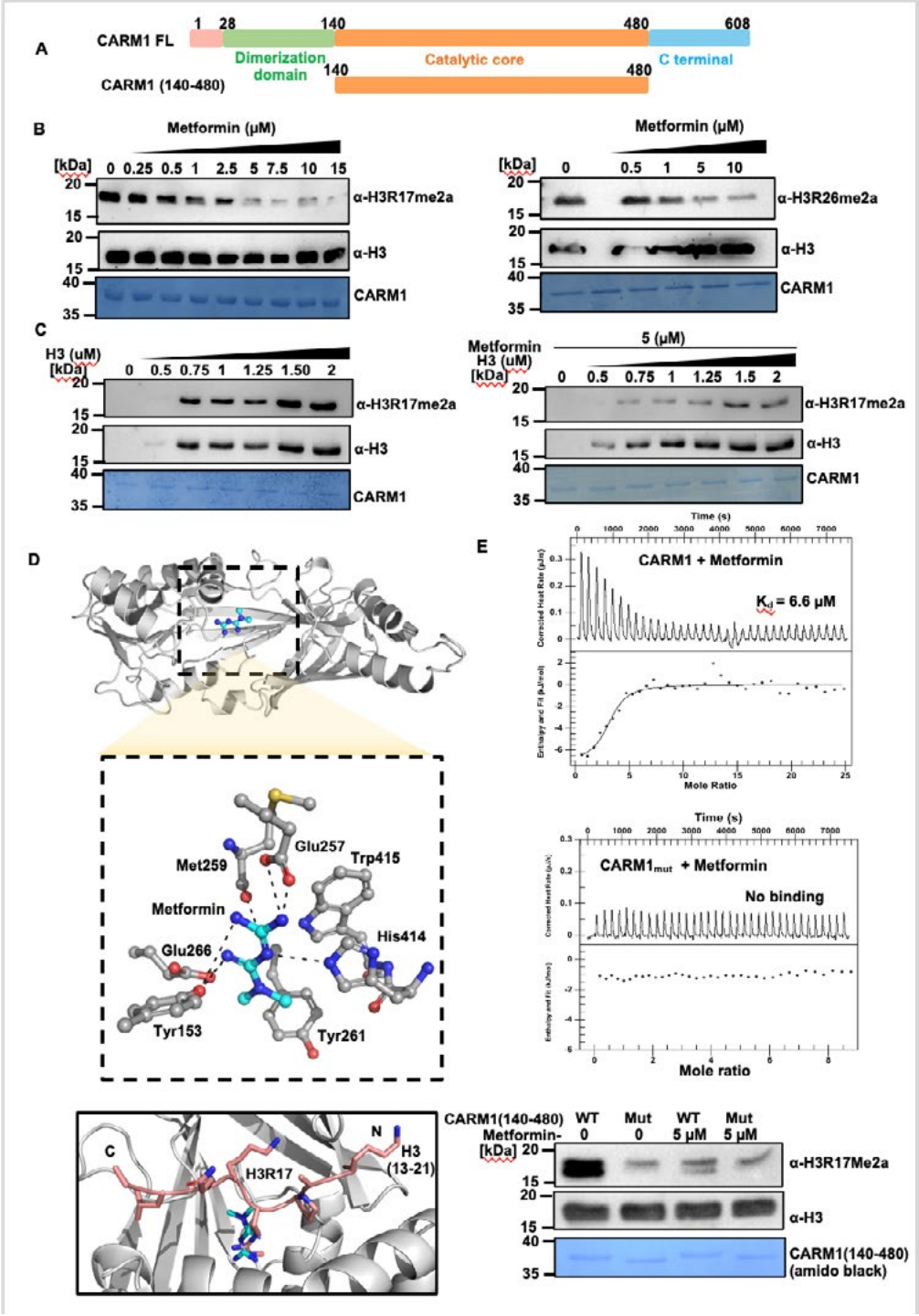


Figure 1: Inhibition of CARM1 methyltransferase activity by metformin in vitro. (A) Domain architecture of human full-length CARM1 and its catalytic core (140-480). (B) In vitro methyltransferase assay with purified hCARM1140-480 and recombinant histone H3 with increasing concentration of metformin. Samples were analysed by western blotting and probed with anti H3R17me2a and H3R26me2a antibodies. (C) In vitro methyltransferase assay with increasing substrate (recombinant H3) concentration in the absence and presence of metformin (5mM). The level of H3R17me2a was monitored by western blotting analysis. (D) Docking studies to show the position of metformin (in ball and stick model in cyan and blue) in the substrate binding pocket of CARM1(PDB ID 2V7E) and superimposition of H3 peptide (13-21, pink) bound CARM1 with metformin occupy the same binding pocket. (E) Isothermal titration calorimetry showing metformin binding to CARM1 wildtype and CARM1mut and HMTase assay using recombinant histone H3 with CARM1 wildtype and CARM1mut.

Future Research Plans

Further studies will be conducted to explore the long-term effects of metformin-induced CARM1 inhibition on epigenetic stability and metabolic health. Investigations will extend to tissue-specific roles of CARM1 in different metabolic organs and its contribution to disease pathogenesis. High-throughput screening will be employed to identify more potent and selective CARM1 inhibitors for therapeutic applications. The potential of metformin or its derivatives in treating cancers linked to CARM1 overexpression will also be evaluated. Additionally, clinical trials may be designed to assess the efficacy of metformin-based epigenetic therapies in diverse patient populations.

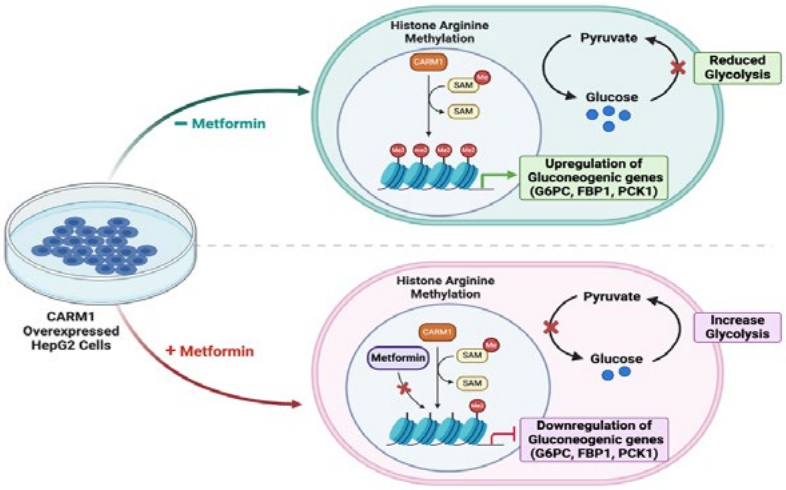


Figure 2: Schematic representation of metformin mediated suppression of CARM1 methylation activity at the gluconeogenic gene promoter.

Extramural / CSIR Funding

1. 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, Department of Science & Technology (DST), 2023-26, 50.2 Lakhs, (CRG/2022/001895).
2. Structural characterization of Zinc finger MYND domain containing protein with GATAD2A subunit of NuRD complex implicated in Neural Differentiation. Department of Biotechnology (DBT), 2023-26, 74.329 Lakhs, (BT/PR45090/MED/122/319/2022).

Publications

1. Dhang, S., Mondal, A., Das, C., Roy, S. (2025) Metformin inhibits the histone methyltransferase CARM1 and attenuates H3 histone methylation during gluconeogenesis. *J Biol Chem.* 301,108271.
2. Singh, V., Mondal, A., Adhikary, S., Mondal, P., Shirgaonkar, N., DasGupta, R., Roy, S., Das, C. (2024) UBR7 E3 Ligase Suppresses Interferon-β Mediated Immune Signaling by Targeting Sp110 in Hepatitis B Virus-Induced Hepatocellular Carcinoma. *ACS Infect Dis.* 10, 3775-3796.
3. Dasgupta, A., Nandi, S., Gupta, S., Roy, S., Das, C. (2024) To Ub or not to Ub: The epic dilemma of histones that regulate gene expression and epigenetic cross-talk. *Biochim Biophys Acta Gene Regul Mech.* 1867,195033.
4. Das, C., Bhattacharya, A., Adhikari, S., Mondal, A., Mondal, P., Adhikary, S., Roy, S., Ramos, K., Yadav, KK., Tainer, JA., Pandita, TK. (2024) A prismatic view of the epigenetic-metabolic regulatory axis in breast cancer therapy resistance. Oncogene. 43,1727-1741.

Dr. Siddhartha Roy, Senior Principal Scientist

Group Members: Sinjini Dhang, SRF; Avradeep Karmakar, SRF; Deep Basu, SRF; Sayan Gupta, SRF; Bhaskar Das, JRF; Bonodip Chowdhury, JRF; Sayani Mukherjee, JRF

Collaborators: Dr. Chandrima Das, Saha Institute of Nuclear Physics, Kolkata

Dr. Subrata Adak and his group members

Identification of TNF-α mRNA binding site in leishmanial glyceraldehyde-3-phosphate dehydrogenase

Research Activities

One of the classical glycolytic enzymes is glyceraldehyde-3-phosphate dehydrogenase (GAPDH), which catalyzes the reversible oxidative phosphorylation of glyceraldehyde-3-phosphate to the higher energy intermediate 1,3-bisphosphoglycerate in the presence of inorganic phosphate and nicotinamide adenine dinucleotide (NAD^+). However, emerging evidences suggest that GAPDH is a moonlighting protein, which exhibits multiple non-glycolytic functions in different subcellular organelles. Apart from glycolytic function, membrane-bound GAPDH displays an important function for membrane fusion, endocytosis and iron transport. Cytosolic GAPDH controls the stability of mRNA, post-transcriptional regulation and translation, and is required for heme insertion of iNOS and ER to Golgi trafficking. GAPDH in nucleus is involved in transcriptional regulation of gene, the preservation of DNA integrity, cell death through apoptosis, as well as nuclear tRNA export. Unexpectedly, numerous human diseases, like tumorigenesis, diabetes and neurodegenerative disorders are dependent on GAPDH structure and function.

Recently, we have shown that the GAPDH protein from *Leishmania major* (LmGAPDH) is localized within the extracellular vesicles (EVs). *Leishmania* EVs are mainly involved in the transporting of various biomolecules into host macrophage during infection. By comparative studies among LmGAPDH overexpression, half knockout (HKO), and complement *Leishmania* promastigotes, HKO cells exhibited lesser virulence property compared to other cell lines when BALB/c mice were inoculated separately with all kinds of cell lines. In addition, ELISA, RT-PCR, and immunoblot data showed that higher TNF-α protein expression occurred during infection of host macrophages with HKO cell lines and its EVs. *In vitro* protein translation studies suggested that the repression of TNF-α expression is directly proportional to LmGAPDH concentration. Furthermore, RNA electrophoretic mobility shift assay (REMSA) studies suggested that LmGAPDH has ability to bind with the AU-rich 3' -UTR region of TNF-α mRNA (TNF-α ARE).

GAPDH lacks canonical RNA-binding consensus sequences, for example RNP motifs, RGG boxes, KH domain or any other known nucleic-acid-binding motifs. It is well-known that AU-rich sequence elements of mRNA are involved in GAPDH binding. The inhibition study of the RNA-GAPDH complex formation by NAD^+, NADH and ATP further indicated that the NAD^+-binding site or (di) nucleotide-binding fold (Rossman fold) is involved in RNA binding. In addition, GAPDH has ability to interact with other RNAs including tRNA, rRNA and viral RNA. A group of researchers established by using deletion mutant that the N-terminal 43 amino acid residues (Rossman fold) of human GAPDH with GST fusion protein are sufficient for TNF-α ARE binding but the precise binding residue(s)

in GAPDH is/are still unexplored. Another group of researchers suggested that the TNF-α ARE-binding site in GAPDH would span beyond the Rossman fold area including the dimer and tetramer interface. Although structure of NAD^+ bound GAPDH are now available, a high-resolution X-ray structure of RNA bound GAPDH is still unknown in the literature.

The aim of our goals is

- Identification of the specific crucial residues, which is involved in TNF-α mRNA binding at NAD^+ domain.
- What is the mechanism for the regulation of GAPDH activity by TNF-α mRNA binding at the molecular level?

RNA electrophoretic mobility shift assay (REMSA) and catalytic activity measurement revealed that the inhibition by TNF-α ARE was competitive with respect to cofactor NAD^+ in LmGAPDH. To identify the TNF-α ARE binding residues of the LmGAPDH, we exploited a systematic mutational analysis of its NAD^+ binding domain. Catalytic activity measurement indicates that both R13 and N336 amino acids in the NAD^+ binding site are absolutely required for activity whereas other mutants including I14A, R16A, D39A and T112A showed higher Km (lower affinity) value for NAD^+ binding and lower catalytic activity. REMSA studies revealed that the replacement of Arg-13 with Ala/Lys or Asn-336 with Ala resulted in complete loss of binding with the TNF-α ARE. I14A, R16A, D39A and T112A residues at or near NAD^+ binding site showed lower binding with the TNF-α ARE compared to the wild-type protein. The protein induced fluorescence enhancement (PIFE) studies and *in vitro* protein translation assay further confirmed the REMSA results. Based on our findings, the NAD+ binding residues in LmGAPDH are important for TNFα ARE binding.

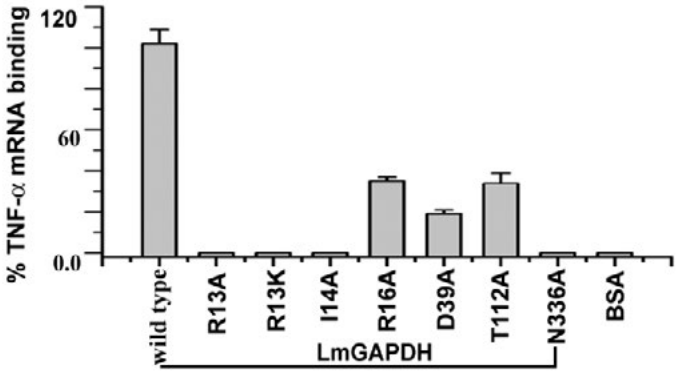


Figure 1: Protein induced fluorescence enhancement studies revealed that the NAD^+ binding residues (R13, I14, N336, D39, R16A and T112) in LmGAPDH are important for TNFα ARE binding.

Future Research Plans

- Comparison of the amino acid sequences of GAPDH from prokaryotic to eukaryotic organisms suggests that mRNA-binding could be evolutionarily conserved. Thus, evolutionarily conserved role of GAPDH in mRNA-binding, possibly depending on the metabolic reprogramming of cells remains to be determined.
- Further x-ray crystal structure of GAPDH and TNF- α ARE complexes are needed to confirm interaction site of TNF- α ARE with GAPDH.

Extramural Funding

- 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).
- Leishmaniasis: Target specific approaches to affect host-pathogen interaction and disease process. CSIR, 2020-25, 300 lakh, MLP-136

Conferences Attended

93rd General meet of the Society of Biological Chemists of India SBC(I), The M.S. University of Baroda, Vadodara, 27-29 December 2024.

Dr. Subrata Adak, Chief Scientist

Group Members: Yuthika Dholey, SRF; Puja Panja, SRF; Gaurab Chowdhury, SRF; Namrata Dhara, SRF; Swastik Biswas, SRF; Ritwick Modak, JRF; Anik Bose, JRF

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 signaling 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.

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 used genomics and computational biology to prove that a large group of Cyanobacteria belonging to subsection IV has the most diversity. Using genomics and transcriptomics as a tool, we have proposed to split the family Hapalosiphonaceae into 3 distinct groups. The group 1 is considered close, where as group 2 is rapidly diverging and undergoing genome expansion. The

extremophiles are characterized by the presence of metabolic gene clusters responsible for anti-microbial and anti-tumorigenic activities (Figure 1). We have shown that a marine Cyanobacteria Oscillatoria salina has water soluble compounds working as a cancer spheroid disintegrating agent with very potent activity (Figure 2). Recently, the anti-microbial compounds derived from this organism is studied extensively. The most significant work our group achieved this year was the discovery of a novel Cyanobacteria species. After extensive analysis, we show that multiple species submitted to Genbank are in fact placed wrongly in different taxonomic clade. We have named this organism as Leptolyngbya iicbica LK after our beloved institution (Figure 3).

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.

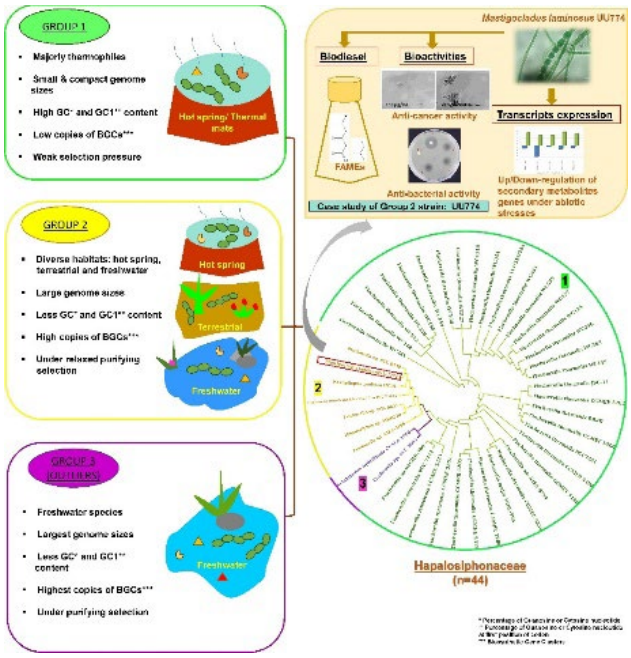


Figure 1: Mastigocladus laminosus UU774 is a hotspring extremophile, belong to the family Hapalosiphonaceae. This is a large family consisting of 3 distinct groups with diverse habitats and genome signatures. We propose vertical splitting of this family into 3 groups based on their genomic profile.

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. National Network Component. Department of Biotechnology (DBT), 2023 – 2028, 169.87 Lakhs, (BT/PR40243/BTIS/137/75/2023)
2. Platform integration for high Throughput multi omics data analysis and text processing. (DBT-Bioinformatics Center), 2022-2027, 227.21464 Lakhs, (BT/PR40137/BTIS/137/35/2022).
3. Development of Genome Consortium Databank from plants and microbial population emerging from India. DBT (National Networking Program), 2023-2028, 16.97 Lakhs. (BT/PR40233/BTIS/137/74/2023).
4. A comprehensive approach to address Antimicrobial Resistance (AMR). CSIR (MMP 075202) (2024-2027).
5. Mycoremediation of Toxic Heterocyclic Organosulfur Compounds: Multi 'Omics' Approach to Unravel the Novel Biodesulfurization Pathway(s) in the Filamentous Fungus Arthrinium malaysianum Grown in Presence of 2-Deoxy Glucose (2DG): Fabrication of Novel Biosorbent for Translational Research. Department of Science & Technology (DST), 2022-2025, 18.39 Lakhs, (TAR/2022/000465).

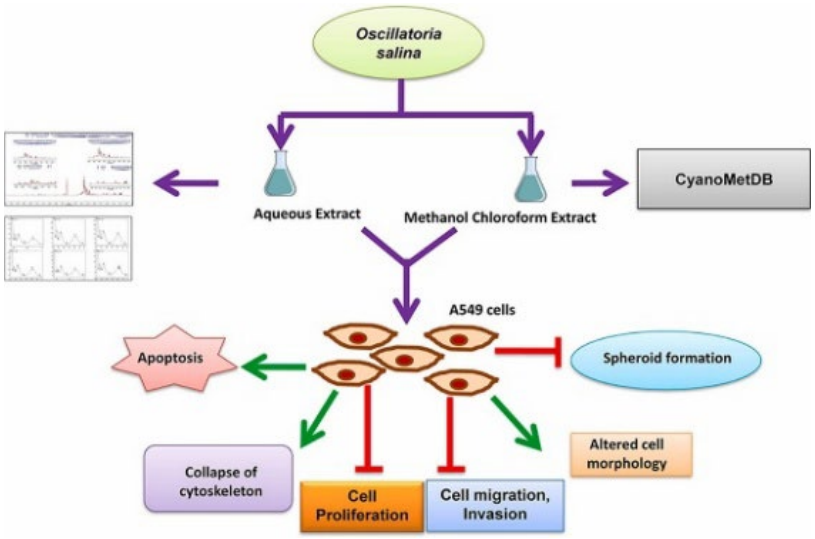


Figure 2: Oscillatoria salina, a marine Cyanobacteria produces a brilliant blue pigment in aqueous extract. This pigment is demonstrated to have apoptosis, cell proliferation, cell migration and invasion over the A 549 cancer cell line.

