Curriculum Vitae
Arindam Talukdar, Ph.D.

SPECIALIZATION/RESEARCH AREAS: Dr. Talukdar lab's primary focus is:

- Addressing the fundamental questions that lie at the interface of chemistry and biology
- Medicinal Chemistry, Chemical Biology, Computational Analysis, Drug Discovery
- Understanding protein-protein interactions.
- To perform rational design and synthesis of novel chemical entities to unravel the molecular mechanism and develop potential treatments for human diseases.

CURRENT POSITION AND ADDRESS:

Senior Principal Scientist
Organic and Medicinal Chemistry Division
Professor, Academy of Scientific & Innovative Research (AcSIR)
Head, Business Development Group
CSIR- Indian Institute of Chemical Biology (IICB)
Adjunct Faculty, National Institute of Pharmaceutical Education and Research (NIPER), Kolkata
4, Raja S. C. Mallick Road, Jadavpur, Kolkata-700032 INDIA
Phone: 9051646141
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https://iicb.res.in/faculty/arindam-talukdar

ACADEMIC/RESEARCH EXPERIENCE/EMPLOYMENT

Degree	Year of Passing	University/Institute	Subjects
B. Pharmacy	1995	Department of Pharmaceutical Sciences, NAGPUR UNIVERSITY, Nagpur, India.	Pharmaceutical Sciences
M. Pharmacy	1997	University Institute of Pharmaceutical Sciences, PANJAB UNIVERSITY, Chandigarh, India	Medicinal Chemistry, Organic Chemistry, Pharmacology
PhD (Chemistry)	2003	CSIR-National Chemical Laboratory (NCL), Pune, India. (University of Pune)	Chemistry, Total Synthesis of natural products, Glycochemistry

From	To	Name of Organization	Position Held
4th January 2004	31st March 2005	Department of Biochemistry, The Ohio State University, USA (Prof. Peng G Wang)	Postdoctoral Researcher
1st April 2005	May 2010	Medicinal Chemistry and Molecular Pharmacology, Purdue University, USA (Prof. mark Cushman)	Postdoctoral Research Associate
June 2010	15 January 2013	Albany Molecular Research Inc. (AMRI) Singapore	Senior Research Scientist
21 January 2013	20 January 2017	CSIR-Indian Institute of Chemical Biology, Kolkata, India	Senior Scientist
21 January 2017	20 January 2021	CSIR-Indian Institute of Chemical Biology, Kolkata, India	Principal Scientist
21 January 2021	Till date	CSIR-Indian Institute of Chemical Biology, Kolkata, India	Senior Principal Scientist

LEADERSHIP EXPERIENCE/ ADMINISTRATIVE ROLE

1. Head of Business Development Group (BDG-IICB) of CSIR-Indian Institute of Chemical Biology since June 2020. Responsible for setting up Drug Discovery Platform and various business-related activities between Industry and IICB.

- As a Head BDG, I look after the MoU/CDA between IICB scientists and third parties.
- Organized multiple Industry-academia meetings among IICB scientists and involved scientists from the Eastern part of India.
- I look after the patent portfolio and mentor/guide the IICB scientists to write patent drafts and protect their inventions by formulating new patents.

2. CSIR-Mission Project. I have been involved in many CSIR projects notably the Antiviral Mission mode project. During the SAR-Cov-2 pandemic, I was actively involved in the conceptualization, formulation, execution and functioning of the HCP-41 mission and CSIR activities related to mitigation strategies of the pandemic situation.
   - As one of the nodal scientists, I assisted the project Director to conceive, formulate and execute the mission. I'm assisting other CSIR labs in their work strategies. I've also motivated other IICB scientists to re-orient their research and contribute to the CSIR mission.
   - I'm also involved as PI related to Non-alcoholic steatohepatitis (NASH).
   -

3. Coordinated three international workshop/symposium for students involved in Drug discovery research:
    - I have coordinated three Indo-Australian workshops and Symposium on "Recent Advances in Drug Development" in 2018, 2019, 2021 and 2022 at CSIR-IICB, Kolkata. Experts from around the world representing both academia and industry came on the same platform to share their experience-based advice on the future of rational drug design.
    - workshop was meant for PhD/Postdoctoral students and young faculties from across India. The objective of the workshop is capacity building and spreading the temper of drug discovery to as many students as possible across India.

4. Industrial Leadership. I worked as a team leader at Albany Molecular Research at Singapore Drug Research Center. I was one of the inventors in the development of the First-in-class inhibitor for epigenetic drug-target SUV39H2 and take the molecule to preclinical stage.
    - As a team leader at Albany Molecular Research Inc, my responsibility was to lead a group of scientists, coordinate among various drug development groups to strategically design and synthesize various HTS hits to validate them. Successful hit-to-lead development into the preclinical stage. (Bicyclic Compound and Use Thereof for Inhibiting SUV39H2. PCT/US2016/0051350).

5. Coordinator at India International Science Festival 2019 (IISF), organized by Ministry of Science & Technology, Ministry of Earth Sciences, and Vijnana Bharati (VIBHA).
    - I was the Coordinator of National Start-up Conclave & Expo. MSMEs from different parts of the country set up their stalls and many delegates visited.
    - I was the focal person coordinating the MSMEs, their logistics and various events for the smooth functioning of the conclave.

6. National Missions. I'm a course coordinator of one course (Separation techniques) offered under CSIR-IICB 'Skill Development Program' as a part of the CSIR National Skill Development Mission.
    - I personally teach and provide hands-on experimentations for two weeks to the students on various techniques used for the separation of small molecules.
    - I actively participate as a member of the CSIR-IICB "JIGYASA" outreach program for Kendriya Vidyalaya students.
    - I teach as well as demonstrated various scientific experiments to school students from class VIII-XI.

INDUSTRIAL EXPERIENCE:

Senior Research Scientist at Albany Molecular Research Inc. (AMRI) Singapore (2010-Jan 2013)

- As a team leader involved as one of the inventors to identify and develop HTS hits to lead validation and put first-in-class molecules against epigenetic targets for further clinical stage.
- US Patent has been filled related to the invention.

RESEARCH & LABORATORY EXPERIENCE:

M. Pharmacy Research Dissertation: Pharmaceutical Chemistry

Title: Synthesis and Mutagenic study of some nitrophenyl thioethers
University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, India
Research Supervisor: Professor Tilak R Juneja (October 1996- June 1997)

Ph.D. Chemistry:

Title: Synthesis of Aza Analogue Of CMI-977, Terminal Disaccharide Unit of *K. pneumoniae* And Some Useful Organic Transformations
CSIR-National Chemical Laboratory, Pune, India (University of Pune)
Research Supervisor: Dr. Mukund K Gurjar

CMI-977 is a potent 5-lipoxygenase (5-LO) inhibitor, which has crossed Phase 2 clinical trial. The project was funded by CytoMed, USA/Millennium Pharmaceuticals USA.

2004-2005 Post-Doctoral Research Associate, Department of Chemistry and Biochemistry, The Ohio State University, Columbus, OH

April 2005- May 2010. Post-Doctoral Research Associate, Medicinal Chemistry and Molecular Pharmacology Division, Purdue University, West Lafayette IN

Independent Scientist at CSIR-Indian Institute of Chemical Biology (IICB) Jan 2013

I joined CSIR-Indian Institute of Chemical Biology (IICB) in late January 2013 and currently, has been promoted to Senior Principal Scientist, Professor, Academy of Scientific & Innovative Research (AcSIR). The Council of Scientific and Industrial Research (CSIR) has 37 research laboratories across India and under the Ministry of Science and Technology, Government of India. My independent research lab aims to answer fundamental questions that lie at the interface of chemistry and biology with the objective to unravel the molecular mechanism and rationally develop a potential treatment for human diseases. At IICB, I have integrated my knowledge gained from the exposure to working in different domains of research and forged a network of collaborations among IICB scientists, scientists from other institutes and international collaborations for the pursuit of original research and their translational development in a multidisciplinary concerted manner. I have initiated programs for autoimmune diseases and metabolic diseases platforms from scratch at IICB from the very scratch without any previous background. I have involved other faculty members in the program and am responsible for guiding/monitoring and the progress of these drug development efforts. The preclinical validation and negotiations with pharma companies for licensing of the portfolio are ongoing.