Publications

1. Mandal, K., Dutta, S., Geeta, A., Maulik, A., Upadhyay, A., Das, A., Behera, S., Tripathy, S. (2024). Genome sequencing of Phytophthora capsici from southern Asia reveals effector polymorphism during the early stage of pathogenesis. *Molecular Plant-microbe Interactions*. 37(5).

2. Das, B, Prusty, A., Dutta, S., Maulik, A., Dahat, Y., Kumar, D., and Tripathy, S. (2024). Exploring the Uncharted Seas: Metabolite Profiling Unleashes the Anticancer Properties of Oscillatoria Salina'. *Heliyon* 10, no. 16.

3. Chakraborty, A., Bodhak, S., Tah, I., Kant, Sashi., Saha, D., Dey, K., Gupta, K., Tripathy, S., and Allu, AR. (2024). Tailored Bioactive Glass Coating: Navigating Devitrification Toward a Superior Implant Performance. *ACS Biomaterials Science & Engineering* 10, 5300–5312.

4. Kant, S, Das, S., Roy, S., and Tripathy, S. (2024). Fungal Cellulases: A Comprehensive Review. *The Nucleus*, 1–17.

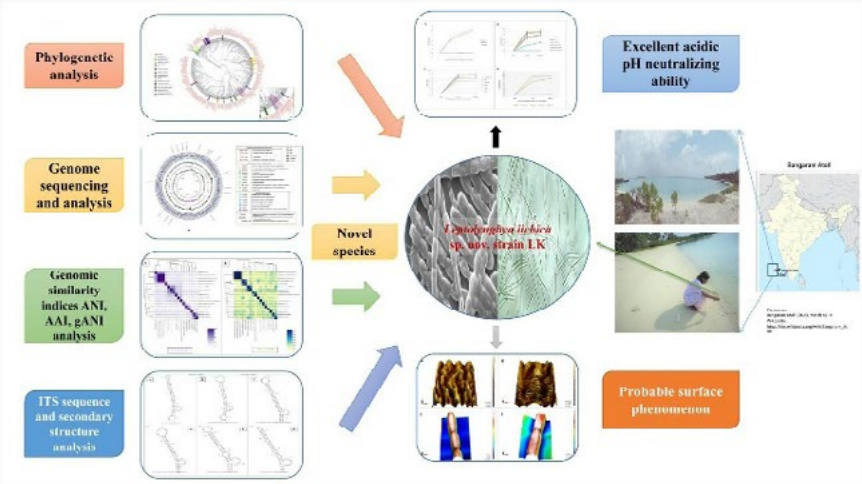


Figure 3: Leptolyngbya iicbica LK, is a native strain found in Lakshadweep Island has profound acid neutralizing properties. This organism was a novel species as is evident from whole genome phylogenetic analysis, Average nucleotide and amino acid identity and by comparative analysis of ITS regions.

5. Geeta, A, Mukherjee, M., Das, B., Dutta, S., Prusty, A., Ghosh, S., Biswas Raha, A., Poddar Sarkar, M., and Tripathy, S. (2024). Distinct Genome Trichotomy in Members of Hapalosiphonaceae Is Guided by Habitat Adaptation with Mastigocladus Laminosus UU774 as a Case Study. *Algal Research.* 82: 103603.

6. Dutta, S, Kothari, S., Singh, D., Ghosh, S., Sarangi, AN., Behera, S., Prajapati, S., Sinha, PK., Prusty, A., and Tripathy, S. (2024). Novel Oceanic Cyanobacterium Isolated from Bangaram Island with Profound Acid Neutralizing Ability Is Proposed as Leptolyngbya Iicbica Sp. Nov. Strain LK'. *Molecular Phylogenetics and Evolution.* 197: 108092.

Conferences Attended

1. Plant Biology in the post genomics era: Strategies for crops and mankind, Sister Nivedita University, Feb 9th 2024, Kolkata.

2. BIC and NNP – Bioinformatics workshop September – 2024.

Invited Lectures

Mistaken Identity: Genomics comes in the rescue of microbes in placing them into right perspective. Graphic Era Hill University, Dehradun, Uttarakhand, India. International Conference on Innovative Sustainable Agriculture & Livestock Technologies during 25th -29th of November, 2024.

Dr. Sucheta Tripathy, Senior Principal Scientist

Group Members: Dr. Bornita Das, DST Women Scientist; Dr. Aditi Maulik, DBT BRC Scientist; Aribam Geeta, SRF; Subhajeet Dutta, SRF; Kajal Mandal, SRF; Aditya Upadhyay, SRF; Sreyashi Das, JRF; Meghashree Guha, JRF; Mondira Banerjee, JRF; Dr. Asharani Prusty, PA; Dr. Shashikant, PA; Vaishnavi, PA; Sreejita Sinha, PA

Collaborators: Dr. Rays Jiang, Professor, UCSF, USA; Dr. Kaushik Biswas, CSIR-CGCRI, Kolkata, India; Dr. Mitun Das, CSIR-CGCRI, Kolkata, India

Dr. Tanaya Bose and her group members

Targeting *Plasmodium falciparum* ribosomes with structure-based antibiotics and natural product-based small molecules to target *Staphylococcus aureus and E. Coli*

Research Activities

Although the core architecture of ribosomes in *Plasmodium falciparum* and *Homo sapiens* is conserved, significant differences exist in the peripheral regions, particularly in the ribosomal RNA (rRNA) expansion segments. These peripheral variations present an opportunity for species-specific targeting. By computationally scanning the *P. falciparum* rRNA, we identified unique, non-conserved regions represented in the figure below that can serve as selective targets for antisense oligonucleotides (ASOs).

The ASOs were designed based on the following criteria:

- Target region length ranging from 10 to 22 nucleotides.
- High solvent-accessible surface area (ASA) of the target nucleotides.

Sequence uniqueness and divergence from human rRNA, confirmed via multiple sequence alignment using Clustal Omega.

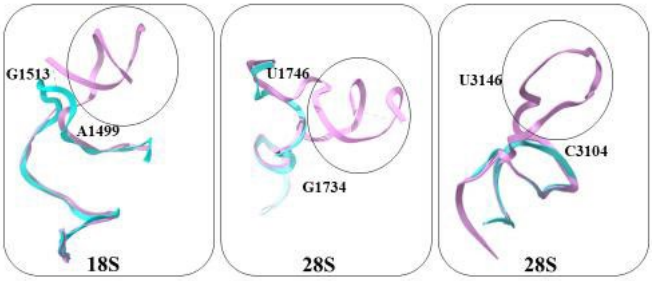


Figure: Representative superposition images of target regions in P. Falciparum (Pink PDB: 3JBO) and H. sapiens (Cyan PDB:4UG0). a. 1499 series. b. 1734 series c. 3104 series The images were created using the UCF ChimeraX package (Pettersen et al., 2004).

In our design strategy, we prioritized rRNA regions on the ribosomal surface, particularly non-conserved, from both the large and small ribosomal subunit of *P. falciparum*, to ensure greater accessibility and functional disruption. These regions are planned to target using antisense DNA or phosphorothioate-modified oligonucleotides. The designed ASOs will be tested *in vitro* using transcription/translation inhibition assays to evaluate their effect on peptide bond formation.

As part of experimental standardization, we have purified *E. coli* ribosomes to serve as controls. Currently, we are actively purifying *P. falciparum* ribosomes from their lysates for testing the efficacy of the designed antisense oligonucleotides.

In parallel, we have initiated collaborative work with Dr. Parasuraman Jaishankar (Scientist, CSIR-IICB) to investigate natural product-based small-molecule inhibitors that target *Staphylococcus aureus* and *E. Coli*. A set of candidate compounds has been synthesized and subjected to preliminary activity screening.

To further elucidate the mechanism of action and binding interactions at the atomic level, selected compounds will be subjected to structural analysis using cryo-electron microscopy. This approach will allow us to visualize compound–ribosome interactions and better understand the inhibition mechanism.

Concurrently, we are scaling up *S. aureus* cultures and purifying ribosomes to support ongoing and future biochemical and structural studies.

Future Research Plans

The suitability of the sequences to serve as antibiotic targets will be determined with an *in vitro* transcription/translation activity assay using luciferase as a reporter gene. The correlation between the inhibition and the targeting of the selected regions will be assessed, upon conjugation of the antisense oligonucleotides with fluorescein, with binding assays on non-denaturing agarose gel and with the use of mismatched oligonucleotide sequences. The efficacy of the antisense oligonucleotides will be tested also on whole *Plasmodium Falciparum* cells. Studying the structure of the 80S from *P. Falciparum* in complex with a bound antisense oligonucleotide molecule will enable us to decipher the molecular details of the mechanism for protein synthesis inhibition.

In future, we plan to study the inhibition of protein synthesis of *Staphylococcus aureus* and *E. Coli ribosome* in presence of the novel small molecules. Once the IC50 of protein synthesis inhibition of the molecules are determined, we will study the structure of the antibiotics bound ribosome using cryo-electron microscopy. This will help us understand the mechanism of binding of the molecule to the ribosome at atomic level.

Extramural / CSIR Funding

Targeting bacterial ribosomes with a new class of antibiotics to overcome antibiotic resistance. DBT-Ramalingaswami fellowship, 2023, 49.5 Lakhs

Publications

1. Rivalta, A., Hiregange, DG., Bose, T., Rajan, KS., Yonath, A., Zimmerman, E., Waghalter, M., Fridkin, G., Martinez-Roman, I., Rosenfield, L., Fedorenko, A., Bashan, A., Yonath, H. (2025). Ribosomes: from conserved origin to functional/medical mobility and heterogeneity. *Philos Trans R Soc Lond B Biol Sci.* 380, 20230393
2. Rajan, KS., Aryal, S., Hiregange, DG., Bashan, A., Madmoni, H., Olami, M., Doniger, T., Cohen-Chalamish, S., Pescher, P., Taoka, M., Nobe, Y., Fedorenko, A., Bose, T., Zimermann, E., Prina, E., Aharon-Hefetz, N., Pilpel, Y., Isobe, T., Unger, R., Späth, GF., Yonath, A., Michaeli, S. (2024). Structural and mechanistic insights into the function of Leishmania ribosome lacking a single pseudouridine modification. *Cell Rep.* 43,114203.

Book Chapters

Rivalta, A., Hiregange, D.G., Bose, T., Fridkin, G., Rajan, K.S., Yonath, A., Zimmerman, E., Bashan, A. and Yonath, H. (2023). Medical Implications of Functional and Destructive Cellular Motions: Curiosity-Driven Open Issues. In Curious Future Insight: Science for a Better Tomorrow (pp. 82-65). Cham: Springer International Publishing.

Invited Lectures

1. Delivered invited talk at Kolkata Biophysics meet, SINP, Kolkata on 2nd April, 2024.
2. Delivered invited lecture at a conference at IIT Delhi titled “SATHI Summit: Advances in cryoEM and 3D Image Processing” on 5th April, 2024

Conferences Attended

Attended brainstorming meeting at U R Rao Satellite Center, ISRO, Bangalore on Astrobiology held on 22nd and 23rd April 2024, Bangalore.

Dr. Tanaya Bose, Senior Scientist

Group Members: Pranay Karmakar, UGC-JRF; Amar Pal, UGC-JRF; Krishna Chakroborty, UGC-JRF

Collaborators: Dr. Parasuraman Jaisankar, Pharmacology & Drug Discovery Division, CSIR-Indian Institute of Chemical Biology, Kolkata; Dr. Rashmi Gaur, Organic and Medicinal Chemistry, CSIR-Indian Institute of Chemical Biology, Kolkata

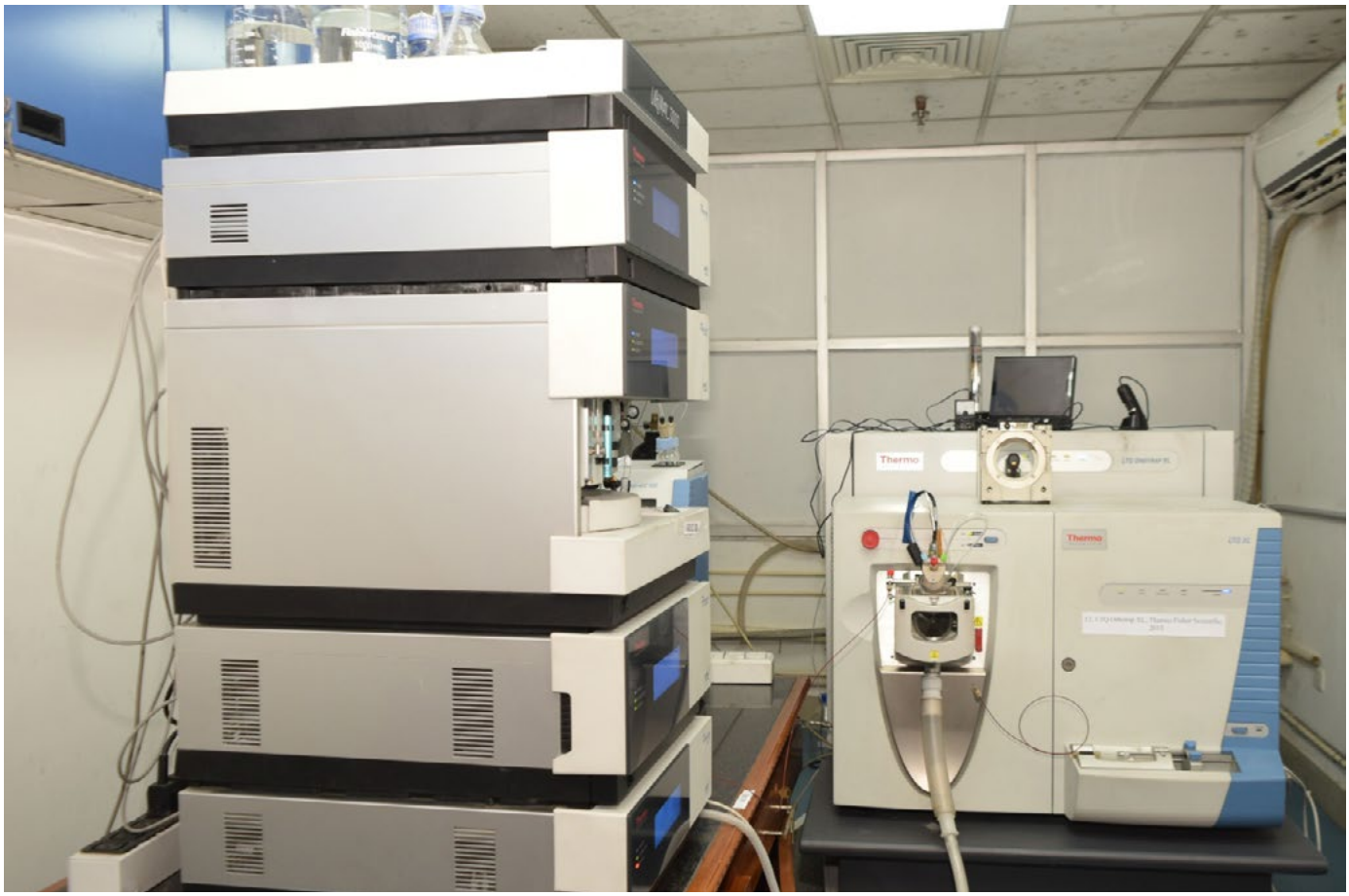
CENTRAL INSTRUMENTATION FACILITY

Central Instrumentation Facility Division (CIF)

Group members of Central Instrumentation Facility Division

CIF provides support to the researchers at CSIR-IICB along with different academic and R&D organizations, that students and faculties includes Universities and Colleges of the country. We have 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. CIF is also providing knowledge and information to the college and university students through different programs that include SDP, open house, etc. For the PhD students, the course on Instrumentation and techniques 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 SDP 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 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.

These facilities of instruments are logically distributed in both the campuses of IICB. The instruments list of CIF is available on the IICB-webpage along with their location and their operators and scientists-in charge. 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, for monitoring 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 coming from different corners of the country.



ORBITRAP

Representatives of AIIMS, New Delhi visiting CIF, CSIR-IICB, Kolkata

Demonstration of instrument at CIF, CSIR-IICB, Kolkata

Demonstration of instrument at CIF, CSIR-IICB, Kolkata

Human Resource: Dr. Sib Sankar Roy (Head), Dr. Indu Bhusan Deb (Deputy Head), Dr. E. Padmanaban, Mr. Sandip Chowdhury, Mr. Sandip Chakraborty, Mr. Jishu Mandal, Mr. Binayak Pal, Mr. Sounak Bhattacharya, Mr. Soumik Laha, Mr. Sandip Kundu, Mr. Santu Paul, Mr. M. Vigneshwaran, Mr. Tapas Chowdhury, Mr. Tarak Prasad Nandi, Mr. Hari Shankar Beni, Mr. Nimai Charan Pradhan, Mrs. Arpita Maji, Mr Arijit Chowdhury, Mr. Nilaksha Swarnakar, and Mr Anirban Manna.

SUPPORT DIVISIONS

Animal House

CSIR-IICB is associated with research in the area of biomedical research; majority of its research projects are reliant on animal experiments. IICB Animal Facility had been established long back; however, it's been up graded time to time to keep pace with the evolving need 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 follows CCSEA guidelines strictly for animal maintenance and experiments. A uniform environment (Room temperature 22 $\pm$ 2^{0}C, relative humidity 50–60%, light and dark schedule 12:12hrs; illumination below 400 lux at 1 mt above the floor) is maintained in the animal facility; the animals are housed in Individually Ventilated Cages (IVC). Animals (mice, rat, hamster, rabbit etc) including transgenic and immune compromised strains of mice are bred and supplied from the in-house breeding colony. Colonies of animals are set up only for the strains which have reasonable demand and animal production is balanced with the experimental requirement to avoid unnecessary culling of animals. They are raised under strict health and genetic monitoring.

Utilization of animals as well as animal experiments is strictly monitored; experiments are performed as approved by the IAEC.

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

Mice, Rat – Sprague Dwaley, Hamster – Syrian Golden, Rabbit – New Zealand (White).

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

Species	Stock on 1st April 2024	No. of animals		Total (A)	No. of animals issued		No. of animals		Total (B)	Stock on 31.3. 2025
		Produced	Purchased		Produced	Purchased	died in-stock	Supplied to other R&D organization		
Mouse	1540	2574	149	4263	2167	135	450	0	2752	1511 *
Rat	252	223	70	545	218	70	82	0	370	175
Hamster	74	45	0	119	17	0	39	0	56	63
Rabbit	58	05	0	63	0	0	16	0	17	47

*Mice /strain	Male	Female	Total
C57 BL/6J	92	225	317
BALB/C	88	84	172
Swiss	24	40	64
FVBN	22	28	50
5XFAD	38	82	120
APOE	21	50	71
PPARA KO	30	37	67
WNT 5 KO	36	58	94
NUDE	40	128	168
Tg	35	38	73
Rag	62	81	143
Cre	45	53	98
NCG-X	05	05	10
NCRI C57bl/6	02	02	04
Total	560	951	1511

Human Reseouce: Dr. A. Konar, Dr. R. Sarkhel, Dr. S. Bhatiya, Mr. S. S. Verma, Mr. R. Sarkar, Mr. J. Midya, Mr. P. Midya, Mr. Lalu Sardar, Mr. G.C..Sardar, Mr. S K. Midya.

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.

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 Questions; prepares year-wise documents on total Patents of CSIR-IICB filed and granted, conducts periodic review of its Patent Portfolio.

Human Resourse: Dr. Upasana Ray (Head), Dr. Ranjan Jana (Deputy Head), Mr. Sandeep Aggarwal, Mrs. Arti Grover and Mr. P. C. Dehury

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.

Jadavpur Campus Server Room

Salt Lake Campus Server Room

Major Implementations (or) Achievements of the IT Division

- Migration of Staff Email Services
- Technical Support for CSIR Portals implementations at CSIR-IICB like e-office, e-hrms, access portal etc.
- Upgradation of Meeting Rooms facilities at both the campuses of CSIR-IICB
- Implementation of Network Setup for GLP falicity at Salt lake Campus

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.
- 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.
- Upgradation of IT System, Technical Documents and Other Special ICT Services from time to time.

Human Resource:

CSIR-IICB Jadavpur Campus: Dr. Debabrata Biswas, Senior Principal Scientist and Head IT Division; 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, IT Division

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 Division under 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 has 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 2024-25 are as follows:

- Repair and Renovation of building, sanitary and water supply services.
- External minor repair and painting works of RL and CF Blocks at CSIR-IICB, Salt Lake Campus, and Repair and renovation of Different rooms (2024-25), Phase-I at CSIR-IICB, Jadavpur, Kolkata. (Civil Works).
- Structural repair and retrofitting works of roof slab and ceiling of Library Journal room at CSIR-IICB Jadavpur campus.
- Roof treatment works of RL Block, CF Block and other buildings at Salt Lake campus and Construction of fire stair roof over RL and CF block and covering the sides of the open stair at CSIR-IICB, Salt lake Campus, Kolkata.
- External repair and painting of Guest House building and Staff Quarter at IICB, Salt Lake campus.
- Setting up off FCP project at CSIR-IICB, Salt Lake Campus, Kolkata (Civil, Electrical and Air Conditioning Work).
- Repair and Renovation of Iron Gate at Scientist Apartment Building at 428, Prince Anwar Shah Road, Kolkata-700045.

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 Repair and renovation of Different rooms (2024-25), Phase-I at CSIR-IICB, Jadavpur, Kolkata.
- Repair and renovation and upgradation of CCTV system
- AMC works for various electrical appliances like DG Sets, Capacitor panels, Fire Detection system, EPBAX System.
- Electrical and associated work for setting up off FCP project at CSIR-IICB, Salt Lake Campus, Kolkata.

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:

- Establishment of Bio-Safety Level-2(BSL-2) Laboratory and associated works on turnkey basis at CSIR-IICB, Jadavpur campus
- Operation service and maintenance of Central Air Conditioning Plants of CSIR-IICB Jadavpur campus to ensure normal activities of the Auditorium and Library.
- Renovation, upgradation and modernization of existing cold room to set up new modular walk-in cold room at ground floor, CSIR-IICB, Jadavpur campus.
- 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 the 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 Reseouce:

Civil Engineering Section: Dr. Nakul C. Maiti (Head), 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: Miss Sheetal and Mr. Sujoy Haldar.

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) & Academic Affairs division (AAD) 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 the group contributes are: activities related to academic administration concerning the research scholars pursuing PhD program at the institute, CSIR-IICB PhD course work, student affairs, post-graduate internship programme, and different other activities of the institute. HRG & AAD provides assistance in the preparation of related documentation and co-ordination of various programs critical to the mission of the Institute.

Dr. Sanjay Dutta, Sr. Principal Scientist & Head, HRG serves as the co-ordinator of the Academic Affairs committee.

Dr. Jayati Sengupta, Chief Scientist serves Chairperson of the Academic Affairs committee (AAC).

Activities, Guidance and Initiatives:

Student Affairs & Academic Affairs

1. CSIR-IICB PhD course work: Management of Course work schedule, curriculum planning and course co-ordination, class schedule and attendance records, coordination with the teachers, management and co-ordination of semester examinations, seminar, and publication of result, issuance of certificates and statement of marks.
2. Scrutinization of applications and documents of research fellows related to their academic records as necessary guidelines during the academic tenure of the student. Maintenance of PhD registration related information.
3. Summer Internship program: co-ordination and management of the program, selection and placement of post-graduate trainees at CSIR-IICB as per the guidelines.
4. Coordination of Academic Affairs committee meeting and related documentations.
5. CSIR-IICB JRF (direct) entrance interview and JRF admissions for PhD under AcSIR @ CSIR-IICB: co-ordination and associated activities for the interview procedure, web notification, vacancy details for the number of JRFs as per guidelines. Maintenance of record of student strength under the guidance of the PhD supervisors at CSIR-IICB.

6. Publication of the PhD course catalogue, academic Calendar and corresponding guidelines for the students enrolled for the PhD course work.
7. Organization of Orientation programme for PhD students enrolled in the CSIR-IICB PhD course work.

Human Resourses : PhD students (as on March 2025)

At a Glance:

Number of existing Research Fellows: 251 (approx.)

(CSIR/UGC/DST/DBT/ICMR)

Number of students awarded PhD degree during 2024-25: 61

(doctorate degree received from AcSIR/University of Calcutta/ Jadavpur University

Summer Internship Program

HRG coordinates Summer Internship Program 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 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 students carried their Summer Internship project work at CSIR-IICB during 2024-25: 39

Learning and instructional support: Academic Affairs

To conduct and coordinate the CSIR-IICB PhD course work is the major focus of this Division which includes various related activities. The division engages towards the academic-administrative guidance for the doctoral students pursuing research work at the institute and also for the AcSIR activities at CSIR-IICB.

The CSIR-IICB "**Academic Affairs Committee (AAC)"** acts as an Advisory Committee to the Academic Affairs Division & HRG in connection with all the activities of the department.

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 structure 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 CW comprises of Basic & Advanced level courses [total 18 credits taken by one student]:

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

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

'Societal program: Problem Understanding and Analysis'

AAD & 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 Course work students for 2024-25 : 55 (Chemistry - 9, Biology - 46)

Human Resource: Dr. Sanjay Dutta, Sr. Principal Scientist, Head HRG, Ms. Debasree Das, Ms. Sutapa Ganguly

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 2024-25: 53

Number of students awarded PhD degree during 2024-25: 29

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.

AcSIR Science club

The Science club of AcSIR was inaugurated on 23rd May 2024 by the Director, AcSIR. The vision of the science club is to create a vibrant platform that cultivates collaboration, innovation, and knowledge exchange among the enlightened minds within the institute. The objective of science club is to foster a culture of curiosity and scientific exchange, in a forum for interdisciplinary discussions, events, contributing to the scientific sphere. Collectively, our aim is to kindle a flame of scientific inquisitiveness and ingenuity, progressing toward fresh horizons of exploration in the fields of chemical biology.

AcSIR Co-ordinator: Dr. Jayati Sengupta, Sr. Principal Scientist CSIR-IICB

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	10	ACS Applied Optical Materials
02	Accounts of Materials Research	11	ACS Applied Polymer Materials
03	ACS Agricultural Science & Technology	12	ACS Bio & Medchem Au
04	ACS Applied Bio Materials	13	ACS Biomaterials Science and Engineering
05	ACS Applied Electronics Materials	14	ACS Catalysis
06	ACS Applied Energy Materials	15	ACS Central Science
07	ACS Applied Engineering Materials	16	ACS Chemical Biology
08	ACS Applied Materials & Interfaces	17	ACS Chemical Health & Safety
09	ACS Applied Nano Materials	18	ACS Chemical Neuroscience

19	ACS Combinatorial Science [Journal of Combinatorial Chemistry (1999 - 2010)]	52	Chemistry of Materials
20	ACS Earth and Space Chemistry	53	Crystal Growth & Design
21	ACS Energy Letters	54	Energy & Fuels
22	ACS Engineering Au	55	Environment & Health
23	ACS Environmental Au	56	Environmental Science & Technology
24	ACS ES & T Engineering	57	Environmental Science & Technology Letters
25	ACS ES & T Water	58	Industrial & Engineering Chemistry Research
26	ACS Food & Science Technology	59	Inorganic Chemistry
27	ACS Infectious Diseases	60	JACS Au
28	ACS Macro Letters	61	Journal of Agricultural and Food Chemistry
29	ACS Materials Au	62	Journal of Chemical & Engineering Data
30	ACS Materials Letters	63	Journal of Chemical Education
31	ACS Measurement Science Au	64	Journal of Chemical Information and Modeling
32	ACS Medicinal Chemistry Letters	65	Journal of Chemical Theory and Computation
33	ACS Nano	66	Journal of Medicinal Chemistry
34	ACS Nano Science Au	67	Journal of Natural Products
35	ACS Omega	68	Journal of Proteome Research
36	ACS Organic & Inorganic Au	69	Journal of the American Chemical Society
37	ACS Pharmacology & Translation Science	70	Journal of the American Society for Mass Spectrometry
38	ACS Photonics	71	Langmuir
39	ACS Physical Chemistry Au	72	Macromolecules
40	ACS Polymer Au	73	Molecular Pharmaceutics
41	ACS Sensors	74	Nano Letters
42	ACS Sustainable Chemistry & Engineering	75	Organic Letters
43	ACS Synthetic Biology	76	Organic Process Research & Development
44	Analytical Chemistry	77	Organometallics
45	Biochemistry	78	Precision Chemistry
46	Bioconjugate Chemistry	79	The Journal of Organic Chemistry
47	Biomacromolecules	80	The Journal of Physical Chemistry A
48	C&EM Global Enterprise	81	The Journal of Physical Chemistry B
49	Chemical & Biomedical Imagine	82	The Journal of Physical Chemistry C
50	Chemical Research in Toxicology	83	The Journal of Physical Chemistry Letters
51	Chemical Reviews		

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 scientists, 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; Mr. Manas Samanta, Sr. Technical Officer (1) (Up to Jun 2024); 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 Division

The planning, monitoring and evaluation (PME) division manages the Institute's plan and non-plan 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, 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 plan and the budget and maintains the expenditure data, monitors and accounts the receipts of cheques as well as online transfer of fund by the sponsors against the project sanctioned, and request for sanctioned fund, and maintains proper record keeping of all aspects of projects. It does regularly interaction with finance division regarding the expenditure carried out against the projects and prepares the data on this a monthly basis. 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. Details of CSIR and other extramural projects sanctioned during the reporting period (sanctioned, ongoing and completed) are provided as separate lists.

Human Resource: Dr. Subhas Chandra Biswas (Chief Scientist & Head), Dr. Ramalingam Natarajan (Senior Principal Scientist & Deputy Head), Mr. Soumalya Sinha (Senior Technician (1)) and Mr. Samir Thami (Senior Technician (1))

Publication and Information Division (P&I)

Group members of Publication & Information Division

The Publication & Information (P&I) Division of CSIR-Indian Institute of Chemical Biology (CSIR-IICB), Kolkata, serves as a vital communication bridge between the Institute and its diverse stakeholders. Entrusted with the responsibility of documenting and disseminating scientific achievements, institutional developments, research highlights, outreach materials and digital content, the division ensures and plays a key role in ensuring that the Institute's work is accurately represented and accessible to the scientific community, policymakers and the general public through annual reports, publications, digital media and information services.

Beyond documentation and dissemination, the P&I Division is actively engaged in science outreach programs aimed at nurturing scientific temper among students and young minds. Through coordinated visits, interactive sessions, exhibitions and awareness programs across schools and colleges in Kolkata and neighbouring regions, the division contributes significantly to science education and public engagement in research. These efforts not only reflect the Institute's commitment to social responsibility but also help inspire the next generation of scientists.

Finally, this Annual Report stands as a testament to CSIR-IICB's ongoing commitment to excellence in scientific progress, innovations, collaborative endeavors and societal engagement over the past year, highlighting the collective efforts of its researchers, staff and supporting divisions.

Human Resource: Dr. Sarita Ghosh, Senior Principal Scientist; Dr. Anirban Manna, Senior Technician (2)

ADMINISTRATIVE SUPPORT DIVISION

Administrative Division

Group Members of Director's Secretariat

Controller of Administration

Administrative Officer

Group Members of Recruitment Section

Group Members of General Section

Group Members of Bill & Cash Section

Group Members of Establishment Section and Medical Cell

Security officer

Administration in CSIR Laboratories involves the management and organisation of resources, people and systems to achieve specific goals and objectives of the Council. It encompasses planning, decision making and implementation of policies and procedures to ensure efficient and effective operation in line with the Institute's mandate. Effective Administration enables organisations to deliver services, achieve outcomes and meet stake-holders' expectations.

The role of Administration is to provide support system to run the Institute smoothly by ensuring adherence and compliance with Govt. of India/CSIR guidelines issued from time to time. General Administrative matters are mainly dealt by concerned Sections of Recruitment, Bill/DDO, Establishment, General, Medical.

Recruitment Section including CR Cell and Legal Vigilance Cell 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. Also, CR, Vigilance and Legal Cell being under the overarch of the Recruitment Section, maintenance of records of performance appraisal, action under CCS (CCA) Rules and Conduct Rules and legal nitty gritty of the Institute are all catered by the Section.

Establishment Section deals with the matters pertaining to personal affairs, related to service records, like maintenance of service books, account of leave, Issue of Identity Certificate for passport, Issue of Employment Certificates, Permissions for study purpose and to apply for outside posts, Permission to travel by air in respect of non-entitled officials, Deputations within and outside CSIR, LTC, Leave Advance etc

Bill Section plays a pivotal role as liaison between Administration and Accounts and besides processing preparation of Monthly Salary/Stipend bills and Arrear Salary/Stipend, TA/DA Claims, Gratuities, effecting Recoveries from Playbills, 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. and it is not limited 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 car booking, bill processing, tendering regarding Hiring of cars/manpower/guest house/canteen & also monthly bills processing of the above mentioned services and also car procurement regarding matter. Air Ticket booking and bills processing for payment of those air ticket/other services like electricity, telephone. Booking of different Seminar hall and

auditorium of the Institute. Purchase of Swamy's handbook, observance of many special days like 26th Jan, 15th Aug, Foundation day (Both IICB and also CSIR), Communal Harmony, Swachhata Pakhawada,Yoga Day etc.

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.

The **Guest House in the CSIR-IICB TRUE Campus** under the aegis of Administration is fully operational now. All efforts to make the best utilisation of the facility was ensured by the Administration. The complete online system makes every booking simple, easy and time saving with 24x7 accessibility. Various in-house meetings, CSIR HRDC/RAB/sister lab led meetings are being held in this campus, regularly.

Human Resource:

Director Secretariat: Mrs. Pratima Banerjee, Private Secretary; Mr. Rabindranath Das, Private Secretary; Mr. Dinesh Mahali, Multi-Tasking Staff; Shri Rahul Dhar, JSA (G)

Administrative Secretariat: Ms. Sumana Majumdar, CoA; Mr. Amrendra Kumar, AO; Shri Kanu Mondal, AO

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; Mrs. Piyasha Kunkri, Junior Stenographer; Md. Farhan Qamar, JSA (G)

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; Shri Rounak Roy, JSA (G); Shri Rakesh Ranjan Kumar, JSA (G)

General Section: Mr. Manish Kr. Pandey, Section Officer (G); Mr. Tanumoy Sen, Senior Secretariat Assistant (Gen); Mr. Ram Kanai Mondal, Senior Secretariat Assistant (Gen); Mrs. Olivia Mondal, JSA(G); Shri Mainak Chakraborty, JSA(G); Shri Aashutosh Singh, ASO(G)

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); Shri Anick Sinha, ASO(G)

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

The Finance and Accounts Division of CSIR-IICB (Council of Scientific and Industrial Research – Indian Institute of Chemical Biology) plays a vital role in ensuring the efficient financial management and accountability of the institute. Its primary functions include budgeting, financial planning, and allocation of funds in accordance with CSIR guidelines and government regulations.

The division is responsible for maintaining accurate accounts of all financial transactions, processing salaries, pensions, and other employee-related financial matters, and ensuring timely payment to vendors and service providers. It also handles internal and external audits, tax compliance, and financial reporting to CSIR headquarters and other regulatory bodies.

Additionally, the division provides support in project accounting, ensuring proper utilization of project funds, and helps in formulating financial policies to enhance transparency and cost-efficiency in research and administrative activities of the institute.

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; Ms. Soumi Guhathakurta, Junior Stenographer; Mr. Pawan Kumar Agrawal, ASO; Mr. Rupam Samanta, JSA; Mr. Manoranjan Adhikari, JSA

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

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 2024-25 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 the Chairman of all the OLIC meetings every quarter (three months).

A quarterly Hindi workshop was organized on 28th May, 2024 (Tuesday) for the technical staffs. Shri Naveen Kumar Prajapati, Consultant, Central Translation Bureau, Ministry of Home Affairs, Kolkata was the speaker of this workshop, where the staff members were imparted training topic on **"Official translation and problem solving in technical aspects"**.

Hindi pakhwada was celebrated from 14th to 27th September 2024. 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 Day and Fourth All India Official Language Conference was organized on 14-15 September 2024 at Bharat Mandapam, Delhi. In which Senior Principal Scientist of the Institute Dr. Umesh Prasad Singh was present.

On 17 September 2024 (Tuesday), Hindi essay and note and draft writing competition was organized in which the staff and researchers of the Institute participated. Mr. L.K. Singh, Hindi Teacher, Hindi Teaching Scheme, Nizam Palace, Kolkata was present as the judge of both these competitions.

Hindi Debate Competition was organized on 18th September, 2024 whose judges were Mr. Mantu Das, Assistant Professor, Hindi Department, Rani Birla Girls College, Kolkata and Dr. Sunanda Rai Choudhary, Associate Professor(Former), Hindi Department, Yogesh Chandra Choudhary College, Kolkata.

On September 23, 2024, a Hindi workshop was organized for administrative staff on the topic 'Official Language Policy and Responsibilities of Union Government' which was conducted by Shri Priyankar Paliwal, Former Senior Hindi Officer, CSIR- Central Glass & Ceramic Research Kolkata & now Consultant, Bharatiya Vidya Mandir.

Hindi Pakhwada closing ceremony and prize distribution program was organized on 27 September 2024. The chief guest of the program was Dr. Rishikesh Roy, Secretary-in-charge and Deputy Director (Official Language), Tea Board, Kolkata and the special guest was Dr. Satya Upadhyay, Principal, Calcutta Girls College, who were welcomed by the Chief Scientist of the Institute, Dr. P. Jaishankar.

The participants who got first, second and third place in all the competitions held from 14 to 27 September 2024 were awarded. Apart from this, the participants who took part in all the competitions were also honored with participation awards. Employees who used more than 10,000 Hindi words for office work also were awarded.

The employees and researchers present in the auditorium of the institute were asked to write a word starting with 'ज' in Hindi and were rewarded for writing the correct word. All the people present were very impressed with the lectures of the chief guest of the program Dr. Rishikesh Roy and the special guest Dr. Satya Upadhyay. In the end, the program concluded successfully with the vote of thanks by the Administrative Officer of the institute, Ms. Sumana Majumdar.

A quarterly Hindi workshop was organized on 24 December, 2024 (Tuesday) for the scientific staff members. Staff members were imparted training topic on “Word Processing on Computer”. The workshop was conducted by Sri Anoop Kumar, Assistant Director, Hindi Teaching Scheme, Ministry of Home Affairs.

A quarterly Hindi workshop was organized on 18th March, 2025 (Tuesday) for the technical staff members. The topic was **“Official translation and problem solving in technical aspects”**. The workshop was conducted by Sri Anoop Kumar, Assistant Director, Hindi Teaching Scheme, Ministry of Home Affairs.

OUTREACH PROGRAMMES

Skill Development Programme

Core members of Skill Development Programme

CSIR Integrated Skill Initiative: Empowering the Future

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 curated 14 high end R&D laboratory oriented training courses. These courses provides an opportunity to our youth for hands-on-training, scientific knowledge, analytical perspective & technical skill for understanding the latest technologies used in a research field. The trainees receive 2-weeks exposure in different skilling programs in various advanced areas of IICB expertise through lectures and practical sessions.The program is led by a team of experienced and renowned faculty members ,who have expertise in their respective fields.They ensure high-quality training and guidance for all participants. Participants get the chance to network with peers and experts in the field through seminars, conferences and interactive sessions. Our program fosters industry and research organisations and enhances employability in sectors related to Biopharmaceutics, Biotechnology, Molecular Biology, Chemistry Bioinformatics and more.

The Courses conducted under CSIR Integrated Skill Development Programme at CSIR-IICB are:

1. Technique for 3D structure reconstruction from Cryo-Electron Microscopy dataset of biological samples
2. High end equipment for clinical applications -Flow cytometry
3. Liquid Chromatography-Mass Spectrometry
4. Clinical Biochemistry, Microbiology and Pathology techniques for biomedical applications
5. High end equipment for clinical applications-Optical Microscopy

6. Nuclear Magnetic Resonance Spectroscopy
7. Real time PCR (Duration:1 week)
8. Protein X-ray crystallography
9. Gas Chromatography Mass Spectrometry
10. Molecular Cloning, Protein expression and structural characterization
11. Separation Techniques for organic molecules
12. Advanced Bioinformatics
13. High Performance Liquid Chromatography
14. X-ray crystallography (Small Molecules)

Skill Development Sessions 2024-2025

In 2024-2025, CSIR-IICB offered 39 certificate courses under its Skill Development Programme through 3 sessions.

The sessions were structured as follows:

First Session (June 2024)

14 skill courses conducted in parallel (conducted from 3rd June to 14th June 2024).

Second Session (Sept 2024)

13 skill courses conducted in parallel (conducted from 2nd Sept to 13th Sept 2024).

Third Session (Jan 2025)

12 skill courses conducted in parallel (conducted from 6th Jan to 17th Jan 2025).