PATENTS

1. PROTACS For Ask1 Protein Degradation: Preparation and Use Thereof. Application No: 202311034982 (PI: Dr. A Talukdar)
2. Small molecules for Adoptive T-cell therapy (ACT) through activation of the mTOR signalling pathway, preparation and use thereof. Application No: 202311034981 (PI: Dr. A Talukdar and Dr. S Chatterjee)
3. Preparation of Quinazolinediones and use Thereof for Treatment of Non-Alcoholic Fatty Liver Disease. PCT/IN2022/051099. Filing date 25.12.2021. (PI: Dr. A Talukdar and Dr. P Chakrabarti)
4. Quinazolinones Derivatives for Treatment of Non-Alcoholic Fatty Liver Disease, Preparation and Use Thereof. PCT/IN2021/050621. (PI: Dr. A Talukdar and Dr. P Chakrabarti)
5. Bicycle Topoisomerase I Inhibiting Compounds, Process for Preparation And Use Thereof. WO/2019/229765. (PI: Dr. A Talukdar)
6. Purine Based Compounds As Toll-Like Receptor 9 Antagonist. WO/2019/092739-US20200347062B2-Grant Date: 09.11.2021. (PI: Dr. A Talukdar and Dr. D Ganguly)
7. Bicyclic Compound and Use Thereof for Inhibiting SUV39H2. PCT/US2016/0051350.
8. Blocking toll-like receptor 9 signaling with small molecule antagonist. WO2017/163264A1-US10662177B2 Grant Date: 26.05.2020. (PI: Dr. A Talukdar and Dr. D Ganguly)
9. Preparation of 2,5-disubstituted pyrrolidines and tetrahydrothiophenes as leukotrine biosynthesis inhibitors. *PCT Int. Appl. WO 2000001670 A1* 13 Jan 2000, 80 pp. European Patent EP 1115702, 22 February 2002.

PUBLICATIONS

1. Talukdar A.*, Sarkar D. EDITORIAL: Catalyzing the Future of Medicinal Chemistry Research in India. ***Journal of Medicinal Chemistry***, 2023, https://doi.org/10.1021/acs.jmedchem.3c01304 (***In Press***).
2. Bhattacharya D, Li ASM, Paul B, Dastidar UG, Santhakumar V, Sarkar D, Chau I, Li F, Ghosh T, Vedadi M, Talukdar A.* Development of Selective Class I Protein Arginine Methyltransferase Inhibitors through Fragment-Based Drug Design Approach. ***European Journal of Medicinal Chemistry***, 2023, https://doi.org/10.1016/j.ejmech.2023.115713 (***In Press***)
3. Das N, Bhattacharya, D, Bandopadhyay P, Dastidar UG, Paul B, Rahaman O, Hoque I, Patra B, Ganguly D*, and Talukdar A.* Mitigating hERG Liability of Toll-Like Receptor 9 and 7 Antagonists through Structure-Based Design. ***ChemMedChem***, 2023 (e202300069). Selected for CSIR Special Issue by Wiley. https://doi.org/10.1002/cmdc.202300069.
4. Das N, Bandopadhyay P, Roy S, Sinha BP, Dastidar UG, Rahaman O, Pal S, Ganguly D*, and Talukdar A.* Development, Optimization, and In Vivo Validation of New Imidazopyridine Chemotypes as Dual TLR7/TLR9 Antagonists through Activity-Directed Sequential Incorporation of Relevant Structural Subunits. ***Journal of Medicinal Chemistry***, 2022, 65, 17, 11607.

5. Pal S, Ghosh Dastidar U, Ghosh T, Ganguly D, Talukdar A.* Integration of Ligand-Based and Structure-Based Methods for the Design of Small-Molecule TLR7 Antagonists. ***Molecules***, 2022, 27, 13, 4026.
6. McNamara N, Saunders E, Varghese S, Zheng R, Simpson K, Varma DM, Johnson MM, Hasan Zahid MS, Bachelder EM, Ainslie KM, No JH, Koh D, Shum D, Das N, Patra B, Roy J, Talukdar A., Ganguly D, McConville M, Baell J*. Hit-to-lead optimization of novel phenyl imidazole carboxamides that are active against Leishmania donovani. ***European Journal of Medicinal Chemistry***, 2022, 240, 114577. 4026.
7. Talukdar A.* Kundu B, Sarkar D, Goon S, Mondal MA. Topoisomerase I inhibitors: Challenges, progress and the road ahead. ***European Journal of Medicinal Chemistry***, 2022, 236, 114304.
8. Talukdar A.* Mukherjee A, Bhattacharya D. Fascinating Transformation of SAM-Competitive Protein Methyltransferase Inhibitors from Nucleoside Analogues to Non-Nucleoside Analogues. ***Journal of Medicinal Chemistry***, 2022, 65,3, 1662. Selected for Special issue "Epigenetics 2022".
9. Veale, CGL, Talukdar A, Vauzeilles B. ICBS 2021: Looking Toward the Next Decade of Chemical Biology. ***ACS Chemical Biology***. 2022, 17, 4, 728–743
10. Kundu B, Raychaudhuri D, Mukherjee A, Sinha BP, Sarkar D, Bandopadhyay P, Pal S, Das N, Dey D, Ramarao K, Nagireddy K, Ganguly D,* and Talukdar A.* Systematic Optimization of Potent and Orally Bioavailable Purine Scaffold as a Dual Inhibitor of Toll-Like Receptors 7 and 9. ***Journal of Medicinal Chemistry***, 2021, *64*, 9279–9301.
11. Talukdar A.* Ganguly D, Roy S, Das N, Sarkar D. Structural Evolution and Translational Potential for Agonists and Antagonists of Endosomal Toll-like Receptors. ***Journal of Medicinal Chemistry***, 2021, 64, 12, 8010.
12. Pal S, Paul B, Bandopadhyay P, Preethy N, Sarkar D, Rahaman O, Goon S, Roy S, Ganguly D,* Talukdar A.* Synthesis and characterization of new potent TLR7 antagonists based on analysis of the binding mode using biomolecular simulations. ***European Journal of Medicinal Chemistry***, 2021, 210, 112978.
13. Bezerra GA, Holenstein A, Foster WR, Xie B, Hicks KG, Bürer C, Lutz S, Mukherjee A, Sarkar D, Bhattacharya D, Rutter J, Talukdar A. Brown PJ, Luo M, Shi L, Froese DS,* Yue WW.* Identification of small molecule allosteric modulators of 5,10-methylenetetrahydrofolate reductase (MTHFR) by targeting its unique regulatory domain. ***Biochimie***, 2021. 183, 100.
14. Kundu B, Sarkar D, Chowdhuri SP, Pal S, Das SK, Das BB, and Talukdar A.* Development of a metabolically stable topoisomerase I poison as anticancer agent. ***European Journal of Medicinal Chemistry***, 2020, *202*, 112551.
15. Mukherjee A, Raychaudhuri D, Sinha BP, Kundu B, Mitra M, Paul B, Bandopadhyay P, Ganguly D,* and Talukdar A.* A Chemical Switch for Transforming a Purine Agonist for Toll-like Receptor 7 to a Clinically Relevant Antagonist. ***Journal of Medicinal Chemistry***, 2020, 63, 4776.
16. Bhowmik D, Pal S, Lahiri A, Talukdar A*, Sandip Paul*. Emergence of multiple variants of SARS-CoV-2 with signature structural changes. 2020. bioRxiv preprint. doi: 10.1101/2020.04.26.062471.
17. Pal S, Talukdar A.* Compilation of Potential Protein Targets for SARS-CoV-2: Preparation of Homology Model and Active Site Determination for Future Rational Antiviral Design. 2020. ChemRxiv. doi: 10.26434/chemrxiv.12084468.