The Courses conducted and Number of Candidates trained during the 2024-25 are tabulated below:

Course	Session-I	Session-II	Session-III	Grand Total
Technique for 3D structure reconstruction from Cryo-Electron Microscopy dataset of biological samples	04	05	05	14
High end equipments for clinical applications -Flow cytometry	12	11	06	29
Liquid Chromatography-Mass Spectrometry	10	06	07	23
Clinical Biochemistry,Microbiology and Pathology techniques for biomedical applications	08	09	08	24
Nuclear Magnetic Resonance Spectroscopy	06	04	07	17
High end equipments for clinical applications-Optical Microscopy	07	06	06	19
Real time PCR (Duration:1 week)	10	10	09	29
Protein X-ray crystallography	10	05	-	15
X-Ray crystallography (Small molecules)	02	04	02	08
Gas Chromatography Mass Spectrometry	06	03	08	17
Molecular Cloning,Protein expression and structural characterization	11	11	12	34
Separation Techniques for organic molecules	04	-	06	22
Advanced Bioinformatics	10	10	15	35
High Performance Liquid Chromatography	07	07	-	14
Total	**107**	**91**	**91**	**289**

Glimpses of CSIR-IICB Skill Development Programme

Practical sessions during Skill Development Programme

Training Program on Course-Real time PCR

Training Program on Course-Protein X-ray crystallography

Training program on Course-Cryo EM:Sample optimization and 3D structure reconstruction

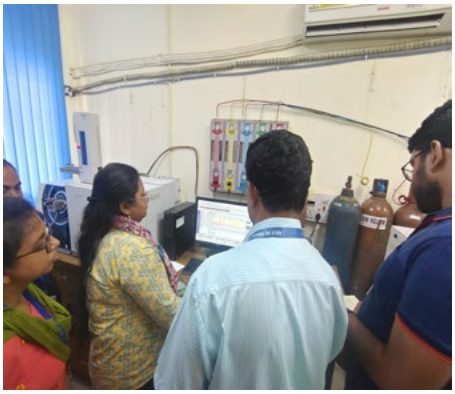
Training program on Course-Molecular Cloning,Protein expression and structural characterization

Training program on Course-Liquid Chromatography-Mass Spectrometry

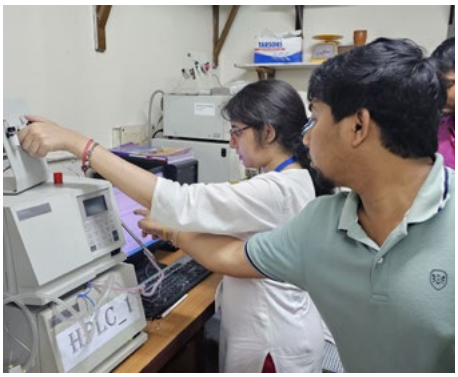
Training program on Course-Nuclear Magnetic Resonance Spectroscopy

Training program on Course-Separation Techniques for organic molecules

Training Program on Course-Advanced Bioinformatics



Training Program on Course-Gas Chromatography Mass Spectrometry



Training Program on Course-High Performance Liquid Chromatography

Training program on High end equipment for clinical applications -Flow cytometry

Training Program on Course-Clinical Biochemistry,Microbiology and Pathology techniques for biomedical applications

Skill Development Programme Valedictory Day

Training session conducted from June 03-14, 2024

Training session conducted from September 02-13, 2024

Training session conducted from Jan 6 -17, 2025

Glimpses of course completion certificate received by trainees

CSIR Jigyasa Programme

CSIR-IICB Team members of CSIR Jigyasa Progmmme

The **CSIR Jigyasa Programme** is a pioneering initiative of the **Council of Scientific and Industrial Research (CSIR)** aimed at connecting the scientific community with school students to ignite curiosity, innovation and a spirit of inquiry. Through this programme, CSIR laboratories across the country collaborate with schools to promote scientific temperament and hands-on learning among young minds.

As a key contributor to this national mission, **the CSIR-Indian Institute of Chemical Biology (CSIR-IICB), Kolkata** plays a vital role in bringing science closer to students. With its rich legacy in biomedical and chemical research, CSIR-IICB actively engages with school students through interactive sessions, laboratory visits, scientific demonstrations and mentorship opportunities. The institute opens its doors to inquisitive learners, encouraging them to explore the fascinating world of life sciences and interdisciplinary research.

CSIR-IICB's participation in the Jigyasa programme reflects its commitment to nurturing future scientists and promoting a culture of scientific inquiry. By bridging the gap between classroom learning and real-world research, the institute contributes meaningfully to the development of a scientifically empowered nation.

Various outreach programmes for science awareness under CSIR Jigyasa banner, during 2024-25, are listed below:

1. An outreach activity was organized under CSIR Jigyasa program at CSIR-IICB on May 29, 2024. Students from Kachiamara Hemchandra High School, Kultali, South 24 parganas, were shown interesting chemical reactions in one of the Chemistry Laboratory of CSIR-IICB. The working principle and analysis procedure of confocal microscope and XRD were also demonstrated to them.

2. 'The Wonder of Chemistry: Magic Show' by Dr. Indu Bhusan Deb, Senior Principal Scientist, CSIR-IICB for the student participants of the Annual Day Celebration of Kolkata Nivedita Shakti, was organized under CSIR Jigyasa Programme on June 12, 2024.

3. Under CSIR-Jigyasa programme, two lectures were arranged at Lakshminarayanpur Sitanath High School (H.S.), Mathurapur -1 Block, South 24parganas on July 03, 2024. Dr. Saikat Majumder, Senior Scientist, CSIR-IICB talked about the 'Immunology of B and T cells'. In addition, Dr. Ashim Paul, Senior Scientist, CSIR-IICB delivered a lecture on the 'Chemistry of molecules and Biomolecules in daily life'.

4. An outreach programme was organized at Narayanpur High School, South 24 parganas on July 11, 2024 under CSIR Jigyasa banner. Dr. Jayati Sengupta, Senior Principal Scientist, CSIR-IICB delivered a Lecture on 'The astounding molecular machine for protein synthesis inside living cells: The ribosome' while Dr. Indu Bhusan Deb, Senior Principal Scientist, CSIR-IICB demonstrated some Chemistry experiments to the students.

5. Students of Satish Chandra Memorial School, Chakdaha, Nadia, West Bengal visited CSIR-IICB on August 23, 2024 under CSIR Jigyasa Programme.

6. Two CSIR Jigyasa Programmes were conducted on August 20, 2024 at Chinsurah Deshbandhu Memorial High School (H.S.) and Chinsurah Balika Bani Mandir (H.S.). In both schools, Dr. Krishnananda Chattopadhyay, Chief Scientist, CSIR-IICB delivered lectures on Neurodegenerative Diseases, which were followed by Quiz Contests.

7. Students from Kaswara Yeasin Mondal Sikshaniketan, Hooghly visited CSIR-IICB under CSIR Jigyasa programme on October 03, 2024.

8. On the occasion of 83rd CSIR Foundation Day, an Open House Programme for school children was organized on September 26, 2024 at CSIR-IICB under CSIR Jigyasa Banner.

9. As a part of the OWOT event an outreach programme was organized at CSIR-IICB on November 12, 2024. Students from Jadavpur Vidyapith visited CSIR-IICB during the occasion.

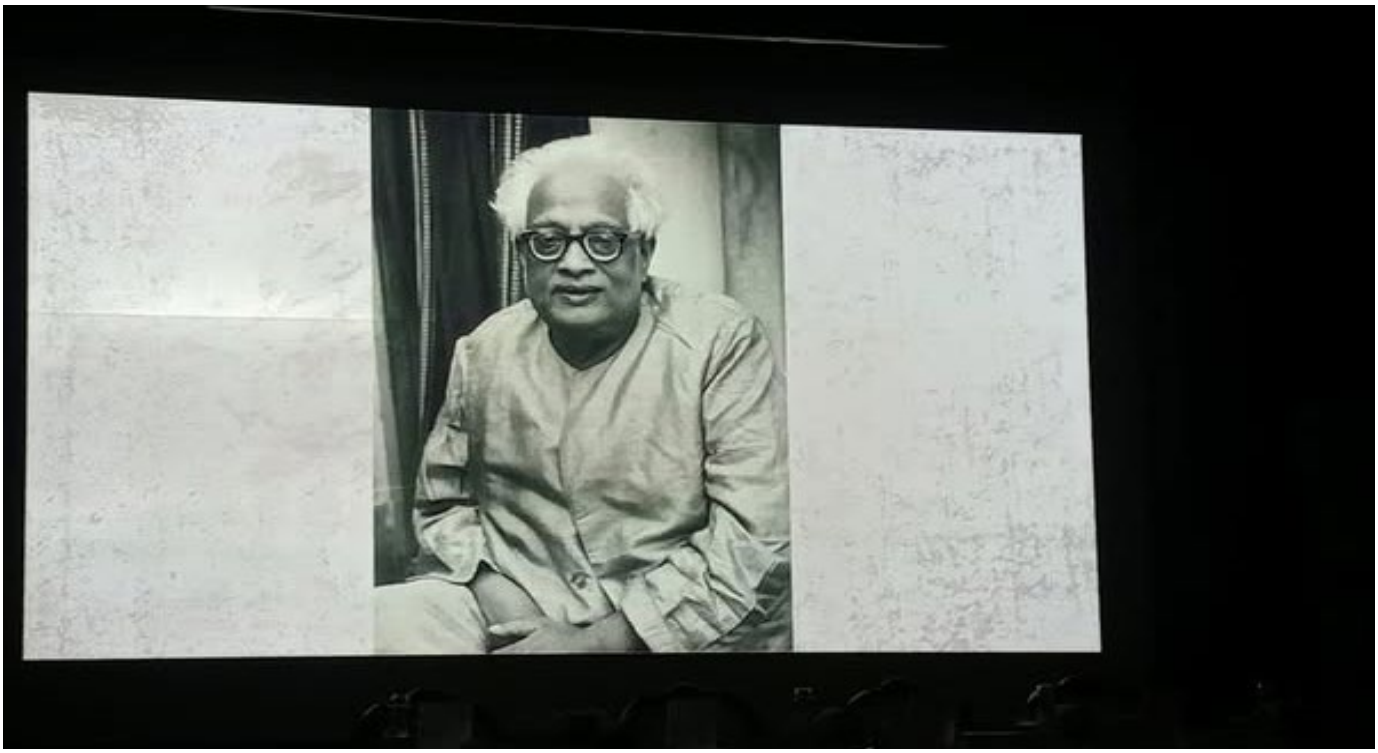
10. An outreach programme was organized under CSIR Jigyasa banner at PM Shri Kendriya Vidyalaya Santragachhi, Howrah on December 13.12.2024. Dr. Sib Sankar Roy, Chief Scientist, CSIR-IICB and Dr. Sarita Ghosh, Senior Principal Scientist and Jigyasa Nodal from CSIR-IICB visited KV Santragachi to organise the event. Dr. Roy delivered a lecture on 'Curiosity Driven Scientific Research in Disease Biology'.

11. CSIR Jigyasa Scientific Aptitude Assessment for the school students was organized at CSIR-IICB on December 20, 2024. Total 30 students from PM Shri Kendriya Vidyalaya Santragachi and PM Shri Kendriya Vidyalaya No 2, Saltlake participated in the event. Dr. Sarita Ghosh, Senior Principal Scientist and Jigyasa Nodal from CSIR-IICB, Dr, Saikat Majumder, Senior Scientist, Dr. Smrutisanjita Behra, Scientist, Dr. Debasis Nayak, Scientist and Dr. Anirban Manna, Senior Technician (2) actively participated to make the event successful.

12. Students from G.D. Birla Centre for Education visited CSIR-IICB, Saltlake campus on January 29, 2025 under CSIR Jigyasa programme.

13. Students from eight different schools visited CSIR-IICB, Jadavpur campus on January 30, 2025 under CSIR Jigyasa programme.

14. On the occasion of National Science Day, a Screening of a Movie on Professor Satyendra Nath Bose was organized on February 28, 2025 under CSIR Jigyasa Programme



15. A CSIR Jigyasa programme was organized on March 19, 2025 at Narayantala Ramkrishna Vidyamandir, Narayantala, Basanti, South 24 Parganas. Two Lectures were delivered on 'তথ্য অনেক কিন্তু সত্য এক' (There are many facts but only one truth) by Dr. Rupasri Ain, Chief Scientist, CSIR-IICB and on 'Basic concepts of stereochemistry of organic compounds' by Dr. Sarita Ghosh, Senior Principal Scientist, CSIR-IICB.

Other Outreach Programmes

1. Fourth Semester MSc students from the Department of Human Physiology, Vidyasagar University and M.Sc.Environmental Science Students from University of Calcutta visited CSIR-IICB for the Educational Tour on April 25, 2024.

2. As a part of scientific social responsibilities (SSR) under the Core Research Grant no. CRG/2021/006717, SERB, DST, Govt. of India, a workshop on "Careers in Chemical Sciences" was arranged by Dr. Ranjan Jana, Sr. Principal Scientist, CSIR-IICB on 23rd July at CSIR-IICB. Students from Mahishadal Gayeswari Girls' High School, Mahishadal, Purba Medinipur, West Bengal, India joined in the workshop.

3. Students from the Department of Chemistry, Sitananda College, Purba Medinipur, visited CSIR-IICB Jadavpur Campus for an educational tour on January 17, 2025. The Royal Society of Chemistry, Eastern India Section will bear the travel expenses for the tour.

4. Students from Department of Botany, Berhampur University, Berhampur, Odisha visited CSIR-IICB, Jadavpur campus on March 4, 2025.

5. Twenty students from Microbiology and Bioinformatics Department, Atal Bihari Vajpayee University, Bilaspur, Chhattisgarh visited CSIR-IICB, Jadavpur campus on March 18, 2025.

VISIT OF DIGNITARIES AND OTHER EVENTS


68th CSIR-IICB Foundation Day was celebrated in a befitting manner on April 02, 2024. Prof. Vinod Kumar Singh, Padma Shri awardee, Namita Gautam Chair Professor, Department of Chemistry, IIT-Kanpur, and Chairperson of the Recruitment & Assessment Board (RAB) at CSIR graced the occasion as Chief Guest. Prof. Aditya Prasad Dash, Padma Shri awardee, Ex-Vice Chancellor, Central University of Tamil Nadu and the Mentor of CSIR-IICB, was present as the Guest of Honour of the programme. A 'Science and Magic Workshop' was conducted in the afternoon by Prof. Anil Kumar from the Department of Chemistry, IIT Bombay, Powai, Mumbai.

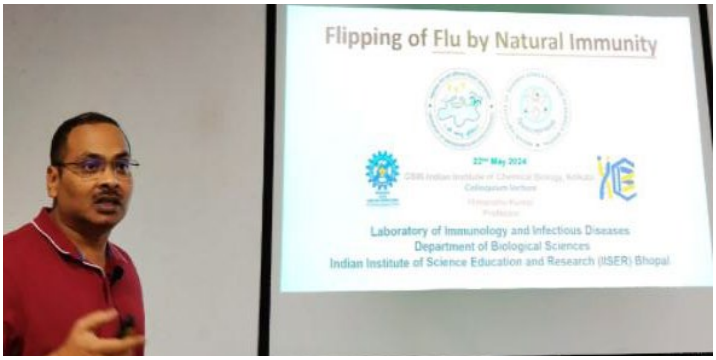
A delegation from the National Academy of Sciences, Belarus visited CSIR-IICB to explore opportunities of bilateral scientific cooperation.

"The Swachhata Pakhwada 2024" is being observed at CSIR-IICB from 1st May to 15th May, 2024.



CSIR-IICB celebrated 'Rashtriya Boudhik Sampada Mahotsav' & World Intellectual Property Day. An interactive program on the theme "Patent Filing and Informatics for Students and Researchers" on May 10, 2024.

CSIR-IICB celebrated National Technology Day on May 13, 2024. Professor Kaustuv Sanyal, Director, Bose Institute, Kolkata delivered a special lecture on 'The Centromere Code Hypothesis'.



Prof. Himanshu Kumar, Professor and Head, Biological Sciences, Laboratory of Immunology & Infectious Disease Biology, IISER Bhopal delivered a colloquium lecture on May 22, 2024

AcSIR Science Club@CSIR-IICB was inaugurated on May 23, 2024 CSIR-IICB, Kolkata. Prof. Manoj Kumar Dhar, Director, AcSIR graced the occasion as Chief Guest.

Mr. Sanjeev Kumar, Director, Communication and Information Services, JNU, New Delhi delivered a lecture on "Use of e-office and other ICT Applications in the Institution on May 24, 2024

Dr. Shashi Gujar, Executive Director, Cancer Immunotherapy, Innovation & Global Partnerships, Faculty of Medicine, Dalhousie University, Canada, delivered a guest lecture on May 24, 2024

सीएसआईआर-भारतीय रासायनिक जीवविज्ञान संस्थान में दिनांक 28 मई, 2024 को तकनीकी कर्मचारियों के लिए हिंदी कार्यशाला का आयोजन किया गया।

Professor Uday Maitra, Department of Organic Chemistry, Indian Institute of Science (IISc), Bangalore, delivered a special lecture on 'From a Chemical Curiosity to a Portable Device', which was followed by a science magic show, "Chemistry is Fun" on June 04, 2024

CSIR-IICB organized the International Day of Yoga (IDY) countdown event on June 6, 2024

Prof. Amit Kumar from the Department of Chemistry of IIT Patna, delivered a lecture on 'Glycosylation and Glycodiversification: An Important Aspect of Carbohydrate Chemistry' on June 11, 2024

The 10th International Yoga Day was celebrated at CSIR-IICB on June 21, 2024

CSIR-IICB organised a three-day induction workshop on GLP Principles during June 25-27, 2024

CSIR-IICB, Kolkata, conducted the 2nd Workshop for Handling and Care of Laboratory Animals during July 1-5, 2024 at CSIR-IICB, Salt Lake Campus

Prof. Jayanta Chatterjee, Associate Professor, Molecular Biophysics Unit (MBU) of the Indian Institute of Science, delivered a Special Guest Lecture on "From super secondary structures to antibody engineering: Our journey with reverse turns" on July 8, 2024

Dr. Rajan Sankaranarayanan, Outstanding Scientist from CSIR-CCMB, Hyderabad, delivered a lecture on 'Chiral proofreading during protein biosynthesis and its evolutionary implications' as a part of the Colloquium Lecture Series-Biology: 2024-25 on July 10, 2024

Dr. Phalguni A. Alladi, Scientist-F from NIMHANS, Bangalore, delivered a Special Guest Lecture on "Comprehending Parkinson's Disease: our Basic & Translational Approaches" on July 18, 2024

CSIR-IICB celebrated 'National Sports Day' on August 29, 2024.

CSIR-IICB participated in the Global Bio-India 2024, currently being held in New Delhi, with a focus on leveraging bio-partnering opportunities, and building network within the Biotech sector.

सीएसआईआर-आईआईसीबी कोलकाता में हिंदी पखवाड़ा कार्यक्रम के अंतर्गत दिनांक 18/09/2024 को वाद-विवाद प्रतियोगिता का आयोजन किया गया। इस प्रतियोगिता के निर्णायक के रूप में डॉ. सुनंदा राय चौधरी, एसोसिएट प्रोफेसर, हिंदी विभाग (पूर्व), योगेश चंद्र चौधरी कॉलेज एवं श्री मंटू दास, सहायक प्रोफेसर, रानी बिड़ला गर्ल्स कॉलेज, कोलकाता उपस्थित थे।

BIC & NNP Bioinformatics Workshop/ Annotation Jamboree 2025 was organised during September 23 - 28, 2024

CSIR-IICB celebrated 83rd CSIR Foundation Day on September 30, 2024. Prof. Santishree Dhulipudi Pandit, the Vice Chancellor of Jawaharlal Nehru University, New Delhi and CSIR Society member graced the occasion as the Chief Guest. Professor Aditya Prasad Dash, Padmashri Awardee and the mentor of CSIR-IICB, was present as the Guest of Honor. The foundation day Lecture was delivered by Prof. Praveen K. Vemula from iBRIC-inStem.

An awareness workshop on Ethics in Research, was organised on October 03, 2024 at CSIR-IICB. Prof. Chandrima Shaha, J. C. Bose Chair Distinguished Professor and Dr. Syamal Roy, ICMR Emeritus scientist addressed the gathering on the occasion.

Prof. Srinivas M, Director AIIMS, New Delhi and CSIR council member along with a team of AIIMS researchers/clinicians visited CSIR-IICB on October 20, 2024 for a collaborative research meeting.

Two-day training programme on e-procurement during 20-21 September, 2024, as a part of the three-months long campaign on preventive vigilance. Shri Sailesh Kumar Soni, Deputy Director, ISTM, DoPT, New Delhi was present as the expert.

The 9th Ayurveda Day was celebrated at the CSIR-IICB, Salt Lake Campus, Kolkata, on October 25, 2024, in collaboration with the Central Ayurveda Research Institute (CARI), Kolkata.

On October 29, 2024 the entire community of CSIR-IICB came together to celebrate fitness and unity at the Fit India Swachhta Freedom Run 5.0!