18. Kundu B, Das SK, Paul Chowdhuri S, Pal S, Sarkar D, Ghosh A, Mukherjee A, Bhattacharya D, Das BB,* and Talukdar A.* Discovery and Mechanistic Study of Tailor-Made Quinoline Derivatives as Topoisomerase 1 Poisons with Potent Anticancer Activity. ***Journal of Medicinal Chemistry***, 2019, *62*, 3428.
19. A Mukherjee, S Mishra, NK Kotla, K Manna, S Roy, B Kundu, Bhattacharya D, Saha KD, Talukdar A.*. Semisynthetic Quercetin Derivatives with Potent Antitumor Activity in Colon Carcinoma. ***ACS Omega***, 2019, *4*, 7285.
20. Kundu B, Sarkar D, Ray N, Talukdar A.* Understanding the Riboflavin Biosynthesis Pathway for the Development of Antimicrobial Agents. ***Medicinal Research Reviews***. 2019, 1-34.
21. Pal S, Kumar V, Kundu B, Bhattacharya D, Preethy N, Reddy MP, Talukdar A.* Ligand-based Pharmacophore Modeling, Virtual Screening and Molecular Docking Studies for Discovery of Potential Topoisomerase I Inhibitors. ***Computational and Structural Biotechnology Journal***, 2019, *17*, 291.
22. Paul B, Rahaman O, Roy S, Pal S, Satish S, Mukherjee A, Ghosh AR, Raychaudhuri D, Bhattacharya R, Goon S, Ganguly D* and Talukdar A.* Activity-guided Development of Potent and Selective Toll-like Receptor 9 Antagonists. ***European Journal of Medicinal Chemistry***, 2018, *159*, 187.
23. Liu CSC, Raychaudhuri D, Paul B, Chakrabarty Y, Ghosh AR, Rahaman O, Talukdar A, Ganguly D. Cutting Edge: Piezo1 Mechanosensors Optimize Human T Cell Activation. ***Journal of Immunology***, 2018. pii: ji1701118.
24. S Roy, B Paul, A Mukherjee, B Kundu, Talukdar A.* Copper-catalyzed selective C–N bond formation with 2-amino, 2-hydroxy and 2-bromo-5-halopyridine. ***RSC Advances***, 2017, *7*, 44366.
25. Roy S, Mukherjee A, Paul B, Rahaman O, Roy S, Maithri G, Ramya B, Pal S, Ganguly D,* and Talukdar A.* Design and Development of Benzoxazole Derivatives with Toll-like Receptor 9 Antagonism. ***European Journal of Medicinal Chemistry***, 2017, *134*, 334-347.
26. Talukdar A, Zhao Y, Lv W, Bacher A, B. Illarionov, M. Fischer, and Mark Cushman. O-Nucleoside, S-Nucleoside, and N-Nucleoside Probes of Lumazine Synthase and Riboflavin Synthase. ***J. Org. Chem***., 2012, *77*, 6239-6261.
27. Mayhoub SA, Talukdar A, and Mark Cushman. A Highly Efficient Oxidation of Benzyl Methyl Ethers with NBS Selectively Affords Either Aromatic Aldehydes or Aromatic Methyl Esters. ***J. Org. Chem***., 2010, *75*, 3507-3510.
28. Talukdar A, Morgunova E, Duan J, Meining W, Foloppe N, Nilsson L, Bacher A, Illarionov B, Fischer M, Ladenstein R, Mark Cushman. Virtual Screening, Selection and Development of a Novel Structural Scaffold for Inhibition of Lumazine Synthase. ***Bioorg Med Chem***. 2010, *18*, 3518-3534.
29. Talukdar A, Breen M, Bacher A, Illarionov B, Fischer M, Georg G, Ye QZ, and Mark Cushman. Discovery and Development of a Small Molecule Library with Lumazine Synthase Inhibitory Activity. ***J. Org. Chem***., 2009, *74*, 5123–5134 (Feature JOC Article).
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32. Kim HY, Talukdar A, and Cushman, M. Regioselective synthesis of *N*-β-hydroxyethylaziridines by ring-opening reaction of epoxides with aziridine generated in situ. ***Organic Letters***, 2006, *8*, 1085.
33. Luo S, Zhu, L, Talukdar A, Mi X, Cheng J-P, Wang PG. Recent Advances in Rear Earth-Metal Triflate catalyzed Organic Synthesis in Green Chemistry. ***Mini-Reviews in Organic Chemistry 2005****, 2. 546.*
34. Zhu L, Talukdar A, Zhang G, Kedenburg JP, Wang PG. A divergent synthesis of uncommon sugars from furanaldehyde. ***Synlett,*** 2005, 1547.
35. Gurjar, MK, Talukdar A. Synthesis of terminal disaccharide unit of *Klebsiella pneumoniae*. ***Tetrahedron***, 2004, *60*, 3267.
36. Talukdar A. Unusual conversion of sugar oximes to sugar nitriles with ruthenium catalysts. ***Synthetic Communications***, 2002, *32*(22), 3503.
37. Gurjar, MK, Talukdar A. Heck reaction of (*S*)-N-Cbz-allyl glycine *tert*-butyl ester with aromatic halides. ***Synthesis***, 2002, 315.
38. Juneja, TR, Talukdar A*, Gupta, RL. Mutagenicity of Sulfoscanate: a comparative study. ***Mutation Res***., 2002, *518*, 155-161.
39. Chorghade MS, Gurjar MK, Talukdar A. Fascinating Excursions into Chiral Chemistry: An Insider's Perspective. ***CHIMICA OGGI Chemistry Today*** 2002, *20,* 20.
40. Juneja, TR, Talukdar A*, Mehta N, Gupta, RL. Effect of various alkyl and unsaturated substituents on the mutagenicity of some nitrophenyl thioethers. ***Mutation Res***., 2001, *495*, 97-102.
41. Gurjar MK, Sadalapure K, Adhikari S, Sarma BVNBS, Talukdar A, Chorghade MS. Kinetic resolution of aryl glycidyl ethers: A practical synthesis of optically pure β-blocker (*S*)-Metoprolol. ***Heterocycles***, 1998, *48*, 1471.

BOOK CHAPTER

1. Bromhexine: Into the spotlight. Chapter 57; Viral, Parasitic, Bacterial, and Fungal Infections. Arindam Talukdar, Dipika Sarkar, Dipayan Sarkar. Elsevier. 2022.
2. Molecular Docking for Computer-Aided Drug Design. Chapter-21; Computational Approaches Toward Development of Topoisomerase I Inhibitor: A Clinically Validated Target. Arindam Talukdar, Sourav Pal. Elsevier. 2021.
3. Protein–Protein Interaction Regulators. Chapter-13; Small Molecule Modulators of Endo-lysosomal Toll-like Receptors. Arindam Talukdar, Ayan Mukherjee, Dipyaman Ganguly. Protein–Protein Interaction Regulators. Royal Society of Chemistry. 2020.
4. N-Nitroso Compounds. Chapter-3; Nitric Oxide Donors and its Applications. Arindam Talukdar, Wang P. G. 2004. Wiley-VCH, Germany.