CSIR-IICB hosted a Curtain Raiser Event of India International Science Festival (IISF) on October 29, 2024, with three extremely fascinating Guest Lectures by Prof. Gobardhan Das, Director, IISER Bhopal, Prof. Avanish Kumar Srivastava, Director, CSIR-AMPRI, Bhopal, and Prof. Irishi N. N. Namboothiri, Senior Professor, Department of Chemistry, IIT Bombay.

CSIR-IICB at the CSIR pavilion of IISF Expo 2024 at IIT Guwahati, Assam during November 30 – December 3, 2024

Celebration of Janjatiya Gaurav Divas on November 15, 2024 and Janjatiya Gaurav Varsh and 150th Birth Anniversary of Bhagwan Birsa Munda at CSIR-IICB, Kolkata

The 'Health Care - Thematic Conclave on Mental Health and Well-Being' was organised at CSIR-IICB as a part of the 'One Week, One Theme' (OWOT) campaign aims to highlight innovative technological advancements across CSIR's network of laboratories during November 11-12, 2024. Dr. Jitendra Singh, the Hon'ble Minister of Science and Technology and Earth Sciences, delivered a video address. Dr. N. Kalaiselvi, Director General of CSIR and Secretary of DSIR, formally inaugurated the conclave at Dr. J.C. Ray Auditorium, CSIR-IICB, Kolkata. The event attracted leaders from academia, industry, clinical settings, and non-profit organizations engaged in dementia and related mental health research. A highlight of the program was a panel discussion focusing on the opportunities and challenges of translational research in healthcare. Additionally, poster presentations by young researchers and visits from school and college students added to the event's dynamic and inclusive nature. A MoU was exchanged between CSIR-IICB and Albert David Ltd. on the occasion.

Dr. Rahul Purwar, Professor, Department of Biosciences and Bioengineering, IIT Bombay delivered a Colloquium Lecture on November 22, 2024

Dr. Rakesh K Tyagi, Professor, Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi delivered a Special Guest Lecture on 'Genomic bookmarking by nuclear receptors: a novel dimension in epigenetic control' on December 6, 2024

A scientific talk on 'Structure guided design to enhance stability and efficacy of viral vaccines' was delivered by Prof. R. Varadarajan from IISc, Bangalore on December 20, 2024 at CSIR-IICB, Kolkata.

सीएसआईआर-आईआईसीबी में दिनांक 24 दिसंबर, 2024 (मंगलवार) को वैज्ञानिक कर्मचारी सदस्यों के लिए हिंदी कार्यशाला का आयोजन किया गया। श्री अनुप कुमार, सहायक निदेशक, हिंदी शिक्षण योजना, गृह मंत्रालय इस कार्यशाला के वक्ता के रूप में उपस्थित थे।

CSIR-IICB hosted a 6-Day CME Program, sponsored by The Ministry of AYUSH, on "Reverse Pharmacology of Traditional Medicine using Modern Biomedical Techniques," during February 3-8, 2025

2nd Collaborative Research Meeting with AIIMS, New Delhi was held on February 9, 2025 at CSIR-IICB

On February 26, 2025, the CSIR Vigyan Rath visited CSIR-IICB, Kolkata.

National Science Day celebration on February 28, 2025. Prof. Ullas Kolthur-Seetharam, Director of CDFD, Hyderabad, was the Chief Guest and Prof. Ashutosh Ghosh, former VC, University of Calcutta was the Guest of Honor.

Prof. Seyed E. Hasnain, Padma Shri Awardee, Distinguished Professor at Sharda University, NCR and National Science Chair at IIT, Delhi delivered a Special Colloquium Lecture on March 3, 2025 at CSIR-IICB, Kolkata.

International Women's Day was celebrated at CSIR-IICB, Kolkata throughout March 04-13, 2025

CSIR-IICB participated in the celebration of the 130th Birth Anniversary of Satyendra Nath Bose and the centenary year of Bose-Einstein statistics, during March 8-9, 2025, at IIT Kharagpur Research Park, Kolkata, West Bengal.

A colloquium lecture on 'Targeting Metabolic Vulnerability in Acute Myeloid Leukemia' was delivered by Dr. Vikram Mathews, Director & Senior Professor Dept. of Haematology, Christian Medical College, Vellore, on March 28, 2025.

KEY PERFORMANCE INDICES

Awards/Honours

Sl. No.	Awardee	Award
1	Prof. Vibha Tandon, Director	Received the 1st AV Rama Rao Award for her contribution in Chemical Sciences on the occasion of 33rd CRSI National Symposium in Chemistry and CRSI-ACS Lectures organized by Dr. Reddy's Laboratories Ltd. during July 04 - 06, 2024.
2	Dr. Subhas Chandra Biswas, Chief Scientist	Elected as a fellow of The National Academy of Sciences, India
3	Dr. Debabrata Biswas, Senior Principal Scientist	Elected as member of the Guha Research Conference 2024
4	Dr. Dipyaman Ganguly, Senior Principal Scientist	Elected as member of the Guha Research Conference 2024
5	Dr. Subhajit Biswas, Principal Scientist	Elected as a fellow of West Bwngal Academy of Science and Technilogy 2025
6	Dr. Aakriti Garg, Project Associate II	Young Researcher Award 2024 (1st Rank) in Pharmaceutical Sciences for excellence in research work presented in Fifth Science Conclave-cum-National Biomedical Research Competition (NBRCOM), 20224 by Society of Young Biomedical Scientists, India
7	Dr. Deepshikha Ghosh, Project Associate II	Young Researcher Award 2024 (4th Rank) in Oral Presentation (Life Sciences) in Fifth Science Conclave-cum-National Biomedical Research Competition (NBRCOM), 20224 by Society of Young Biomedical Scientists, India
8	Ms. Priyanka Panigrahi, SRF	Young Researcher Award 2024 (4th Rank) in Oral (Virtual) Presentation (Health Science) in Fifth Science Conclave-cum-National Biomedical Research Competition (NBRCOM), 20224 by Society of Young Biomedical Scientists, India
9	Mr. Subhajeet Dutta, SRF	ISME19 Travel Grant, ANRF-SERB and CSIR Foreign Travel Grant to present our work in the 19th International Symposium on Microbial Ecology (ISME19), Cape town, South Africa, 18-23 August, 2024.
10	Ms. Aribam Geeta, SRF	Federation of European Microbiological Society travel award, DBT CTEP travel award and ANRF SERB travel award to present our research work in European Workshop on the Biology of Cyanobacteria EWBC2024) in Seville, Spain, from September 3-6, 2024.
11	Mr. Asharani Prusty, Project Associate	ISME19 Travel Grant for attending 19th International Symposium on Microbial Ecology (ISME19), Cape town, South Africa, 18-23 August, 2024.
12	Ms. Shreya Sen Sarma, DST-WISE, PhD Fellow	Young Researcher Award-2024, at 11th Convention, Society for Ethnopharmacology, India [SECON-2024], November 15-16, 2024, Gangtok, Sikkim, India
13	Mr. Biswajit Singh, Project Assistant	RSC-Best poster award – 2024, at 11th Convention, Society for Ethnopharmacology, India [SECON-2024], November 15-16, 2024, Gangtok, Sikkim, India
14	Ms. Somashree Bose, SRF	Received First Prize for Poster Presentation at 'Emerging Trendes in Advanced Materials (ETAM 0225)' held at CSIR-CGCRI, Kolkata during February 6-7, 2025
15	Ms. Ashmita Mukherjee, SRF	Financial Assistance from Science and Engineering Research Board for participating in "Termis World Congress, USA (25 June, 2024 to 28 June, 2024)"
16	Mr. Souradip Paul, SRF	Awarded a grant to completely offset his student dues for onsite boarding, lodging and registration for attending 'EMBO Workshop CELLULAR MATTERS: A deeper look into the complex cytoplas' going to be held on May 18-22, 2025. (Award letter dated 12.3.2025)

List of MoU Signed and agreements during 2024-25

Sl. No.	Name of the Party/Company with Address	Type of Agreement	Date of Execution
1	ICAR-Indian Institute of Rice Research Dr. Smrutisanjita Behera	Material Transfer Agreement	17.05.2024
2	Depart of Biotechnology (DBT) Dr. Siddhartha Roy	Memorandum of Agreement for Research Support (Grant-In-Aid)	25.06.2024
3	Depart of Biotechnology (DBT) Dr. Sourish Ghosh	Memorandum of Agreement for Research Support (Grant-In-Aid)	02.07.2024
4	Depart of Biotechnology (DBT) Dr. Sucheta Tripathy	Memorandum of Agreement for Research Support (Grant-In-Aid)	02.07.2024
5	Depart of Biotechnology (DBT) Dr. Sucheta Tripathy	Memorandum of Agreement for Research Support (Grant-In-Aid)	02.07.2024
6	Depart of Biotechnology (DBT) Dr. Joy Chakraborty	Memorandum of Agreement for Research Support (Grant-In-Aid)	09.07.2024
7	Depart of Biotechnology (DBT) Dr. Sudipta Das	Memorandum of Agreement for Research Support (Grant-In-Aid)	17.09.2024
8	Indian Institute Of Science Education and Research, IISER, Bhopal	Memorandum of Agreement for Research Collaboration	30.09.2024
9	Symbol Discovery Ltd.	Non-Disclosure Agreement (NDA)	09.10.2024
10	Albert David Limited.	Non-Disclosure Agreement (NDA)	11.11.2024
11	LifeCare Innovations Pvt. Ltd.	Non-Disclosure Agreement (NDA)	16.12.2024
12	Depart of Biotechnology (DBT) Dr. U. Mabalirajan	Memorandum of Agreement for Research Support (Grant-In-Aid)	19.02.2025

Patents Filed/Granted 2024-25

Granted in India

Sl. No.	Country	Title	Inventors	Comp. Filing Date	Application No.	Grant Date	Patent No.
1	India	Quinazolinones Derivatives for Treatment of Non-Alcoholic Fatty Liver Disease, Preparation and Use Thereof	Talukdar Arindam, Chakrabarti Partha, Sarkar Dipayan, Chowdhury Saheli, Goon Sunny, Das Subrata, Das Nirmal, Sarkar Dipika	29-Jun-2020	202011027502	26-Mar-2025	563803

Granted Abroad

Sl. No.	Country	Title	Inventors	Grant Date	Patent No.
1	Kenya	An Easy-To-Use Diagnostic System for Rapid Dengue Virus Detection Using Fluorescence-Based Molecular Probes	Biswas Subhajit, Ghosh Surajit, Sukla Soumi, Mondal Prasenjit	15-May-2024	KE 1006

Filed in India

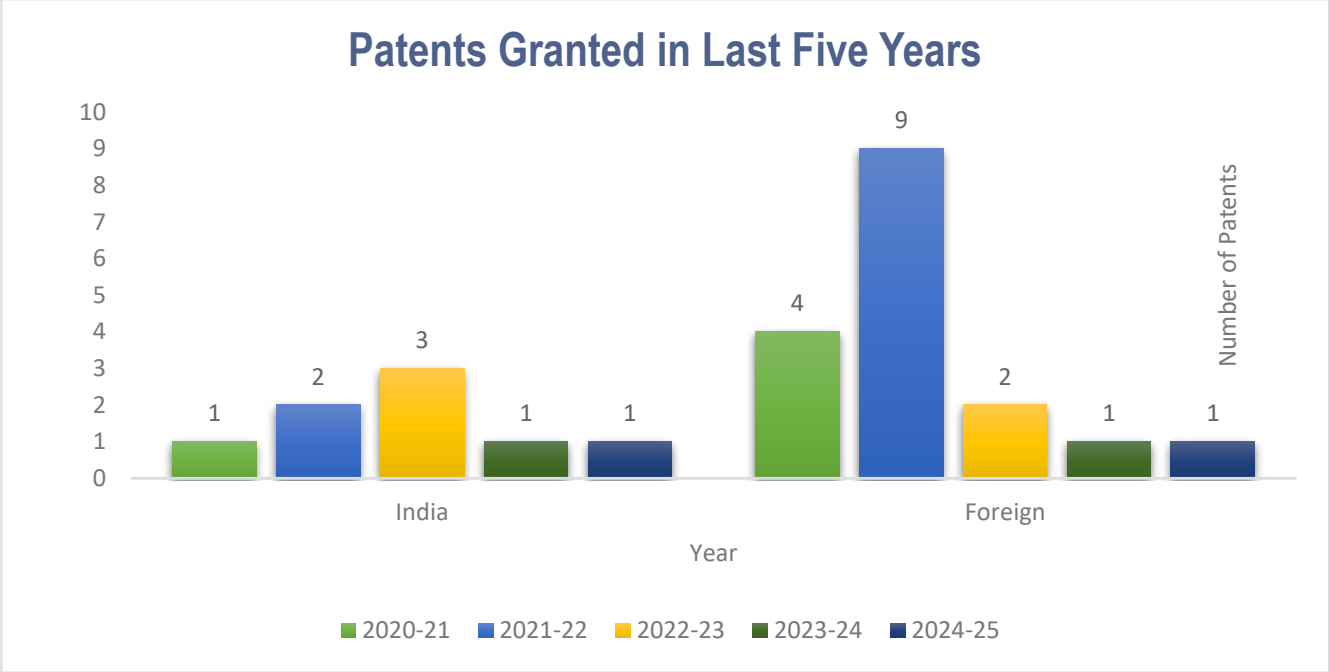
Sl. No.	Title	Inventors	Prov. Filing Date	Comp. Filing Date	Application No.
1	Process for Synthesis of Mandipropamid	Indrajit Das, Jayanta Saha, Sumit Biswas, Subhadeep Ghosh	---	26-Apr-2024	202411033733
2	Green Synthesis of Green Fluorescent Silver Nanodots Capped with Naringenin	Nakul Chandra Maiti, Anupam Maity, Uttam Pal, Kaushik Bera, Shubham Kundu, Rajdip Misra, Krishnendu Khamaru, Mrinmay Bhunia	24-May-2024	29-Apr-2025	202411040868
3	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-Jul-2024	05-Mar-2025	202411016656
4	Composition for Treating Ovarian Cancer and A Preparation Method Therefor	Deepak Kumar, Amit Kumar Srivastava, Sib Sankar Roy, Shreya Sen Sarma, Subhankar Bose	13-Sep-2024	---	202411045945
5	An Improved Process for Synthesis of Trifloxystrobin	Indrajit Das, Abhijit Bankura, Subhadeep Ghosh, Sumit Biswas, Jayanta Saha, Kumaresh Das	---	03-Oct-2024	202411075609
6	An Antiviral Compound and Process for Preparation Thereof	Subhadeep Palit, Bhim Majhi, Rimita Saha, Sanjay Dutta	---	11-Nov-2024	202411087083
7	2-Phenyl Indole Compounds As Anti-Viral Agents, Preparation and Use Thereof	Arindam Talukdar, Binita Patra, Israful Hoque, Nirmal Das, Biswajit Kundu, Krishan Gopal Thakur, Rajesh Ringe, Nittu Singh, Akshay Joshi, Ravneet Singh Chawla, Bokara Kiran Kumar, Alna Kuriyickal Martin, Yogesh Sardana, Renuga Devi, Balamurugan Kanagasabai, Uddipta Ghosh Dastidar, Soupayan Pal, Trisha Ghosh, Dipyaman Ganguly, Jafar Sarif	---	30-Jan-2025	202511008623
8	Improved Synthetic Method for 6-Acetyl-8-Cyclopentyl-5-Methyl-2-Substituent-Pyrido[2,3-D]Pyrimidin-7(8H)-One, A Key Intermediate in the Manufacture of Palbociclib	Indubhusan Deb, Moumita Saha, Koushik Naskar, Writhabrata Sarkar	---	28-Feb-2025	202511018215

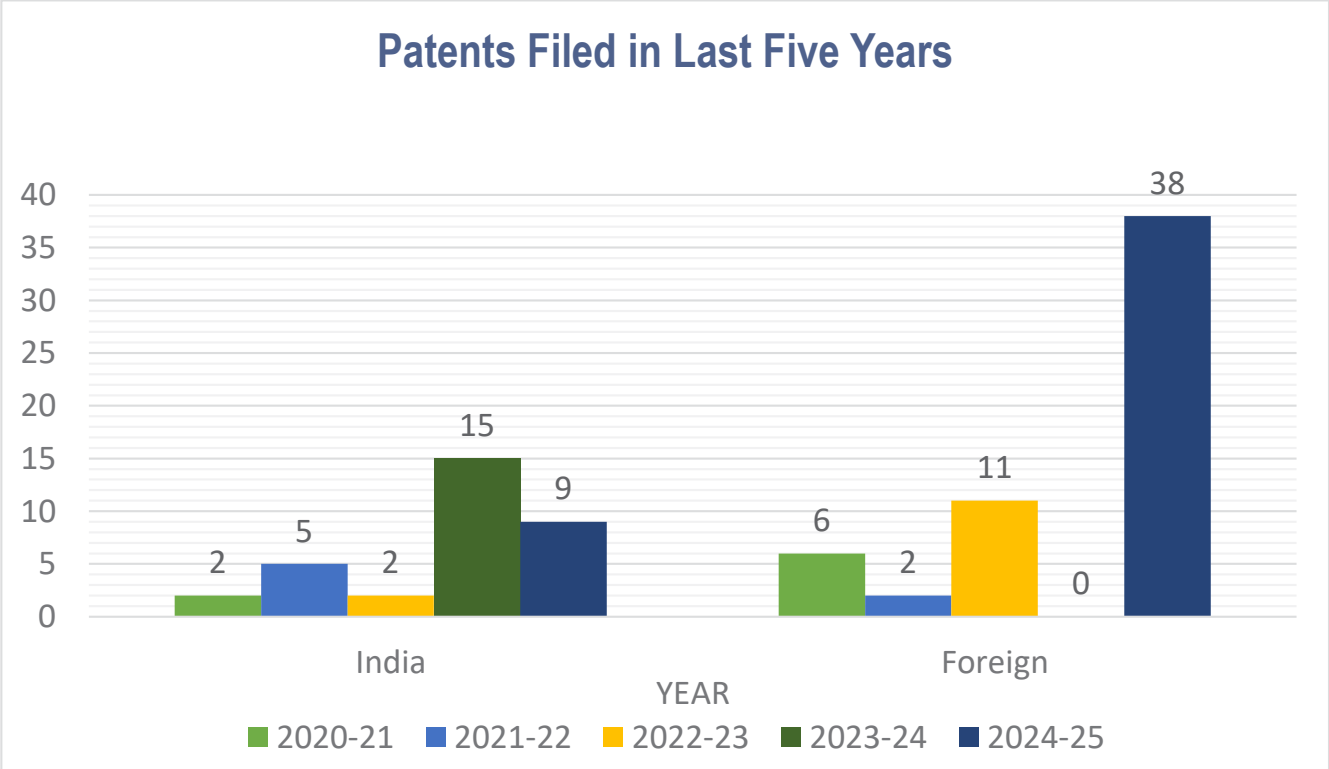
Applications Filed in Foreign Countries

Sl. No.	Country	Title	Inventors	Application No.
1	WO	Liposomal Formulation for Treatment of Visceral Leishmaniasis	Nahid Ali, Nicky Didwania, Mohd Kamran, Abdus Sabur, Sarfaraz Ahmad Ejazi	PCT/ IN2024/050371
2	US	An Improved Synthetic Method for the Preparation of Indole-3-Carboxylic Acid Derivatives: Useful Key Intermediate for the Synthesis of Several Biologically Active Molecules Including Tropisetron	Indubhusan Deb, Arup Bhowmik	18/702220
3	US	A Process For The Preparation of 2,7-Dihydroxyfluorenone Useful for the Synthesis of Tilorone And Its Salts	Parasuraman Jaisankar, Indubhusan Deb, Pinaki Bhattacharjee	18/702639
4	AU	An Improved Synthetic Method for the Preparation of Indole-3-Carboxylic Acid Derivatives: Useful Key Intermediate for the Synthesis of Several Biologically Active Molecules Including Tropisetron	Indubhusan Deb, Arup Bhowmik	2022370641
5	CA	An Improved Synthetic Method for the Preparation of Indole-3-Carboxylic Acid Derivatives: Useful Key Intermediate for the Synthesis of Several Biologically Active Molecules Including Tropisetron	Indubhusan Deb, Arup Bhowmik	3235833
6	CA	A Process for the Preparation of 2,7-Dihydroxyfluorenone Useful for the Synthesis of Tilorone and Its Salts	Parasuraman Jaisankar, Indubhusan Deb, Pinaki Bhattacharjee	3235754
7	JP	A Process for the Preparation of 2,7-Dihydroxyfluorenone Useful for the Synthesis of Tilorone and Its Salts	Parasuraman Jaisankar, Indubhusan Deb, Pinaki Bhattacharjee	2024-523808
8	AU	A Process for the Preparation of 2,7-Dihydroxyfluorenone Useful for the Synthesis of Tilorone and Its Salts	Parasuraman Jaisankar, Indubhusan Deb, Pinaki Bhattacharjee	2022369156
9	JP	An Improved Synthetic Method for the Preparation of Indole-3-Carboxylic Acid Derivatives: Useful Key Intermediate for the Synthesis of Several Biologically Active Molecules Including Tropisetron	Indubhusan Deb, Arup Bhowmik	2024-523753
10	CN	A Process for the Preparation of 2,7-Dihydroxyfluorenone Useful for the Synthesis of Tilorone and Its Salts	Parasuraman Jaisankar, Indubhusan Deb, Pinaki Bhattacharjee	202280070984.3
11	RU	An Improved Synthetic Method For The Preparation Of Indole-3-Carboxylic Acid Derivatives: Useful Key Intermediate For The Synthesis Of Several Biologically Active Molecules Including Tropisetron	Indubhusan Deb, Arup Bhowmik	2024111157
12	SG	In Vitro Protease-Based Sars-Cov-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	11202402800V
13	WO	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	PCT/ IN2024/050437
14	US	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	18/704638
15	CA	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	3236403
16	SA	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	SA 1120242193
17	BR	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	BR 11 2024 008107 9
18	JP	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	2024-525341
19	ZA	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	2024/03266
20	AE	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	P2024-01063
21	AU	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	2022379143