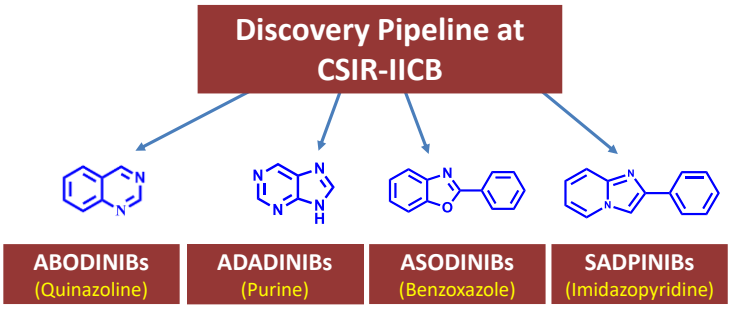
HIGHLIGHTS OF CONTRIBUTIONS TO THE AREA OF SPECIALIZATION

I have an interdisciplinary background with a Master's degree in Pharmaceutical Chemistry from Panjab University Chandigarh and Ph.D degree in Chemistry from CSIR-National Chemical Laboratory (NCL), Pune. My Ph.D. research was an amalgamation of fundamental discovery followed by industrial applications. **The industrial project was funded by CytoMed, USA/Millennium Pharmaceuticals USA** towards stereoselective development of a drug candidate CMI-977 and its analogues. CMI-977 completed the Phase 2 clinical trial. *The key methodology that was developed was extended for the commercial manufacturing of stereoselective β-blocker drugs in the Indian industry*. I spent six years in the USA as a postdoctoral fellow at The Ohio State University and Purdue University, where I obtained training in glycobiology, glycochemistry, and various aspects of Chemical Biology and Medicinal chemistry related to drug discovery. Thereafter, I had a very impactful industrial stint for two-and-half years working as a Senior Research Scientist at Albany Molecular Research Inc, Singapore. As a team leader, I was instrumental in developing and validating first-in-class epigenetic target small molecules from high-throughput screening into the pre-clinical stage. The industry awarded me with inventorship. I joined CSIR-Indian Institute of Chemical Biology (IICB) in January 2013 as a Senior Scientist. Recently I have been promoted to Senior Principal Scientist with merit. The following are the major outputs/outcomes of our research group:

i. Advancement of the fundamental concept of medicinal chemistry drug discovery.
ii. Seminal contribution to the field of medicinal chemistry in general.
iii. Empowering and training PhD and Master's students in drug discovery concepts and strategies, which will foresee the advancement of Indian drug discovery research in coming years.
iv. Providing a conceptual drug discovery model for the medicinal chemistry community for the future generation of the potential drug candidate.
v. Conducting workshops on medicinal chemistry concepts for students (I have conducted four such workshops with international speakers and hands-on training for students across India free of any charges).
vi. Publishing our work in high-impact journals for recognition of Indian Medicinal Chemistry research.
vii. Patenting our work for possible commercialization.

The main contribution is towards the Discovery and Development of dual TLR7 and TLR9 Antagonists for autoimmune diseases at CSIR-IICB. The human innate immune system is the first line of defense against the invasion of pathogenic microorganisms. Toll-like receptors (TLRs), mostly expressed on antigen-presenting cells such as dendritic cells, are germline-encoded pattern recognition molecules that play key roles in innate immunity by regulating inflammation. Among the family of TLRs, TLR3, TLR7, TLR8, and TLR9 have been identified in humans that are located inside the endosomal compartments (pH = 4.5−6.5) of the immune cells and they recognize nucleic acids of both pathogenic origin and self-origin. Aberrantly activation of endosomal TLR7/8/9, initiates autoreactive inflammation in different autoimmune diseases such as systemic lupus erythematosus (SLE), psoriasis, Sjögren's syndrome and systemic sclerosis. The

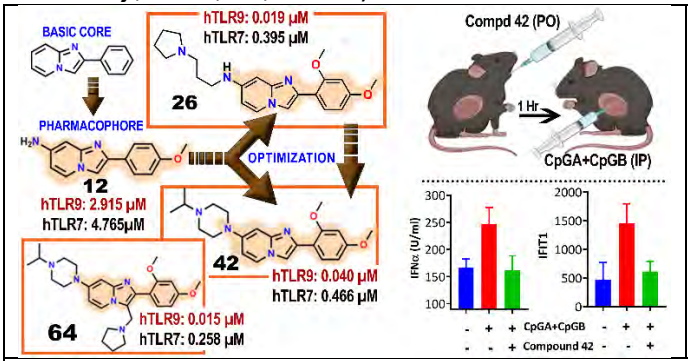
role of TLR7/9 is well established and can serve as an ideal therapeutic target for novel drug discovery, leading to the amelioration of these diseases. The lab is involved in conceptualizing, rationally designing, developing, and validating dual and selective antagonists for the nucleic acid-recognizing TLRs (TLR7 and TLR9) for devising novel therapeutic strategies in relevant clinical contexts. An exhaustive pipeline consisting of molecules from Purine, Quinazoline and Imidazopyridines.

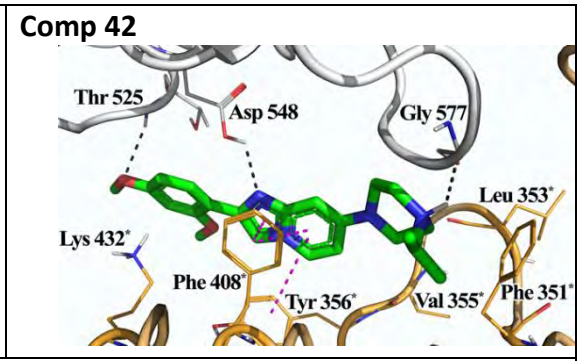


Till now the work resulted in two GRANTED patents (WO/2019/092739- US20200347062B2- **Granted** Date: 09.11.2021; WO2017/163264A1- US10662177B2 **Granted** Date: 26.05.2020) and many publications in reputed medicinal chemistry journals.
Advanced-level talk is ongoing with Pharmaceutical industries for licensing out these patented CSIR technologies. The RC members appreciated the success of the project.

DIFFERENT STRATEGIES ARE EMPLOYED FOR DRUG DISCOVERY.

Strategic Development of New Chemotypes. High-throughput screening to identify new chemotypes is often out of the reach of academics. Our strategy is to develop a new chemotype "imidazopyridine" as dual TLR7/TLR9 antagonists from the basic molecular framework and deducing the chemical spaces through sequentially incorporating relevant structural subunits to identify minimal pharmacophoric features, thereby sculpting the SAR (***Journal of Medicinal Chemistry***, **2022**, *65*, 11607).