Sl. No.	Country	Title	Inventors	Application No.
22	CN	An Improved Synthetic Method for the Preparation of Indole-3-Carboxylic Acid Derivatives: Useful Key Intermediate for the Synthesis of Several Biologically Active Molecules Including Tropisetron	Indubhusan Deb, Arup Bhowmik	202280075279.2
23	WO	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	PCT/ IN2024/050526
24	WO	A Composition for Treating Parkinson's Disease	Deepak Kumar, Joy Chakraborty, Priyanka Yatham, Chayan Banerjee, Shreya Sen Sarma	PCT/ IN2024/050529
25	EP	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	22886340.3
26	RU	A Process for the Preparation of 2,7-Dihydroxyfluorenone Useful for the Synthesis of Tilorone And Its Salts	Parasuraman Jaisankar, Indubhusan Deb, Pinaki Bhattacharjee	2024113284
27	EP	An Improved Synthetic Method for the Preparation of Indole-3-Carboxylic Acid Derivatives: Useful Key Intermediate for the Synthesis of Several Biologically Active Molecules Including Tropisetron	Indubhusan Deb, Arup Bhowmik	22883134.3
28	KR	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	10-2024-7017182
29	WO	Detection System for Alzheimer's Disease Using Magnetic Resonance Image Processing and Machine Learning Techniques	Saikat Chakrabarti, Subhrangshu Das, Priyanka Panigrahi	PCT/ IN2024/050632
30	CN	In Vitro Protease-Based SARS-COV-2 Spike Protein Cleavage Assay System	Upasana Ray, Prem Prakash Tripathi, Feroza Begum, Amit Kumar Srivastava	202280080895.7
31	CN	Preparation of Quinazolinediones and Use Thereof for Treatment of Non-Alcoholic Fatty Liver Disease	Arindam Talukdar, Partha Chakrabarti, Dipayan Sarkar, Saheli Chowdhury, Sunny Goon, Abhishek Sen, Uddipta Ghosh Dastidar, Binita Patra, Israful Hoque	202280085647.1
32	JP	Preparation of Quinazolinediones and Use Thereof for Treatment of Non-Alcoholic Fatty Liver Disease	Arindam Talukdar, Partha Chakrabarti, Dipayan Sarkar, Saheli Chowdhury, Sunny Goon, Abhishek Sen, Uddipta Ghosh Dastidar, Binita Patra, Israful Hoque	2024-538441
33	US	Preparation of Quinazolinediones and Use Thereof for Treatment of Non-Alcoholic Fatty Liver Disease	Arindam Talukdar, Partha Chakrabarti, Dipayan Sarkar, Saheli Chowdhury, Sunny Goon, Abhishek Sen, Uddipta Ghosh Dastidar, Binita Patra, Israful Hoque	18/723847
34	EP	Preparation of Quinazolinediones And Use Thereof for Treatment of Non-Alcoholic Fatty Liver Disease	Arindam Talukdar, Partha Chakrabarti, Dipayan Sarkar, Saheli Chowdhury, Sunny Goon, Abhishek Sen, Uddipta Ghosh Dastidar, Binita Patra, Israful Hoque	22910395.7
35	WO	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 f Mandipropamid	Indubhusan Deb, Imtiaj Mondal, Koushik Naskar, Shantonu Roy	PCT/ IN2024/052299
36	WO	Dihydrobenzo[B,E]Pyrroloazepines Hybrids and A Process for the Preparation Thereof	Indubhusan Deb, Shantonu Roy, Koushik Naskar, Imtiaj Mondal	PCT/ IN2025/050321
37	WO	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	PCT/ IN2025/050394
38	WO	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	PCT/ IN2025/050418

Patents at a Glance





List of research fellow to receive their doctorate degree at CSIR-IICB during 2024-25

Sl. No.	Name of PhD awarded recipient's	Name of PhD Supervisor	University	Date of Award	Title of the Thesis
1	Dr. Aakriti Garg	Dr. P. Jaisankar (Guide) & Dr. Sreya gupta (Co-guide from NIPER-Kolkata)	NIPER, Kolkata	April 23, 2024	Development of Indole Based Novel Fluorescence Probes for Organelle Specific Live Cell Imaging
2	Dr. Achyut Bora	Dr. Sanjay Dutta	AcSIR	January 20, 2025	Elucidating the therapeuic opportunities in DNA abasic sites and repair pathways in cancer cells
3	Dr. Ananya Ganguly	Dr. Malini Sen	University of Calcutta	April 25, 2025	Functional Analysis of WISP3 and PPRD Linked WISP3 Mutants
4	Dr. Anoy Kumar Das	Dr. Subhas C. Biswas	University of Calcutta	March 04, 2024	Understanding the Role of Cell Cycle Molecules in Neurodegenarative Diseases
5	Dr. Anwesha Kar	Dr. Shilpak Chatterjee	AcSIR	December 03, 2024	CD38 mediated Terminal Exhaustion of T cells: Mechanism and Implications
6	Dr. Ashmita Mukherjee	Dr. Krishnananda Chattopadhyay & Co.PI-Dr. Paulomi Ghosh & Dr. Indu Bhusan Deb	AcSIR	February 18, 2025	Extraction of Keratin from human hair and fabrication of keratin-based biomaterial for hemorrhage control
7	Dr. Atanu Pramanik	Dr. Saumen Datta	Jadavpur University	February 10, 2025	Structural and Functional Insights of Virulence Proteins and Associated Factors from *Pseudomonas aeruginosa*
8	Dr. Bhaskar Basu	Dr. Mrinal K. Ghosh	University of Calcutta	May 02, 2024	Deciphering New Interacting Partners of the Deubiquitinase USP7, and the Consequential Effects on Cancer Development
9	Dr. Bhaswati Paul	Dr. R. Natarajan	AcSIR	October 07, 2024	Design and Development of Novel Metal-Organic Cages and Cage-Frameworks for Molecular Recognition and Sensing
10	Dr. Bishnu Prasad Sinha	Dr. Dipyaman Ganguly	AcSIR	May 16, 2024	Exploration of type I IFN mediated pathogenesis and validation of targeted therapies in a preclinical model of psoriasis
11	Dr. Chandra Sova Mandi	Dr. Sanjay Dutta	University of Calcutta	March 21, 2024	Understanding of Nucleic Acids Interactions with Quinoxaline Based Small Molecules and Their Biological Impact
12	Dr. Chayan Banerjee	Dr. Joy Chakraborty	AcSIR	February 18, 2025	Involvement of Monoamine oxidase in neurodegeneration: therapeutic aspects
13	Dr. Chinmoy Banerjee	Dr. Uday Bandyopadhyay	University of Calcutta	May 07, 2024	Functional Identification and Characterization of DNA Binding Property of *Plasmodium falciparum* Alba3 (Pfalba3) Protein
14	Dr. Debanjan Saha	Dr. Uday Badyopadhyay	Jadavpur University	May 13, 2024	Studies on the Structure & Function of HAM1, An Atypical Nucleotide Cleansing Protein of the Human Malignant Malaria Parasite
15	Dr. Deepshikha Ghosh	Dr. Sib Sankar Roy	University of Calcutta	July 30, 2024	Elucidating the Functional and Regulatory Mechanisms of Ets1 Proto-Oncoprotein in Tumor Progression
16	Dr. Devendra Shukla	Dr. Amit Kumar Srivastava	AcSIR	December 30, 2024	Dephering the role of miR-379-5p in ovarian cancer progression and chemoresistance
17	Dr. Dluya Samuel Thagriki	Dr. Upasana Ray	AcSIR	May 14, 2024	Role of NS1 protein in dengue virus entry
18	Dr. Dwipanjan Sanyal	Dr. Krishnananda Chattopadhyay	University of Calcutta	May 03, 2024	Exploring the effect of Evolutionary Selection on Protein Conformational Space Using Model systems
19	Dr. Esha Pandit	Dr. Nakul Chandra Maiti	University of Calcutta	January 13, 2025	Structural And Aggregational Aspects of Alpha Synuclein Variants
20	Dr. Ishani Banerji	Dr. Sucheta Tripathy (guide) & Dr. S.N. Bhattacharyya (co-guide)	AcSIR	April 16, 2024	Differential post-transcriptional regulation of cytokine mRNAs during activation phase of macrophage: mechanism and consequence in inflammatory response
21	Dr. Jafar Sarif	Dr. Dipyaman Ganguly	AcSIR	November 10, 2024	Exploring novel regulators of innate immune system in health and autoimmunity

Sl. No.	Name of PhD awarded recipient's	Name of PhD Supervisor	University	Date of Award	Title of the Thesis
22	Dr. Jayanta Saha	Dr. Indrajit Das	AcSIR	May 07, 2024	Linearly conjugated dienes and trienes: syntheses and reactivity under visible light, and thermal conditions
23	Dr. Krishnendu Khamaru	Dr. Nakul C Maiti & Dr. Biswadip Banerji	Jadavpur University	September 05, 2024	Transition Metal-free Oxygen Activation by Ammonium Based Ionic Liquids for Selective Oxidation Reactions: Experimental and Theoretical Studies
24	Dr. Lopamudra Das	Dr. Nakul Chandra Maiti	University of Calcutta	December 16, 2024	Lipid-Protein Interaction and Its Implications in Human Diseases
25	Dr. Md Asmaul Hoque	Dr. Dipyaman Ganguly	AcSIR	January 20, 2025	Exploring the role of PIEZO1 Mechanosensors in the cell biology of cellular infections
26	Dr. Moumita Roy	Dr. Joy Chakraborty	AcSIR	January 08, 2025	A study on mitochondrial membrane protein interaction during mitophagy: relevance to neurodegeneration
27	Dr. Mukul Dutta	Dr. Susanta Kar	AcSIR	September 06, 2024	Dissecting the role of cellular metabolic pathways in regulating alternative activation of macrophages during experimental visceral leishmaniasis
28	Dr. Nandini Chatterjee	Dr. Subhas C. Biswas	University of Calcutta	July 08, 2024	Studies on Cell Division Cycle 25 A (Cdc25A) Phosphatase in Models of Neurodegenerative Diseases
29	Dr. Prabir Kumar Gharai	Dr. Surajit Ghosh	University of Calcutta	June 11, 2024	Design and Development of New Small Molecule for Neurogenesis and Cellular Imaging
30	Dr. Pratitusti Basu	Dr. Arun Bandyopadhyay	University of Calcutta	June 12, 2024	Identification of Circulatory Plasma Proteins and Their Implications in Progression of Atherosclerosis
31	Dr. Priti Chatterjee	Dr. Sib Sankar Roy	University of Calcutta	August 27, 2024	Interplay of Growth Factor Signaling and Metabolic Adaptations in Tumour Cells Promoting Oncogenesis
32	Dr. Priya Baid	Dr. Jayati Sengupta	University of Calcutta	August 29, 2024	Structural Elucidation of Ribosome-associated Canonical and Non-canonical Factors: A Paradigm for Pathogen-specific Drug Target
33	Dr. Priya Darshani	Dr. Deepak Kumar	NIPER, Kolkata	June 19, 2024	Phytochemical and Bioactivity Screening of Natural Product Compounds from Selected Indian Aromatic and Medicinal Plants
34	Dr. Purbita Bandopadhyay	Dr. Dipyaman Ganguly	AcSIR	June 26, 2024	Role of plasmacytoid dendritic cells in sterile inflammation
35	Dr. Rajni Shaw	Dr. Mrinal K. Ghosh	University of Calcutta	December 13, 2024	Dead-Box RNA Helicase P68:Elicidating Its Novel Involvement in Regulating Chemoresistance in Cancer
36	Dr. Ranit D Rozario	Dr. Dipyaman Ganguly	AcSIR	October 04, 2024	Exploring novel regulators of plasmacytoid dendritic cells
37	Dr. Rumela Bose	Dr. Rupasri Ain	Jadavpur University	July 02, 2024	Prion: a novel regulator of spiral artery remodeling at the material-fetal interface
38	Dr. Saheli Chowdhury	Dr. Partha Chakrabarti	University of Calcutta	June 07, 2024	Delineating the Role of Ubiquitin-Proteasome System in Non-Alcoholic Fatty Liver Disease
39	Dr. Shaheda Tabassum	Dr. Mrinal K. Ghosh	University of Calcutta	April 09, 2024	Elucidating The Novel Molecular Mechanisms Behind the Oncogenecity Of Dead -Box RNA Helicase p68
40	Dr. Shashi Kant	Dr. Sucheta Tripathy	AcSIR	June 27, 2024	Delineating the genome and transcriptome of a newly identified fungus *Apiospora malaysiana* for efficient cellulose degradation and development of different biomaterials for potential commercial application
41	Dr. Shipra Kanti Jena	Dr. Rupasri Ain	AcSIR	November 10, 2024	Molecular signatures regulating Epithelial Mesenchymal Transition (EMT) in placental development and trophoblast stem cell differentiation
42	Dr. Shreya Bhattacharjee	Dr. Subrata Adak (guide) & Dr. S.N. Bhattacharyya (co-guide)	AcSIR	October 04, 2024	Role of Extracellular Vesicles Mediated Cross-Communication In Modulation of Inflammatory Responses In Macrophages and T Cells
43	Dr. Snehanshu Chowdhury	Dr. Shilpak Chatterjee	AcSIR	May 03, 2024	Rewiring metabolic programming increases anti-tumor efficacy of $CD8^+$ T cells
44	Dr. Soham Sengupta	Dr. Malini Sen	University of Calcutta	January 22-Jan-25	Influence of Wnt Signalling on Bacterial Commensals

Sl. No.	Name of PhD awarded recipient's	Name of PhD Supervisor	University	Date of Award	Title of the Thesis
45	Dr. Soumita Goswami	Dr. Subhas C. Biswas	University of Calcutta	February 18, 2025	Studies on Role of Microglia in The Pathophysiology of Alzeimer's Disease
46	Dr. Sreemoyee Chakraborty	Dr. Smrutisanjita Behera (guide) & Dr. S.N. Bhattacharyya (co-supervisor)	AcSIR	October 04, 2024	Balanced expression and export of miRNA in mammalian cells: role of RNA binding proteins and metalloproteases in miRNA homeostasis
47	Dr. Suman Maji	Dr. R. Natarajan	AcSIR	April 16, 2024	Covalent organic cages and cocrystals for molecular recognition and sensing
48	Dr. Sumangal Roychowdhury	Dr. Krishnananda Chattopadhyay	University of Calcutta	June 07, 2024	Studies of Liquid-Liquid Phase Separation Using Model Proteins
49	Dr. Syamantak Ghosh	Dr. Suvendra Nath Bhattacharyya	University of Calcutta	December 04, 2024	Identification Of Extracellular microRNA Targeting Machineries in Mammalian Cells
50	Dr. Tanima Mandal	Dr. Amit Kumar Srivastava	AcSIR	December 30, 2024	Understanding and Targeting Translesion DNA Synthesis in Lung Cancer
51	Dr. Tanushree Das	Dr. Krishna Das Saha	University of Calcutta	June 27, 2024	Evaluation of Anticancer Activity of Nanoparticles of Tea Extract and EGCG In Colon Cancer Cell Lines
52	Dr. Varsha Gupta	Dr. Surajit Ghosh	University of Calcutta	June 25, 2024	Neurogenic Potential of Imidazole- Based Small Molecules
53	Dr. Vivek Kumar Gupta	Dr. P. Jaisankar & Dr. Hemanta K. Majumder	University of Calcutta	April 19, 2024	Development of Inhibitors of DNA Topoisomerases of *Leishmania* And Their Potential as Therapeutic Agents From Natural and Synthetic Origin
54	Dr. Yatham Priyanka	Dr. Deepak Kumar	NIPER, Kolkata	May 31, 2024	Analytical, phytochemical, and formulation studies on *Ferula assa-foetida L.* oleo-gum-resin
55	Dr. Bhim Majhi	Dr. Sanjay Dutta	AcSIR	April 16, 2024	Development of fused heterocyclic compounds targeting nucleic acids
56	Dr. Rimita Saha	Dr. Sanjay Dutta	AcSIR	January 20, 2025	Exploration of quinoxaline-induced structural changes in nucleic acids as a regulator of cell death and viral translation
57	Dr. Pratiti Mandal	Dr. Partha Chakrabarti	AcSIR	March 07, 2025	Studying metabolic perturbations in cancer using synthetic compounds
58	Dr. Prosenjit Das	Dr. Sib Sankar Roy & Dr. Shampa Mallick	Jadavpur University	October 28, 2024	Studies on lipid-induced mitochondrial dysfunction and associated immune-metabolic perturbations: an approach towards novel therapeutic interventions
59	Dr. Naqiya Ambareen	Dr. Subhas Chandra Biswas	AcSIR	January 28, 2025	Understanding the role of autophagy in the pathophysiology of Alzheimer's disease
60	Dr. Rupsha Mondal	Dr. Joy Chakraborty	AcSIR	January 20, 2025	Managing mitochondria from dopamine: halting Parkinson's disease
61	Dr. Asharani Prusty	Dr. Sucheta Tripathy	AcSIR	January 20, 2025	Unveiling Oscillatoria salina: multi-omics insights into metabolic profiling, stress resilience, and therapeutic applications

Higher Qualification Attained by CSIR-IICB Personnel during 2024-25

Sl. No.	Name of the Employee	Designation	Details of the Higher Qualification
1	Shri Shubhendu Ghosh	Assistant Engineer (Air. Cond.)	Attained Bachelor Degree in Mechanical Engineering from Jadavpur University on 24.12.2024 vide O.M. No. Admn.9(2150)/15 dated 21.01.2025
2	Dr. Anirban Manna	Senior Technician (2)	Attained Ph. D. Degree (Science) in Biotechnology from the University of Calcutta on 14.07. 2023 vide O.M. No. Admn.9(1644)/98 dated 20.01.2025.
3	Shri Alok Ray	Assistant Section Officer (General)	Attained 'Bachelor of Arts' from India Gandhi National Open University (IGNOU) on December 30, 2024 vide O.M. No. Admn.9(1510)/95 dated 15.05.2025.
4	Shri Debtanu Pal	Senior Secretariat Assistant (General)	Attained Bachelor of Arts from Swami Vivekananda Subharti University on 24.07.2025 vide OM No. Admn. 9 (2145)/15 dated 28.04.2025.