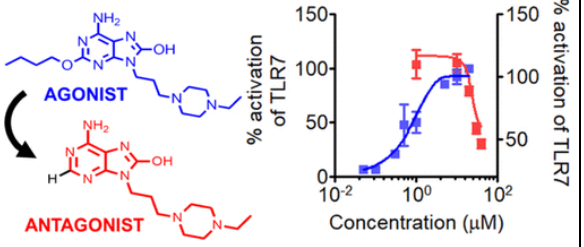




Development, Optimization, and In Vivo Validation of New Imidazopyridine Chemotypes as Dual TLR7/TLR9 Antagonists through Activity-Directed Sequential Incorporation of Relevant Structural Subunits. Das N, Bandopadhyay P, Roy S, Sinha BP, Dastidar, UG, Rehman O, pal S, Ganguly D,* & **Talukdar A** ***. *Journal of Medicinal Chemistry***, **2022,** 65, 17, 11607. https://doi.org/10.1021/acs.jmedchem.2c00386

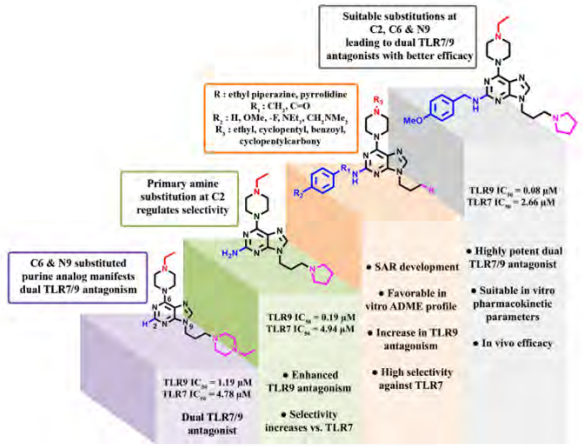
Switching Agonist to Antagonist in Purine Scaffold. We hypothesize that both agonist and antagonist of TLR7 bind at a similar site thus, might share similar chemical-structural features for

receptor affinity. We mapped the path for transforming agonist to antagonist through a single-point '***Chemical Switch***' in TLR7 ligands that can reverse their functional activity. The removal of the butoxy group at C2 position of the TLR7 purine agonist transforms the TLR7 agonist into TLR7 antagonist (***Journal of Medicinal Chemistry***, **2020**, *63*, 4776).



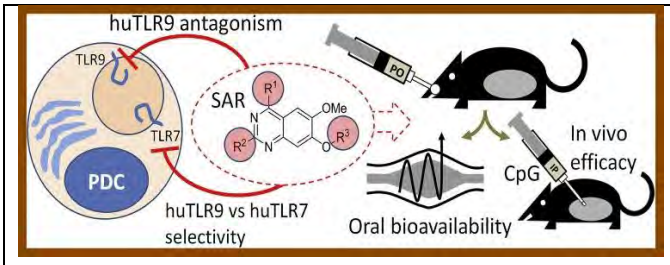
A Chemical Switch for Transforming a Purine Agonist for Toll-like Receptor 7 to a Clinically Relevant Antagonist. Mukherjee A, Raychaudhuri D, Sinha BP, Kundu B, Mitra M, Paul B, Bandopadhyay P, Ganguly D,* and **Talukdar A*.** ***Journal of Medicinal Chemistry***, **2020**, 63, 4776. https://doi.org/10.1021/acs.jmedchem.0c00011 .

Lead Optimization Toward Dual TLR7/TLR9 Antagonists. The lead validation through systematically optimizing via in-vitro DMPK, in-vivo pharmacokinetics, in-vitro and in-vivo toxicity assessment, in-house pharmacodynamic mouse model and finally establishing the efficacy of the lead candidate in a preclinical psoriasis mouse model of the autoimmune disease (***Journal of Medicinal Chemistry***, **2021**, 64, 9279).



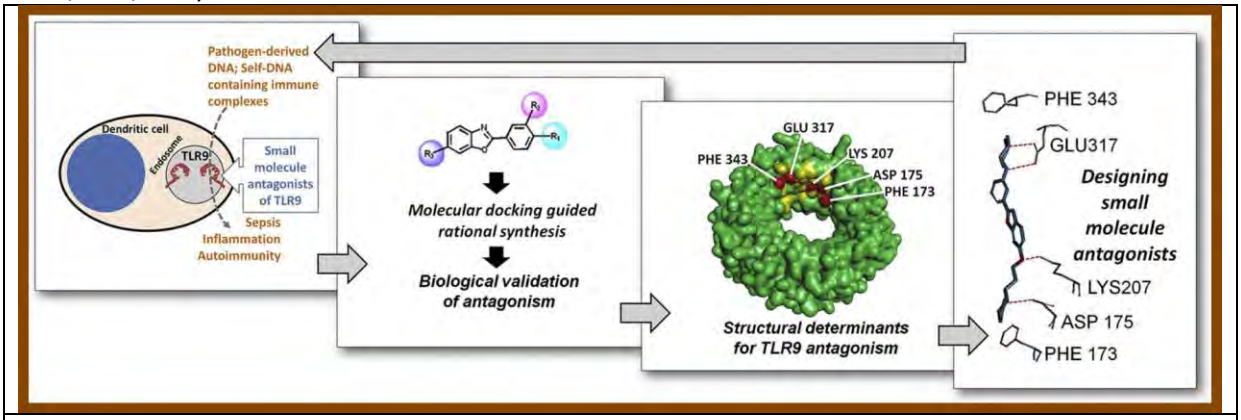
Systematic Optimization of Potent and Orally Bioavailable Purine Scaffold as a Dual Inhibitor of Toll-Like Receptors 7 and 9. Kundu B, Raychaudhuri D, Mukherjee A, Sinha BP, Sarkar D, Bandopadhyay P, Pal S, Das N, Dey D, Ramarao K, Nagireddy K, Ganguly D,* and **Talukdar A***. ***Journal of Medicinal Chemistry***, **2021,** *64*, 9279. https://doi.org/10.1021/acs.jmedchem.1c00532.

Activity Guided Rational Design from Quinazoline Scaffold. Through an activity-guided approach, we have identified chemical features in orally bioavailable quinazoline core that are essential for selective hTLR9 inhibition as well as dual TLR7 and TLR9 inhibition. (***European Journal of Medicinal Chemistry***, **2018**, 159, 187).



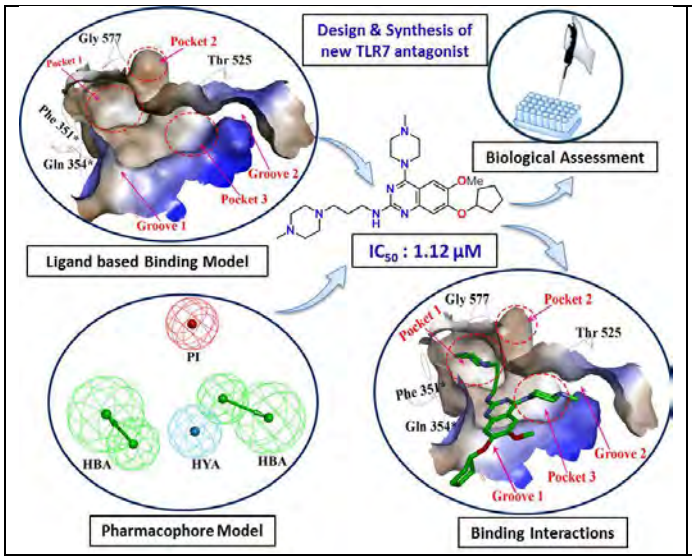
Activity-guided Development of Potent and Selective Toll-like Receptor 9 Antagonists. aul B, Rahaman O, Roy S, Pal S, Satish S, Mukherjee A, Ghosh AR, Raychaudhuri D, Bhattacharya R, Goon S, Ganguly D*, **Talukdar A***. ***European Journal of Medicinal Chemistry***, **2018**, 159, 187. https://doi.org/10.1016/j.ejmech.2018.09.058.

Optimization of Existing Benzoxazole Scaffold. The study was initiated from a known E6446 hTLR9/hTLR7 antagonist We provided a correlation between our binding mode hypothesis and hTLR9 antagonistic activity for future development (***European Journal of Medicinal Chemistry***, **2017**, 134, 334).



Design and Development of Benzoxazole Derivatives with Toll-like Receptor 9 Antagonism. Roy S, Mukherjee A, Paul B, Rahaman O, Roy S, Maithri G, Ramya B, Pal S, Ganguly D,* **Talukdar A***. ***European Journal of Medicinal Chemistry***, **2017**, 134, 334-347. https://doi.org/10.1016/j.ejmech.2017.03.086.

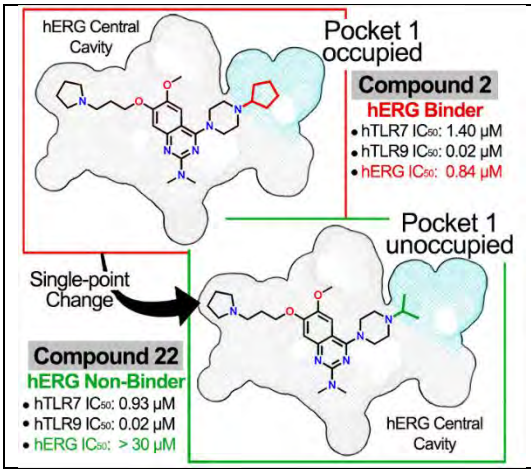
Design Facilitated by Universal Binding Model. The unusual topology of the ligand binding surface of TLR9 and TLR7 lacks conventional pockets. We proposed a hypothetical binding model to design TLR9 and TLR7 antagonists paving the way for a rational design (***European Journal of Medicinal Chemistry***, **2021**, 210, 112978; ***Molecules***, **2022**, 27, 13, 4026). Our hypothetical model was validated through the X-ray co-crystal structure of TLR7 published in Nature Comm. by Tojo et. al. doi: https://doi.org/10.1038/s41467-020-19025-z.



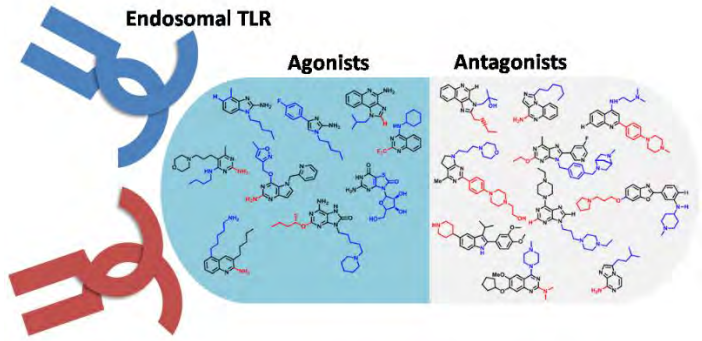
Synthesis and characterization of new potent TLR7 antagonists based on analysis of the binding mode using biomolecular simulations. Pal S, Paul B, Bandopadhyay P, Preethy N, Sarkar D, Rahaman O, Goon S, Roy S, Ganguly D,* **Talukdar A *.** ***European Journal of Medicinal Chemistry***, **2021**, 210, 112978.

Strategy to Mitigating hERG Liability. hERG is a primary **ANTI-TARGET in the drug development** process as the K+ channel encoded by hERG plays an important role in cardiac re-polarization.

The present study describes a coordinated strategy to integrate the understanding from structure-based protein-ligand interaction to develop **non- hERG binders** with IC50 > 30 µM with retention of TLR7/9 antagonism through a ***single point change*** in the scaffold. (***ChemMedChem***, **2023**, e202300069. doi: 10.1002/cmdc.202300069).

	Mitigating hERG Liability of Toll-Like Receptor 9 and 7 Antagonists through Structure-Based Design. N Das, D Bhattacharya, P Bandopadhyay, UG Dastidar, B Paul, Rahaman O, Hoque I, Patra B, Ganguly D, **Talukdar A*.** ***ChemMedChem***, **2023**, e202300069. doi: 10.1002/cmdc.202300069).

Perspective. We published a perspective highlighting rational approaches to elucidate the structural attributes of small molecules capable of agonism or antagonism or of elegantly switching between the two. This understanding can provide the framework for future development (***Journal of Medicinal Chemistry***, **2021**, 64, 12, 8010).

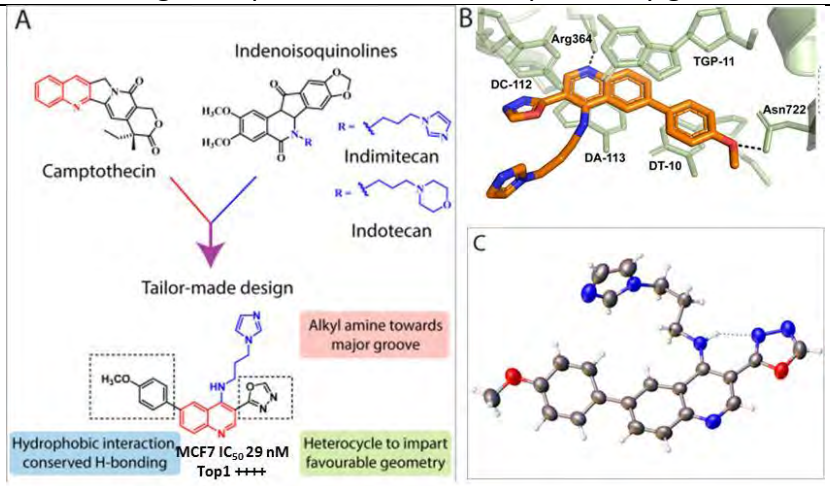
	Structural Evolution and Translational Potential for Agonists and Antagonists of Endosomal Toll-like Receptors. **Talukdar A,*** Ganguly D, Roy S, Das N, Sarkar D. **Journal of Medicinal Chemistry**, **2021**, 64, 12, 8010.

Research contributions towards the Design and Development of *non-camptothecin'* topoisomerase I (Top1) inhibitors for cancer chemotherapy

In various tumor cells, Top1 is over-expressed than the normal cells; hence, modulating the Top1 activity in tumor cells to block DNA replication and cell division has made Top1 an attractive drug target for anticancer therapy. Anticancer drugs like camptothecin (CPT) and its FDA-approved derivatives (Topotecan and Irinotecan) selectively trap Top1-DNA cleavable complexes, which can account for the killing of dividing malignant cells by 'Top1 poisons'. Topotecan and irinotecan are used for advanced colorectal carcinomas and ovarian cancers, which emphasizes the significance of Top1 as a drug target. However, CPTs are not ideal drug molecules due to their toxicity, an inherently unstable chemical structure that is rapidly inactivated in the plasma due to hydrolysis

of lactone E-ring and suffers from rapid cellular efflux via membrane pumps (Pgp). As a result, there is great interest in the development of '*non-camptothecin*' Top1 inhibitors as anticancer agents.

Hypothesis driven Conceptual Design. *Here we have successfully developed and patented (WO2019229765) a new class of potent and selective Top1 poison based on the quinoline core with improved physicochemical properties as well as potency than camptothecin.* The design was initiated based on the structural features of known ligands/poison that bind through the network of interactions in the active site of the human Top1 enzyme. *Our selective lead Top1 poison is bicyclic in nature, unlike polycyclic camptothecins or indenoisoquinolines.* Strategically placed C4 nitrogen atom along with a heterocycle at the C-3 position would form an intramolecular hydrogen bonding (proved through crystal study), which imparts requisite polycyclic geometry and suitable curvature essential for stabilizing the Top1−DNA cleavage complex. Our Top1 poison does not intercalate with DNA nor react with Top1 enzyme but could stabilize covalent Top1-DNA intermediate to form a ternary complex. We have also provided mechanistic insight of Top1 inhibition through live cancer cell imaging and through mutation study. Unlike CPTs, they can stabilize Top1−DNA cleavage complexes even after 5 h proved by gamma-H2AX assay.