Training of manpower during 2024-25

Sl. No.	Name of the Trainee	Name of the Training Programme	Date and Place
1	Shri Rabindranath Das, Private Secretary	Planning of Life after Retirement	June 10-12, 2024 at CSIR-HRDC, Ghaziabad
2	Shri Rajib Ray, Section Officer (S&P)	Records – Management, Administration and Preservation	June 20-21, 2024 at CSIR-HRDC, Ghaziabad
3	Shri Sukhendu Biswas, ASO (G)		
4	114 Registered participants from CSIR-IICB	A three-day induction workshop on GLP (Good Laboratory Practices) Principles	June 25-27, 2024 at CSIR-IICB, Kolkata
5	Dr. Jaisankar, Chief Scientist	CSIR Skill Coordinators' conclave and Brainstorming on Future skills	November 21-22, 2024 at CSIR-IMMT, Bhubaneswar
6	Dr. Upasana Ray, Principal Scientist		
7	Ms. Arti Grover, Sr. Technical Officer (2)		
8	Ms. Sanhita Ganguly, Section Officer (G)	Hands-on Workshop for the IGoT Nodal Officers of CSIR	December 17-19, 2024 at CSIR-HRDC, Ghaziabad
9	Dr. Shirish Bhatiya, Scientist	Fundamentals of Animal Experimentation	January 27-31, 2025 at CSIRCDRI, Lucknow
10	Ms. Moumita Majumder, Private Secretary	Annual meet for all senior level incumbents of Stenographic Cadre	March 21-22, 2025 at CSIR-HRDC, Ghaziabad

Completed Extramural/Sponsored/Consultancy Projects (2024-25)

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	Role of endoplasmic reticulum (ER) stress induced UPR signalling in regulating the metabolic fitness and functionality of CD8+ T cells in cancer	GAP 417	Dr. Shilpak Chatterjee	351.12	DBT, Wellcome Trust	01.01.2020	31.12.2024
2	The steroid sensitizing role of RXR-Gamma, a nuclear receptor, in the pathogenesis of emphysema	GAP 432	Dr. U. Mabalirajan	28.29	SERB, Govt. of India	05.02.2021	04.07.2024
3	Exploring the role of DNAse1L3in obesity –associated metaflammation and type2 diabetes	GAP 433	Dr. Dipyaman Ganguly	26.41	CEFIPRA	01.03.2021	30.06.2024
4	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	24.09.2024
5	Regulation of trophoblast development anda placental pathophysiology by long non-coding RNA	GAP 437	Dr. Rupasri Ain/ Dr. Partha Chakrabarti	51.87	SERB, Govt. of India	12.07.2021	11.07.2024
6	Development of visible-light photoredox and transition metal dual catalytic alkene difunctionalization reactions	GAP 439	Dr. Ranjan Jana	25.06	SERB, Govt. of India	20.12.2021	19.12.2024
7	Translocation and regulation of an unusual novel PAS domain containing phosphoglycerate kinase in Leishmania	GAP 440	Dr. Subrata Adak-	35.75	SERB, Govt. of India	30.12.2021	29.12.2024
8	Understanding the regulatory role of co-activator binding protein PIMT in the pancreatic Beta cells of diabetic animals and T3c diabetic (chronic pancreatisis) humans	GAP 441	Dr. Partha Chakrabarti	12.96	SERB, Govt. of India	31.12.2021	30.12.2024
9	Evaluation of insulin-like growth factor 2 (IGF2) as a potential epigenetic biomarker and therapeutic target to abolish the metabolic memory in diabetic retinopathy	GAP 442	Dr. G. Senthil Kumar	37.74	ICMR, Govt. of India	26.12.2021	25.12.2024
10	Clinical role of a pair of novel mutations in BCR-ABL1 towards therapy switch in imatinib-resistant chronic myeloid leukemia	GAP 443	Dr. Arindam Talukdar	79.93	LADY TATA Memorial Trust	04.02.2022	03.02.2025
11	Functional dissection of Jmjd3 during embryonic and adult hippocampal neurogenesis	GAP 444	Dr. Prem Prakash Tripathi	42.22	SERB, Govt. of India	23.02.2022	22.02.2025
12	Phase II/III clinical trials of an indigenously-developed hepatitis E vaccine and evaluating its immune correlates	GAP 445	Dr. Dipyaman Ganguly	57.80	BIRAC	09.02.2022	30.11.2024
13	In quest of novel drug targets : Investivation on structural dynamics of the mycobacterium ribosome using high-resolution cryo-electron microscopy	GAP 446	Dr. Jayati Sengupta	38.10	SERB	28.03.2022	27.03.2025
14	Investigation of the regulation of plant immunity by sphingolipids in rice	GAP 452	Dr. Smrutisanjita Behra	27.77	SERB	13.12.2022	12.12.2024
15	Reverse pharmacology of traditional medicine using modern biomedical techniques	GAP 489	Dr. P. Jaisankar	9.00	CCRAS, Ministry of Ayush	03.02.2025	08.02.2025
16	Determination and analysis of biological activities of Identified Molecules from Mistletoe	SSP 458	Dr. P. Jaisankar	21.24	Swasthaniketan Integrated Healthcare & Research Foundation	01.02.2023	31.01.2025

Sanctioned and Implemented Extramural/ Sponsored/Consultancy Projects (2024-25)

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	Odd-skipped related-1 in cardiac hypertrophy	GAP 482	Dr. Rupasri Ain	57.05	DBT Govt of India	30.04.2024	29.04.2027
2	Functional characterisation of patient derived single cell spheroids from Oral Squamous Cell Carcinoma to decipher clinical heterogeneity: A Tool for drug Screening and Radiation Sensitivity	GAP 483	Prof. Vibha Tandon	96.80	LADY TATA Memorial Trust	04.07.2024	03.07.2027
3	Tuning Lipid Droplets for Antiviral Interventions in Brain	GAP 484	Dr. Sourish Ghosh	79.42	DBT, Govt of India	20.05.2024	19.05.2027
4	Understanding the functional role of co-activator binding protein PIMT in macrophage mediated insuling resistance in rodents and humans	GAP 485	Dr. Partha Chakrabarti	31.67	DBT, Govt of India	05.07.2024	06.07.2027
5	Long coding RNA signature and function in trophoblast stem cell differentiation	GAP 486	Dr. Rupasri Ain	70.00	DBT, Govt of India	11.07.2024	10.07.2027
6	Decoding the epigenetic foot-print in vascular smooth cells induced by trophoblast cells: Implications in placental morphogenesis	GAP 487	Dr. Rupasri Ain	71.20	DBT, Govt of India	23.09.2024	22.09.2027
7	Role of small non-coding RNAs sorted inside extracellular vesicles for RNA persistence	GAP 488	Dr. Sourish Ghosh	38.23	SERB, Govt. of India	28.10.2024	27.10.2027
8	Reverse pharmacology of traditional medicine using modern biomedical techniques	GAP 489	Dr. P. Jaisankar	9.00	CCRAS, Ministry of Ayush	03.02.2025	08.02.2025
9	Towards Discovery and development of novel drugs and pharmaceuticals	GAP 490	Dr. Deepak Kumar	976.30	Ministry of Earth Sciences, Govt of India	27.01.2025	26.01.2027
10	Elucidating the role of aberrant IL-17 neutrophil axis in driving Type I diabetes pathogenesis	GAP 491	Dr. Saikat Majumder	72.00	ICMR	10.03.2025	09.03.2028

Ongoing In-House Projects (2024-25)

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	343.00	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	1008.10	29.06.2021	28.06.2026
3	Discovery & Pre-clinical Development of Antivirals for COVID-19 & other Diseases.	HCP 41	Dr. Arindam Talukdar	247.00	08.11.2021	31.03.2023
4	Indian Breast Cancer Genome Atlas	HCP 43	Dr. Shilpak Chatterjee	22.75	02.11.2021	31.03.2026
5	Phenome India-CSIR Health Cohort Knowledgebase	HCP 47	Dr. Partha Chakrabarti	1044.36	31.08.2022	31.03.2027
6	CSIR JIGYASA 2.0 Virtual Laboratory Integration Project	HCP 101	Dr. Sarita Ghosh	12.50	27.07.2022	31.03.2026
7	Innovative processes and technologies for Crop Protection Chemicals (Agromission 2)	HCP 49	Dr. Indrajit Das	199.89	11.04.2023	31.03.2026
8	Active Pharmaceutical Ingredients for Affordable Health Care (API-AHC)	HCP 50	Dr. Indu Bhusan Deb	168.00	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	370.00	03.03.2021	31.03.2025
10	Leishmaniasis: Target specific approaches to affect host-pathogen interaction and disease process	MLP 136	Dr. Subrata Adak	300.00	03.03.2021	31.03.2025

Sl. No.	Name of the project	Project code	Name of PI	Total Sanctioned Project Cost (Rs. In Lakhs)	Start Date	Completion Date
11	Modern innovative solutions for Environmental/ Occupational Lung Health challenges using clinical and pre-clinical strategies	MLP 137	Dr. U. Mabalirajan	406.00	03.03.2021	31.03.2025
12	Non-alcoholic Fatty Liver Disease (NAFLD): Novel Pathogenetic mechanism and therapeutic development	MLP 138	Dr. Partha Chakrabarti	499.49	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	410.00	03.03.2021	31.03.2025
14	Development of PROTACs for Targeted Protein Degradation via Small Molecule–Protein Engineering: A Promising New Approach for Treating NAFLD/NASH	FTT070504	Dr. Arindam Talukdar	147.00	01.04.2024	31.03.2026
15	Phytopharmaceutical Mission, Phase III	MMP075201	Dr. Deepak Kumar/Dr. Umesh Prasad Singh	180.76	18.03.2024	31.03.2027
16	A comprehensive approach to address Antimicrobial resistance AMR	MMP075202	Dr. Sanjay Dutta	495.14	01.08.2024	31.03.2027
17	SMASH-ACT: Small Molecule mTOR modulation for Adoptive T cell Therapy (ACT)	FBR070304	Dr. Shilpak Chatterjee	69.90	01.04.2024	31.03.2026
18	Vesicular Transmission of Flavivirus & Its Role in Neurodegeneration	FBR070305	Dr. Sourish Ghosh	69.44	01.04.2024	31.03.2026
19	Mechanistic understanding of tumor suppressor role of human EAF1 in renal cell carcinoma through regulation of selective expression of apoptotic genes.	FIR070304	Dr. Debabrata Biswas	99.00	01.04.2024	31.03.2026
20	National facility for secondary and tertiary (preclinical validation) screening of small molecules and phytopharmaceuticals against India's dominant diseases	FCP512406	Dr. U. Mabalirajan	534.00	01.04.2024	31.03.2026
21	Identification of modulators from natural origins that impede β-amyloid induced proteasome inhibition	RDSF000001	Dr. Joy Chakraborty	25.30	01.04.2024	31.03.2025
22	Deciphering the crosstalk between hepatic steatosis and Atherosclerosis: Modulating the AEBP1-PPARγ axis in maintaining cholesterol Homeostasis	RDSF000002	Dr. Dhabaleswar Patra	24.70	01.04.2024	31.03.2025
23	Seeding excellence: advancing cellular therapies for key Indian diseases	RDSF000003	Dr. U. Mabalirajan	30.00	01.04.2024	31.03.2025
24	Optimizing Guanosine-based Biomaterial Synthesis with Machine Learning for Artificial Skin Generation	RDSF000004	Dr. Manish Debnath	20.00	01.04.2024	31.03.2025
25	Prioritized Equipment Fund (PEF) to procure "600 MHz NMR"	PEF P50	Dr. R. Natarajan	800.00	01.04.2024	31.03.2026

Publications in Peer Reviewed Journal (Jan'24 – Dec'24)

1	Ganguly, D. (2024) Multi-omics studies in interpreting the evolving standard model for immune functions, *Briefings in Functional Genomics*, **23**, 75-81
2	Pramanik, A.; Datta, S. (2024) Structural and functional insights of itaconyl-CoA hydratase from Pseudomonas aeruginosa highlight a novel N-terminal hotdog fold, *FEBS Letters*, 598, 1387-1401
3	Darshani, P.; Sen Sarma, 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*, **9**, 49013-49022
4	Shukla, D.; Mandal, T.; Srivastava, A.K. (2024) Neil 1 deficiency facilitates chemoresistance through upregulation of RAD18 expression in ovarian cancer stem cells, *Biochemical and Biophysical Research Communications*, **712**, 149907
5	Talukdar, P.; Pal, S.; Biswas, D. (2024) Post-translational modification-dependent oligomerization switch in regulation of global transcription and DNA damage repair during genotoxic stress, *Nature Communications*, **15**, 4128
6	Maity, N.; Konar, A.; Hazra, S. (2024) αB-crystallin mini-peptides support corneal healing in vitro and in vivo in rabbit model, *International Journal of Ophthalmology*, **17**, 1772-1779
7	Liu, C.S.C.; Mandal, T.; Biswas, P.; Hoque, M.A.; Bandopadhyay, P.; Sinha, B.P.; Sarif, J.; DRozario, R.; Sinha, D.K.; Sinha, B.; Ganguly, D. (2024) Piezo1 mechanosensing regulates integrin-dependent chemotactic migration in human T cells, *eLife*, **12**, RP91903
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11	Shee, S.; Khamaru, K.; Banerji, B. (2024) Hydrazone Based pH-Responsive Configurational Molecular Rotary Switches Containing a New Conjugated π-Electronic Framework, *European Journal of Organic Chemistry,* **27**, e202400981
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13	Mondal, I.; Naskar, K.; Roy, S.; Purkait, A.; Deb, I. (2024) Synergistic [4+1] Spiroannulation and Selective Ring-Opening Strategy toward γ-Spirolactams, *Organic Letters*, **26**, 9859-9864
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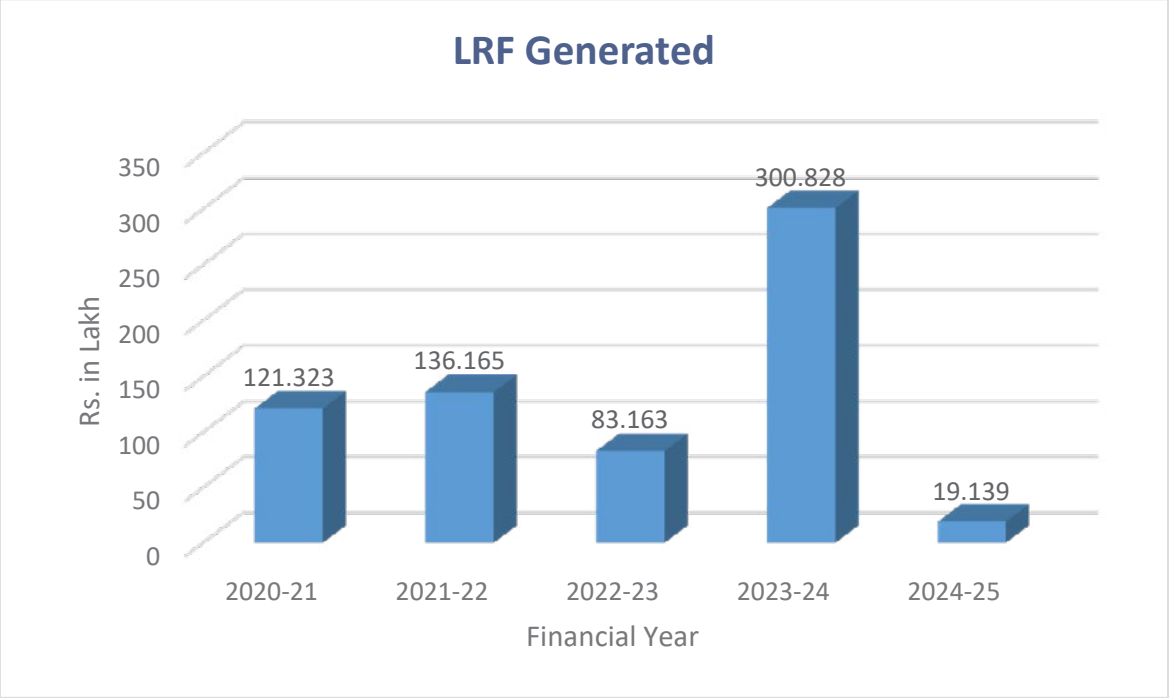
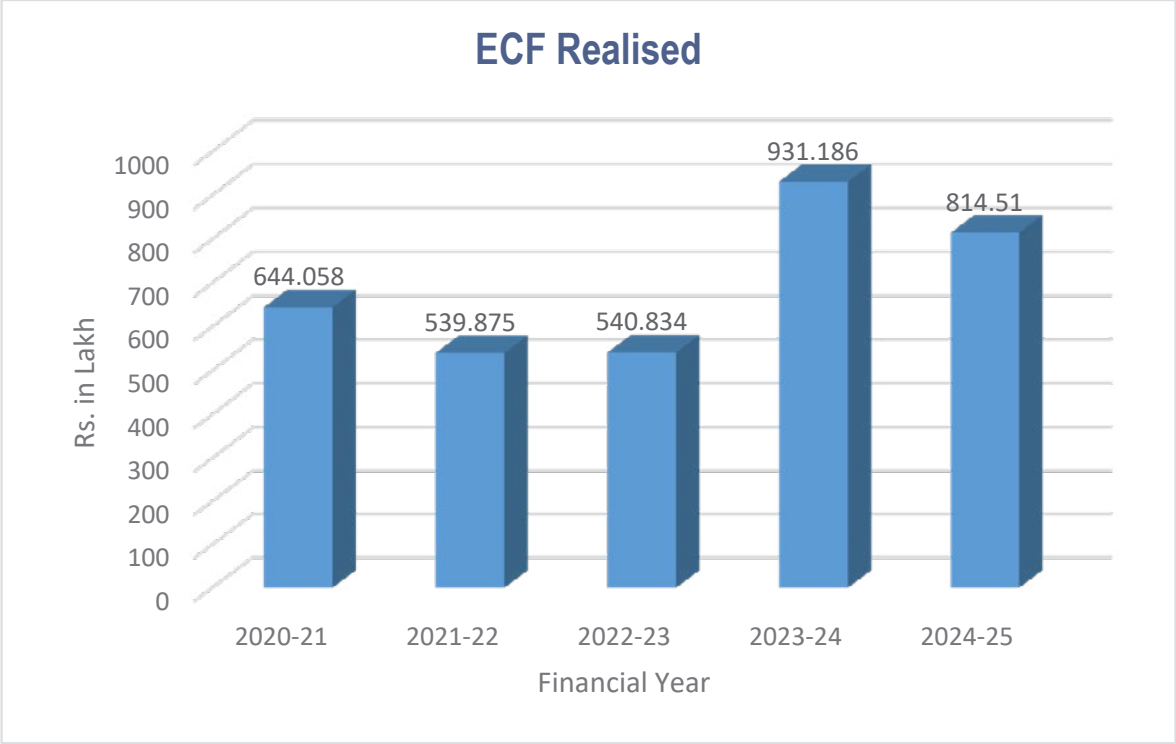
159	Panigrahi, P.; Das, S.; Chakrabarti, S. (2024) CCADD: An online webserver for Alzheimer's disease detection from brain MRI, *Computers in Biology and Medicine*, **177**, 108622

Books/Book Chapters Published

1	Ghosh MK*, Kumar S and Basu M (2024). Ubiquitin Specific Protease 7 (USP7) – Role in Human Pathologies and Potential Targeting Opportunities in Cancer. *Handbook of Proteases in Cancer: Cellular and Molecular Aspects*. Published by *Tayler & Francis*. *In press*
2	Ghosh MK*, Roy S, Chatterjee M, Begam S and Basu M (2024). The Dichotomous Role of CHIP in Cancer. *Handbook of Proteases in Cancer: Cellular and Molecular Aspects*. Published by *Tayler & Francis*. *In press*
3	Shreya Bandopadhyay, Udit Dey, Parna Chakraborty, Pallabi Debnath, Subhadip Kundu, Debabrata Laik, Sib Sankar Roy* (2024) The Role of Matrix Metalloproteinases MMP2 and MMP9 in Ovarian Cancer Progression; Chapter-9; *Handbook of Proteases in Cancer: Cellular and Molecular Aspects; Ed by Sajal Chakraborti,* eBook Published 13 December 2024; eBook ISBN9781003394716; CRC Press; DOIhttps://doi.org/10.1201/9781003394716.
4	Bhattacharyya, A, Ali, N, Gayen, S. 2024. diagnostic approaches for neglected tropical diseases in West Bengal: *A comprehensive review in Current Advances in Microbiology*. Published by Dr. Rajyasri Neogy, Vijaygarh Jyotish Ray College, Kolkata. ISBN: 978-81-969267-6-2.
5	Debnath, M., and Deb, P. (2025). Fluorescent carbon nanoparticles: Fundamentals, structure, fluorescent properties and mechanisms, challenges and future perspectives. In *Fluorescent Carbon Nanoparticles* (pp. 1-41). Elsevier.
6	Bidisha Das, Joy Chakraborty, Krishnananda Chattopadhyay (2025) Emerging Techniques in Cellular and Biomolecular Research; (Springer Nature Singapore); *Biochemical and Biophysical Methods in Molecular and Cellular Biology*; pages 1-28.
7	Rivalta, A., Hiregange, D.G., Bose, T., Fridkin, G., Rajan, K.S., Yonath, A., Zimmerman, E., Bashan, A. and Yonath, H. (2023). *Medical Implications of Functional and Destructive Cellular Motions: Curiosity-Driven Open Issues. In Curious Future Insight: Science for a Better Tomorrow* (pp. 65-82). Cham: Springer International Publishing