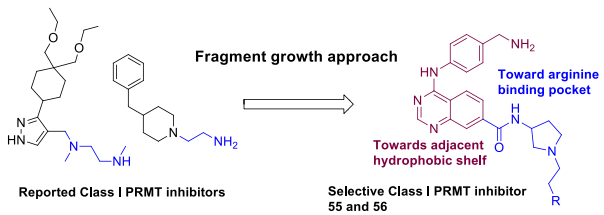
Discovery and Mechanistic Study of Tailor-Made Quinoline Derivatives as Topoisomerase 1 Poisons with Potent Anticancer Activity. Kundu B, Das SK, Paul Chowdhuri S, Pal S, Sarkar D, Ghosh A, Mukherjee A, Bhattacharya D, Das BB,* and **Talukdar A*. *Journal of Medicinal Chemistry*, 2019**, *62*, 3428.

Development of a metabolically stable topoisomerase I poison as anticancer agent. Kundu B, Sarkar D, Chowdhuri SP, Pal S, Das SK, Das BB, and **Talukdar A*. European Journal of Medicinal Chemistry**, **2020**, *202*, 112551.

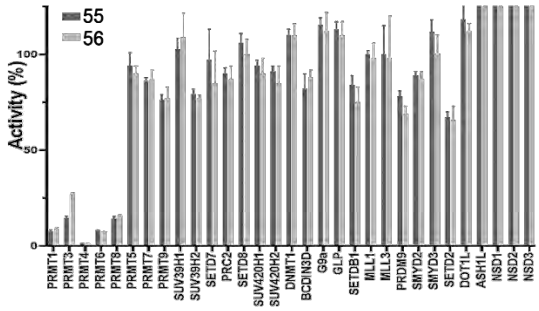
CHEMICAL EPIGENETICS: In collaboration with Structural Genomics Consortium (SGC Canada)

SGC is funded by eight pharmaceutical companies. Along with SGC, we have developed selective class I protein arginine methyltransferase inhibitors through a fragment-based drug design approach. Methyltransferases are enzymes that regulate epigenetic traits of multicellular organisms by catalyzing the methylation of specific lysine and arginine residues which control chromatin compaction, cellular differentiation and repression or activation of transcription. Methyltransferases catalyze the transfer of methyl group from the cofactor *S*-adenosyl- L-

methione (SAM) to substrate peptides and are mainly classified into protein arginine methyltransferase (PRMTs) and protein lysine methyltransferase (PKMTs). However aberrant expression of methyltransferases is linked with diseases like cancer, diabetes, muscular disorders, neurodegenerative diseases, inflammatory disorders etc. Since epigenetic mutations are reversible in nature, a promising therapeutic approach includes targeting these aberrantly expressed epigenetic proteins. Several potent small molecule fragment inhibitors containing flexible alkyl amino side chains, thought to be a possible arginine mimic of Class I PRMTs are present in the literature, which are pan inhibitors of Class I PRMT. We have established a fragment-based drug design approach towards the development of potent Class I PRMT inhibitors with good potency and displayed ~ 100-fold selectivity when tested against a panel of human methyltransferase comprising of lysine methyltransferases (PKMTs), DNA and RNA methyltransferases (DNMTs/ RNMT's).

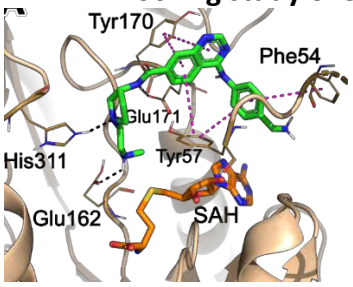


Fragment-based Design of Class I PRMT Inhibitor

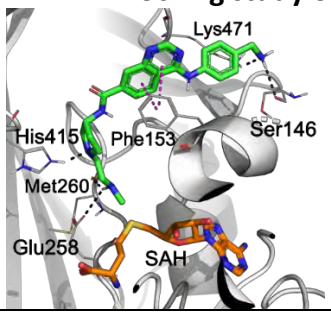


Selectivity of 55 and 56 and against a panel of 31 HMTs at 10 µM

PMRT1: Docking study of 56



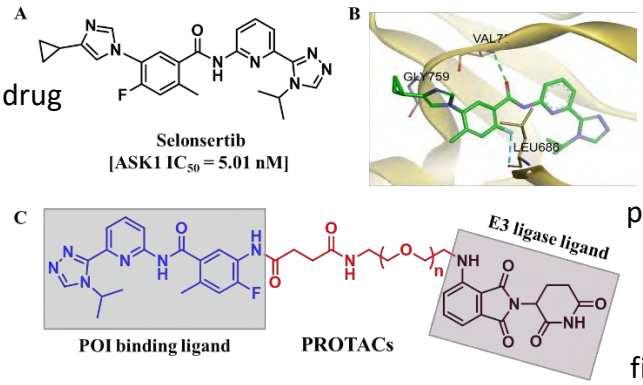
PRMT4: Docking study of 56



Subsequently, we mapped the systematic evolution of selective SAM-competitive heterocyclic non-nucleoside inhibitors from nucleoside inhibitors. This fascinating transition has resolved several issues inherent to nucleoside analogs such as poor pharmacokinetics leading to poor in vivo efficacy. We firmly believe that the strategies described herein will serve as a template for the future development of drugs in general.

Selonsertib-Based PROTAC for Targeted Degradation of Apoptosis Signal-Regulating Kinase 1 (ASK1)

ASK1 is a mitogen-activated protein kinase (MAPK) that transduces apoptotic signals from a variety of stresses. p38 mitogen-activated protein kinases (P38α and β) and c-Jun N-terminal kinases (JNK1, 2, and 3) are key mediators of the cellular stress response. However, prolonged P38 and JNK signaling are associated with many human diseases, including arthritis, dementia, and multiple organ dysfunctions. Attempts to prevent P38- and JNK-mediated disease using small molecule inhibitors of P38 or JNK have generally been unsuccessful. ASK1, an upstream regulator of P38 and JNK, has emerged as an alternative target for limiting P38- and JNK-mediated disease. Furthermore, ASK1 inhibition or deficiency has repeatedly limited the pathologic activation of P38 or JNK in a disease-specific manner. Recently, a promising ASK1 inhibitor, Selonsertib failed in phase 3 clinical trial against NASH-linked cirrhosis, or stage 4 fibrosis. In this context, PROteolysis TArgeting Chimeras (PROTACs) represent a new class of promising therapeutic modalities that hijacks E3 ligases and the ubiquitin-proteasome system (UPS), leading to selective degradation of the target proteins has been employed as an alternative strategy. We have designed and synthesized a set of hetero-bifunctional PROTACs for the targeted proteasomal degradation of ASK1 by hijacking E3 ubiquitin ligase cereblon. Compound HS-26 showed higher degradation efficiency within 1-100 nM, leading to fast, efficient, and prolonged degradation of ASK1 in HepG2 cell lines. Thus, the targeted degradation of ASK1 has great potential and may ultimately be used to achieve lasting, improved human health.



Leadership role in CSIR-Mission Project. I have been involved in many CSIR projects notably the Antiviral Mission mode project (HCP-41). During the SAR-Cov-2 pandemic, I was actively involved in the conceptualization, formulation, execution and functioning of the HCP-41 mission and CSIR activities related to mitigation strategies of the pandemic situation.
As one of the nodal scientists, I assisted the project Director to conceive, formulate and execute the mission. I'm assisting other CSIR labs in their work strategies. I've also motivated other IICB scientists to re-orient their research and contribute to the CSIR mission.