Financial data





Statement of Expenditure upto 31-03-2025

Financial Year: 2024-25 Budget Heads (Rs. in lakh)	31.03.2025 को व्यय विवरण/Expenditure Statement as on 31.03.2025																					
	Lab Grant									HQRF									Lab Reserve		Total	
	Projects			Non-Projects			Total			Projects			Non-Projects			Total			Proj.	Non-Proj.		
1. National Laboratory	Alloc.	Exp.	% Exp.	Alloc.	Exp.	% Exp.	Alloc.	Exp.	% Exp.	Alloc.	Exp.	% Exp.	Alloc.	Exp.	% Exp.	Alloc.	Exp.	% Exp.	Exp.	Exp.	Alloc.	Exp.
A. Grants-in-Aid -Salaries																						
1.Sal. & Sal. Linked Allow.				3251.251	3251.251	100	3251.251	3251.251	100												3251.251	3251.251
2. Other Allowances																					0.000	0.000
(i) Medical Reimbursement				81.486	81.486	100	81.486	81.486	100												81.486	81.486
(ii) Overtime Allowance/Honorarium				3.980	3.980	100	3.980	3.980	100												3.980	3.980
(iii) Leave Travel Concession				20.805	20.805	100	20.805	20.805	100												20.805	20.805
(iv) T.A. (India)	17.676	17.676	100	35.082	35.082	100	52.758	52.758	100												52.758	52.758
(v) T.A. (Foreign)																					0.000	0.000
(vi) Professional Update Allowance							0.000	0.000													0.000	0.000
Total Other Allowances (i to vi)	17.676	17.676	100	141.353	141.353	100	159.029	159.029	100										0.000	0.000	159.029	159.029
A. Total Salaries (1+2)	17.676	17.676	100	3392.604	3392.604	100	3410.280	3410.280	100										0.000	0.000	3410.280	3410.280
B. Grants-in-Aid -General																						
3. P-04 Contingencies	25.167	25.167	100	495.830	495.830	100	520.997	520.997	100	1.390	1.328	96				1.390	1.328	96			522.387	522.325
5. P-05 H.R.D.							0.000	0.000													0.000	0.000
5. P-06 Lab. Maintenance				698.714	698.714	100	698.714	698.714	100												698.714	698.714
5. P-701 Staff Qrs. Maintenance				11.810	11.810	100	11.810	11.810	100												11.810	11.810
6. P07 Chem/Con&ORE	1069.786	1069.786	100	920.690	920.690	100	1990.476	1990.476	100	98.538	97.215	99				98.538	97.215	99		48.052	2089.014	2135.743
7. P-804 Pension & Other retirement benefits				3763.895	3763.895	100	3763.895	3763.895	100												3763.895	3763.895
8. P906 -Advance																						
(i) Conveyance/Computer Advnace							0.000	0.000													0.000	0.000
(ii) House Building Advance							0.000	0.000													0.000	0.000
9. Ohter Heads (for CSIR Hqrs only)																					0.000	0.000
10. P-801 and P-62 ISTADS							0.000	0.000													0.000	0.000
11. P-803 PPO/TNBD							0.000	0.000													0.000	0.000
12. P-805 HRD							0.000	0.000													0.000	0.000
13. P-80508 RAB							0.000	0.000													0.000	0.000
14. P-807 Publicity & Exhibition							0.000	0.000													0.000	0.000
15. P80805 CSIR Guest House (Science Centre)							0.000	0.000													0.000	0.000
16. P80806 Celebrations							0.000	0.000													0.000	0.000
17. P-16 IPTM							0.000	0.000													0.000	0.000
18. P-61 NMTILI (Recurring)																					0.000	0.000
B. Total GIA-General (3 to 18)	1094.953	1094.953	100	5890.939	5890.939	100	6985.892	6985.892	100	99.928	98.543	99				99.928	98.543	99	0.000	48.052	7085.820	7132.487
C. Grants for Creation of Capital Assests																						
1. P-50 Land Cost																					0.000	0.000
2. P-50 Works & Services/Electrical Installations (Lumpsum)				149.502	149.502	100	149.502	149.502	100	70.000	37.016	53				70.000	37.016	53			219.502	186.518
3. P-50 Works & Services/Electrical Installations (other)							0.000	0.000													0.000	0.000
4. P-50 App. & Eqp /Computer Eqp.	224.407	224.407	100	373.466	373.466	100	597.873	597.873	100	464.000	58.844	13	800.000	735.000	92	1264.000	793.844	63		1.400	1861.873	1393.117
5. P-50 Workshop Machinery							0.000	0.000													0.000	0.000
6. P-50 Office Equipments				14.319	14.319	100	14.319	14.319	100												14.319	14.319
7. P-50 Furniture & Fittings				35.610	35.610	100	35.610	35.610	100												35.610	35.610
8. P-50 Library							0.000	0.000													0.000	0.000
(i) Books							0.000	0.000													0.000	0.000
(ii) Journals							0.000	0.000													0.000	0.000
(iii) e-Journal							0.000	0.000													0.000	0.000
9. P-50 Model & Exhibits							0.000	0.000													0.000	0.000
10. P-50 Vehicles				18.505	18.505	100	18.505	18.505	100												18.505	18.505
11. P-50 Tools & Plants							0.000	0.000													0.000	0.000
12. P-50 Software development/procurement/LAN/WAN							0.000	0.000													0.000	0.000
13. P-26 (ICT)							0.000	0.000													0.000	0.000
14. P-702 Staff Qrs. (Const.-Lumpsum)							0.000	0.000													0.000	0.000
15. P-702 Staff Qrs. (Construction) (Other)							0.000	0.000													0.000	0.000
16. P-61 NMTILI (Capital)																					0.000	0.000
C. Total Capital (1 to16)	224.407	224.407	100	591.402	591.402	100	815.809	815.809	100	534.000	95.860	18	800.000	735.000	92	1334.000	830.860	62	0.000	1.400	2149.809	1648.069
Total National Labs (A+B+C)	1337.036	1337.036	100	9874.945	9874.945	100	11211.981	11211.981	100	633.928	194.403	31	800.000	735.000	92	1433.928	929.403	65	0.000	49.452	12645.909	12190.836

20/5/25

अनुभाग अधिकारी (वित्त एवं लेखा)
Section Officer (Finance & Accounts)
सी.एस.आई.आर–भारतीय रासायनिक जीवविज्ञान संस्थान
CSIR-INDIAN INSTITUTE OF CHEMICAL BIOLOGY
कोलकाता- 700 032/Kolkata - 700 032

21.5.25

वित्त एवं लेखा अधिकारी
Finance & Accounts Officer
(सी.एस.आई.आर- भारतीय रासायनिक जीवविज्ञान संस्थान
वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद)
CSIR-Indian Institute of Chemical Biology
(Council of Scientific & Industrial Research)
कोलकाता / Kolkata - 700 032

(₹ in lakhs)

	2020-21	2021-22	2022-23	2023-24	2024-25
LRF Generated	121.323	136.165	83.163	300.828	19.139
ECF Realised	644.058	539.875	540.834	931.186	814.510

(₹ in lakhs)

Statement of Expenditure for Non-CSIR funding agencies & LRF				
Year	ECF		LRF	
	Realised	Expenditure	Generated	Utilised
2024-25	814.510	976.808	19.139	49.452

20/05/25

अनुभाग अधिकारी (वित्त एवं लेखा)
Section Officer (Finance & Accounts)
सी.एस.आई.आर–भारतीय रासायनिक जीवविज्ञान संस्थान
CSIR-INDIAN INSTITUTE OF CHEMICAL BIOLOGY
कोलकाता - 700 032/Kolkata - 700 032

20/05/25

21.5.25

वित्त एवं लेखा अधिकारी
Finance & Accounts Officer
एसआईआर-भारतीय रासायनिक जीवविज्ञान संस्थान
(वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद)
CSIR-Indian Institute of Chemical Biology
(Council of Scientific & Industrial Research)
कोलकाता / Kolkata - 700 032

HUMAN RESOURCE

31 मार्च, 2025 को मानव संसाधन / Human Resource as on March 31, 2025

प्रो. विभा टंडन / Prof. Vibha Tandon
निदेशक, सीएसआईआर-आईआईसीबी / Director, CSIR-IICB

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डॉ. पी. जयशंकर / Dr. P. Jaisankar	मुख्य वैज्ञानिक / Chief Scientist
डॉ. आदित्य कोणार / Dr. Aditya Konar	मुख्य वैज्ञानिक / Chief Scientist
डॉ. के.एन. चट्टोपाध्याय / Dr. K.N. Chattopadhyay	मुख्य वैज्ञानिक / Chief Scientist
डॉ. मृणाल कांति घोष / Dr. Mrinal Kanti Ghosh	मुख्य वैज्ञानिक / Chief Scientist
डॉ. सिब शंकर रॉय / Dr. Sib Sankar Roy	मुख्य वैज्ञानिक / Chief Scientist
डॉ. सौमेन दत्त / Dr. Saumen Datta	मुख्य वैज्ञानिक / Chief Scientist
डॉ. चिन्मय चौधरी / Dr. Chinmay Chowdhury	मुख्य वैज्ञानिक / Chief Scientist
डॉ. सुब्रत आदक / Dr. Subrata Adak	मुख्य वैज्ञानिक / Chief Scientist
डॉ. रुपाश्री ऐन / Dr. Rupasri Ain	मुख्य वैज्ञानिक / Chief Scientist
डॉ. सुभाष चंद्र विश्वास / Dr. Subhas Ch. Biswas	मुख्य वैज्ञानिक / Chief Scientist
डॉ. बिस्वदीप बनर्जी / Dr. Biswadip Banerji	मुख्य वैज्ञानिक / Chief Scientist
डॉ. जयति सेनगुप्ता / Dr. Jayati Sengupta	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. सुचेता त्रिपाठी / Dr. Sucheta Tripathy	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. सैकत चक्रवर्ती / Dr. Saikat Chakrabarti	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. देबब्रत विश्वास / Dr. Debabrata Biswas	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. पार्थ चक्रवर्ती / Dr. Partha Chakrabarti	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. नकुल च. मैती / Dr. Nakul Ch. Maiti	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. रंजन जाना / Dr. Ranjan Jana	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. अरिन्दम तालुकदार / Dr. Arindam Talukdar	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. संजय दत्त / Dr. Sanjay Dutta	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. सिद्धार्थ रॉय / Dr. Siddhartha Roy	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
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डॉ. अमिताव सेनगुप्ता / Dr. Amitava Sengupta	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
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डॉ. रामलिंगम नटराजन / Dr. Ramalingam Natarajan	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
डॉ. सुभजीत विश्वास / Dr. Subhajit Biswas	वरिष्ठ प्रधान वैज्ञानिक / Senior Principal Scientist
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डॉ. यू. मबलीराजन / Dr. U. Mabalirajan	प्रधान वैज्ञानिक / Principal Scientist
डॉ. शिल्पक चटर्जी / Dr. Shilpak Chatterjee	प्रधान वैज्ञानिक / Principal Scientist
डॉ. उपासना रे / Dr. Upasana Ray	प्रधान वैज्ञानिक / Principal Scientist
डॉ. जी सेंथिल कुमार / Dr. G. Senthil Kumar	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. अमित कुमार श्रीवास्तव / Dr. Amit Kr. Srivastava	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. दीपक कुमार / Dr. Deepak Kumar	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. जॉय चक्रवर्ती / Dr. Joy Chakraborty	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. सौरीश घोष / Dr. Sourish Ghosh	वरिष्ठ वैज्ञानिक / Senior Scientist

डॉ. धबलेश्वर पात्रा / Dr. Dhabaleswar Patra	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. प्रेम प्रकाश त्रिपाठी / Dr. Prem Prakash Tripathi	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. सिद्दीक सरकार / Dr. Siddik Sarkar	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. सैकत मजूमदार / Dr. Saikat Majumder	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. असीम पॉल Dr. Ashim Paul	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. तनया बोस / Dr. Tanaya Bose	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. जॉन मोंडल / Dr. John Mondal	वरिष्ठ वैज्ञानिक / Senior Scientist
डॉ. सरस्वती गराई / Dr. Saraswati Garai	वैज्ञानिक / Scientist
श्री संदीप अग्रवाल / Mr. Sandeep Aggarwal	वैज्ञानिक / Scientist
डॉ. स्मृतिसंजिता बेहरा / Dr. Smrutisanjita Behera	वैज्ञानिक / Scientist
डॉ. एमडी जहांगीर आलम / Dr. Md. Jahangir Alam	वैज्ञानिक / Scientist
डॉ. मनीष देबनाथ / Dr. Manish Debnath	वैज्ञानिक / Scientist
डॉ. बिजेश पी. / Dr. Bijesh P.	वैज्ञानिक / Scientist
डॉ. रश्मि गौर / Dr. Rashmi Gaur	वैज्ञानिक / Scientist
डॉ. देबासीस नायक / Dr. Debasis Nayak	वैज्ञानिक / Scientist
डॉ. रतनति सरखेल / Dr. Ratanti Sarkhel	वैज्ञानिक / Scientist
डॉ. भाटिया शिरीषकुमार ईश्वरभाई / Dr. Bhatiya Shirishkumar Ishwarbhai	वैज्ञानिक / Scientist
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श्री पी. गंगोपाध्याय / Mr. P. Gangopadhyay	वरिष्ठ अधीक्षण अभियंता (एआईआर कंड.) / Senior Superintending Engineer (Air Cond.)
डॉ. ई. पद्मनाबन / Dr. E. Padmanaban	प्रधान तकनीकी अधिकारी / Principal Technical Officer
श्री सुसांता रे / Mr. Susanta Ray	वरिष्ठ अधीक्षण अभियंता (सिविल) / Senior Superintending Engineer (Civil)
श्री संदीप चौधरी / Mr. Sandip Chowdhury	वरिष्ठ तकनीकी अधिकारी (2) /Senior Technical Officer (2)
श्रीमती निराली बेज / Mrs. Nirali Bage	कार्यकारी अभियंता (सिविल) / Executive Engineer (Civil)
श्रीमती आरती ग्रोवर / Mrs. Arti Grover	वरिष्ठ तकनीकी अधिकारी (2) / Senior Technical Officer (2)
श्री स्वपन कुमार मंडल / Mr. Swapan Kr. Mondal	वरिष्ठ तकनीकी अधिकारी (2) / Senior Technical Officer (2)
श्री देबाशीष बाणिक / Mr. Debashis Banik	कार्यकारी अभियंता (सिविल) / Executive Engineer (Civil)
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श्री सौमिक लाहा / Mr. Soumik Laha	तकनीकी अधिकारी / Technical Officer
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श्री श्यामल नाथ / Mr. Shyamal Nath	प्रयोगशाला सहायक / Lab. Assistant
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Dr. Sarita Ghosh, Senior Principal Scientist	Member-Secretary

Dihydrofolate formulation for dietary supplementation as an effective nutraceutical supplement and method of preparation thereof

Unmetabolized synthetic folate has been reported in the serum of individuals in developed nations where mandatory folate fortification is implemented. Consequently, there is a shift towards using biological folate derivatives for fortification. In response to this trend, we have developed methods to produce dihydrofolate tablets and capsules with enhanced stability.

The innovation provides an effective nutraceutical for oral administration, serving as a potent agent to enhance overall health and support specific bodily functions, especially in individuals with folate deficiency. The formulation remains substantially stable when stored in various temperature conditions (-20, 8, 23 and 50 °C) for a period of at least 3 months, and methods for preparing these formulations are illustrated.

DHF Stabilized Formulations/Products developed:

Stabilized dihydrofolate powder, Encapsulated dihydrofolate powder, Tablets of dihydrofolate, Tablets of encapsulated-dihydrofolate, Capsules of dihydrofolate, Capsules of encapsulated-dihydrofolate

Dihydrofolate Formulations

USP of Technology: Competitive advantage

Currently, dihydrofolate-based products are not available in the market.

Patent/IPR Details

India Patent Application Number: 202411023759, PCT/IN2025/050394

Market Size/ Potential (India and International)

The global folate market size is valued at around one billion US dollars, and is expected to grow at 6% per year

100% Indigenous

Societal Relevance:

Anaemia due to dihydrofolate deficiency is highly prevalent in India, with folate deficiency being a significant contributing factor. Reports indicate that over 50% of individuals in low-income groups suffer from folate deficiency in India. Unlike synthetic folic acid, dihydrofolate can be readily absorbed and utilised by the body, making it an effective molecule for the amelioration of anaemia.

Technology Transfer Agreement with Thalir Aarogyam LLP. Kozhikode, Kerala on August 05, 2025

Dr. Bijesh P.
(Lead inventor)
Scientist
CSIR-IICB, Kolkata

Dr. Ajana Pathikkal
Designated Partner
ThalirAarogyam

Established in 1935 as the Indian Institute of Medical Research by a group of patriotic scientists and medical professional and later inducted into the Council of Scientific and Industrial Research (CSIR) in 1956, the CSIR-Indian Institute of Chemical Biology (CSIR-IICB) stands as a pioneering research institution of the nation. Since its inception the Institute has played a pivotal role in advancing chemical and biological sciences.

CLSM image of Probe (LipiK 510) specifically bound to the cellular neutral LDs

Picture courtesy:
Dr. P. Jaisankar
Chief Scientist, CSIR-IICB
Patent application no.:202311039884

γ-H2AX staining in 3D spheroid section developed from OVCAR-3 cells

Picture courtesy:
Dr. A.K. Srivastava
Senior Scientist, CSIR-IICB

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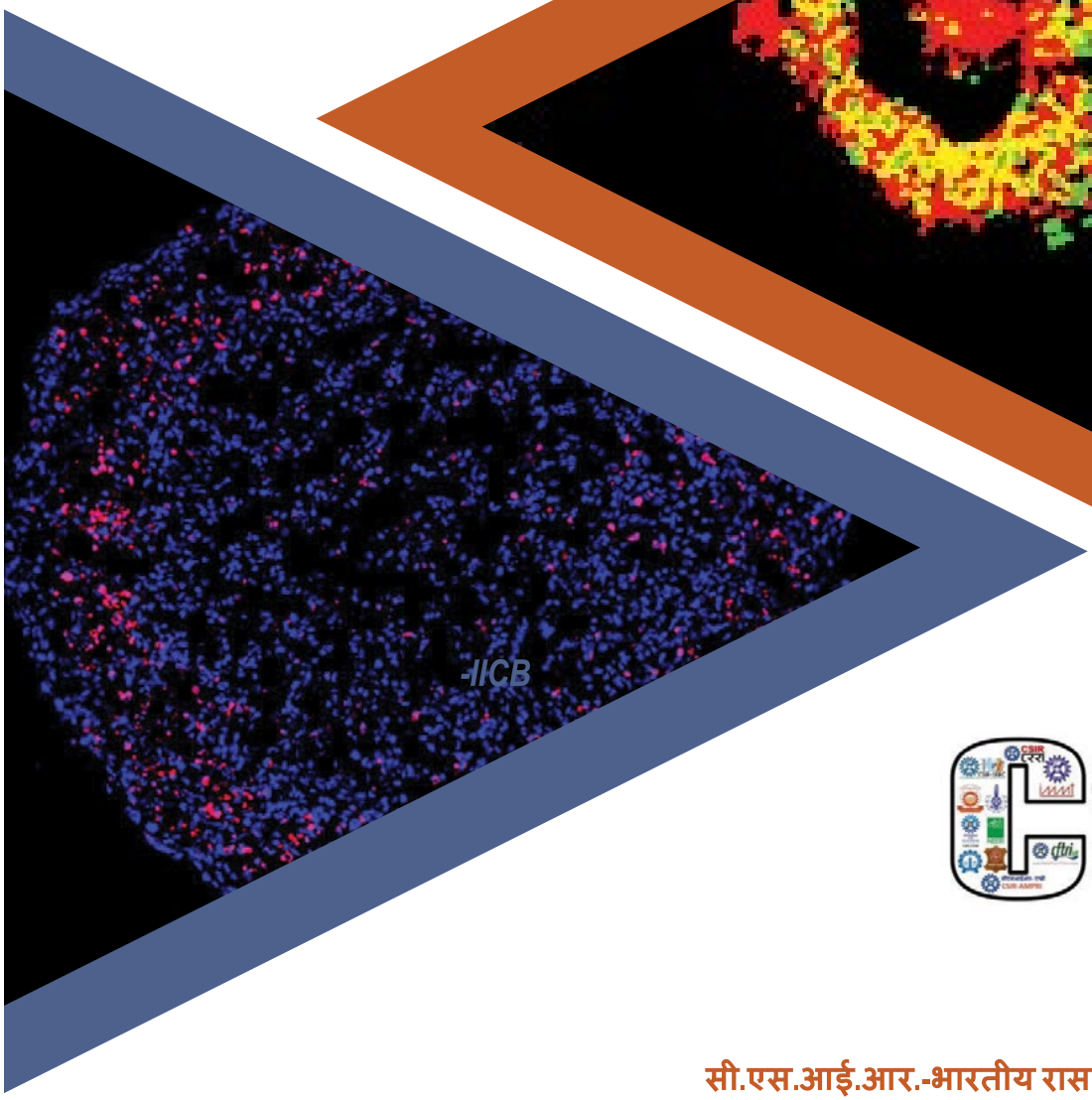
Azadi Ka Amrit Mahotsav



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