Involved in the MLP-138 project as PI of the therapeutic verticle related to Non-alcoholic steatohepatitis (NASH) and systemic autoimmunity MLP-135. As a PI of the sub-vertical, recently two patents were filled. In the MLP project we have filled two patents on our technology.

International Collaborations. Neglected tropical disease (NTDs): Indo-Australia Collaborations with researchers from Monash University and Melbourne University Australia. The program was initiated with GlaxoSmithKline Pharmaceuticals as a shadow partner. As a PI, I am involved in the drug discovery collaboration focused on neglected tropical diseases specifically focused on Leishmaniasis and Chagas disease. The NTDs drug discovery platform is in sync with the Indian Government's vision of 'Eliminating Leishmania'.

Apart from our effort toward drug discovery, we have organized international workshops for students and faculties across India and Australia at IICB Kolkata free of any charges with the objective to build capacity for drug design and spreading awareness of drug discovery strategies among research scholars.

Epigenetic Drug/Probe program with Structural Genomics Consortium (SGC) at the University of Toronto Canada and University of Oxford UK. My research group is involved in a rational drug discovery program to identify selective inhibitors/probe for specific lysine and arginine methyltransferases. These methyltransferases have been implicated in various diseases.

GRANT ACQUISITION

(Intramural, extramural and international bilateral projects) from CSIR, SERB, DST, DBT including Indo-Australian bilateral projects.

Major programs/Projects currently as PI or Co-PI

Sl.No	Title of Project	Project Category	Participating Agencies	Role
1	Antiviral Mission CSIR: Discovery & Pre-clinical Development of Antivirals for COVID-19 & other diseases	National Lab schemes of CSIR HCP-41	CSIR Current	PI and one of the NODAL
2	Development of new drugs for leishmania- an Australia-Indian partnership	Australia-India Strategic Research Fund (AISRF)	DBT	PI
3	Design and Development of Selective inhibitors of protein arginine methyltransferase 1 involved in epigenetic modifications	Core Research Grant (Chemical Sciences)	DST-SERB CRG/2019/000853 Current	PI
4	Development of Drug-target based Assay platforms and screening against COVID 19	COVID-Management	CSIR-MLP-2037	PI
5	Non-alcoholic steatohepatitis (NASH)	Niche Creating Project (CSIR Mission Mode)	CSIR Current MLP-135	Co-PI
6	Deriving a pan-omics diagnostic pipeline for systems level immune health and therapeutic targeting in systemic autoimmunity	Niche Creating Project (CSIR Mission Mode project)	CSIR Current MLP-137	Co-PI
7	Exploring role of Mechanical cues in Immunocellular Regulation	FBR	CSIR Current	Co-PI

8	Clinical role of a pair of novel mutations in BCR-ABL1 towards therapy switch in imatinib-resistant chronic myeloid leukemia	Grant 2021-22 Multi-Institutional Grant	Lady Tata Memorial Trust Current	PI from IICB
9	Probing endosomal toll-like receptor 9 biology using novel small molecule antagonists	Chemical Sciences	DST-SERB EMR/2015/000117	PI

INTERNATIONAL COLLABORATIONS

1. Neglected tropical disease (NTDs): Indo-Australia Collaborations with researchers from Monash University and Melbourne University Australia.

- Program was initiated with GlaxoSmithKline Pharmaceuticals as a shadow partner. As a PI, I'm involved in the drug discovery collaboration focused on neglected tropical diseases specifically focused on Leishmaniasis and Chagas disease. The NTDs drug discovery platform is in sync with the Indian Government's vision of 'Eliminating Leishmania'.
- Apart from our effort toward drug discovery, we have organized international workshops for students and faculties across India and Australia at IICB Kolkata free of any charge with the objective to build capacity for drug design and spreading awareness of drug discovery strategies among research scholars.

2. Epigenetic Drug/Probe program with Structural Genomics Consortium (SGC) at the University of Toronto Canada and the University of Oxford UK.

- SGC is funded by 8 leading pharmaceutical companies.
- My research group is involved in a rational drug discovery program to identify selective inhibitors/probe for specific lysine and arginine methyltransferases. These methyltransferases have been implicated in various diseases.

3. International research collaboration between CSIR-IICB and St. Jude Children's Research Hospital, Memphis, TN, USA.

- I am the coordinator from CSIR-IICB to identify specific areas of synergy and collaboration to jointly carry out research in emerging areas of biomedical sciences and diseases biology of global importance. This MoU/collaboration has opened up immense opportunities for CSIR institutes, especially in the health care theme to collaborate with American Institutes in addition to St. Jude Children's Research Hospital, Memphis, TN, USA.
- Currently, I'm involved with the researchers from St. Jude Children's Research Hospital to jointly formulate the program for student exchange, student internship, and faculty visits to USA.

KNOWLEDGE DISSEMINATION & POPULARIZATION OF SCIENCE

- *Workshop & Symposium at CSIR-IICB*. I have conducted three physical workshops (2018, 2019, 2022) for master's and Ph.D. students across India involved in medicinal chemistry

research. Apart from exposure to international speakers, during the workshop hands-on training with drug design software (Biovia-Discovery studio, Schrodinger) was provided. The workshop was meant for PhD/Postdoctoral students and young faculties from across India. The objective of the workshop is capacity building and spreading the temper of drug discovery to as many students as possible across India.

- Delivered invited Lectures at international conferences/meetings, popular lectures for school students under JIGYASA, a school student-Scientist connecting program.
- Coordinated four workshops with international experts and industry personnel on Drug Discovery strategy for students from across India at CSIR-IICB.
- Organizing committee member of different national and international conferences organized at CSIR-IICB.
- Coordinator of National Start-up Conclave & Expo at India International Science Festival (IISF), held in Kolkata in 2019.
- National Mission. I'm a course coordinator for the CSIR National Skill Development Mission.
- I actively participate as a member of the CSIR-IICB "JIGYASA" outreach program for Kendriya Vidyalaya students.
- VAIBHAV Summit- Participated as a speaker in National/International forum to spread academic drug discovery program for facilitating policy change.
- I was the CSIR-IICB coordinator i-CONNECT- industry-academia meet.

EFFORTS TOWARD POLICY CHANGE

Secretary, Chemical Biology Society (CBS) of India. I have been appointed as Secretary of the Chemical Biology Society of India in March 2023 during the 10th Annual conference held at KIIT University, Bhubaneshwar. The society does Annual Meeting every year and two satellite meetings. The Secretary has a prominent role in the policy decision for propagating chemical biology/medicinal chemistry research in India. I have a greater responsibility to unite the researchers involved in multidisciplinary research in India under the ambit of CBS.

VAIBHAV Summit- Participated as a speaker in a National/International forum to spread academic drug discovery program for facilitating policy change. The program was organized by the Government of India to foster a collaborative research atmosphere among Non-resident Indian Scientists and Indian scientists for the need to facilitate policy change for scientific development.

Global-Co-Chair, Membership Committee, International Chemical Biology Society (ICBS). I'm responsible for integrating the scientists involved in chemical biology research through ICBS across the globe through virtual meetings and emails. I have nominated the National chair of ICBS of various countries to spread awareness of ICBS society.

MEMBERSHIP OF NATIONAL AND INTERNATIONAL SOCIETIES:

- Scientific Expert Review panel at Chemical Probes Portal (http://www.chemicalprobes.org)
- Secretary, Chemical Biology Society, India

- Life member of the Chemical Biology Society, India.
- Global Co-Chair of the Membership Committee, International Chemical Biology Society (ICBS).

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