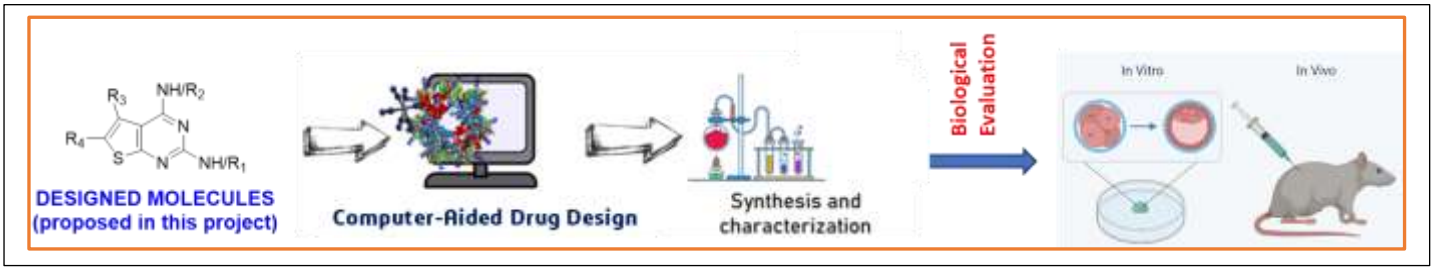
Research Group -Anti-Cancer Drug Discovery

- **Name of Principal Investigator/ Group Leader**: **Dr. Pran Kishore Deb**
- **Research Theme**: Discovery and Development of Novel Chemical Entities for the Treatment of Inflammation, Cancer, Tuberculosis & Malaria
- **Broad Area of Research:**
  - *In silico,* computer-aided drug design of Novel Chemical Entities (NCEs)
  - Synthesis and characterization of NCEs belonging to the Thienopyrimidine Scaffold
  - *In vitro* and *in vivo* anticancer, anti-TB, larvicidal, and anti-inflammatory screening of NCEs

Schematic Representation of the Broad Area of Research



Total Number of Publications by the group: 160

Google Scholar Link: https://scholar.google.com/citations?hl=en&user=isTTsukAAAAJ&view_op=list_works&sortby=pubdate

Top 5 Article: (Vancouver Style)

1. Deb PK, Menon AM, PSR FN, Shruti I, Nidal S, Venugopala KN, et al. Exploring intermolecular interactions and energetics in crystalline substituted thieno[2,3-*d*]pyrimidines. *RSC CrystEngComm*. **2025**;27:2070-2085.
2. Deb PK, Maity P, Sarkar B, Venugopala KN, Tekade RK, Batra S. Insights from Clinical Trials on A2A Adenosine Receptor Antagonists for Cancer Treatment. *ACS Pharmacology & Translational Science*. **2025**;8(6):1498-512.
3. Salou RA, Deb PK, Hourani W, Al-Shar'i N, Al Aboudi A, Venugopala KN, et al. Synthesis, X-ray Crystallography, and Computational Analysis of 2, 4-disubstituted-6, 7-dihydro-5H-cyclopenta[4,5]thieno[2,3-*d*]pyrimidines as COX-2 Inhibitors and Anticancer Agents. *Journal of Molecular Structure*. **2025**:142907.
4. Venugopala KN, Chandrashekharappa S, Deb PK, Al-Shar'i NA, Pillay M, Tiwari P, et al. Identification of potent indolizine derivatives against Mycobacterial tuberculosis: In vitro anti-TB properties, in silico target validation, molecular docking and dynamics studies. *International Journal of Biological Macromolecules*. **2024**;274:133285.
5. Deb PK, Al-Shar'i NA, Venugopala KN, Pillay M, Borah P. In vitro anti-TB properties, in silico target validation, molecular docking and dynamics studies of substituted 1,2,4-oxadiazole analogues against Mycobacterium tuberculosis. *Journal of enzyme inhibition and medicinal chemistry*. **2021**;36(1):869-84.

Patents by the group (38):

Sl. No	Title and Inventors	Application No. & Date	Status
1.	5-(substitutedphenyl)-7-thioxo-7, 8-dihydropyrimido [4, 5-d] pyrimidine-2, 4 (1H, 3H)-dione analogues as antibacterial agents.	**U.S. Patent 12,297,204,** issued **13/5/2025**	Granted
2.	Selective COX-2 inhibition of 2-(substituted benzyl)-3,5, 6,7-tetrahydro-4*H*-cyclopenta[4,5]thieno[2,3-*d*]pyrimidin-4-ones and 4-fluoro-n-(4-oxo-3,5,6,7-tetrahydro-4*H*-cyclopenta[4,5]thieno[2,3-*d*]pyrimidin-2-yl)benzamide as anti-inflammatory agents.	**U.S. Patent 12,227,516B1,** issued **18/2/2025**	Granted
3.	1-(2-(substituted phenyl)-2-oxoethyl)-4-methylpyridin-1-ium bromide as anti-tubercular agents.	**U.S. Patent 12,227,480**, issued **18/2/2025**.	Granted
4.	5-(Substitutedphenyl)-7-thioxo-7,8-dihydropyrimido[4,5-d]pyrimidine-2,4(1H,3H)-dione analogues as antibacterial agents.	**U.S. Patent 18/736710, A1**, issued **13/2/2025**.	Granted
5.	5-(substitutedphenyl)-7-thioxo-7,8-dihydropyrimido[4,5-*d*]pyrimidine-2,4(1*H*,3*H*)-dione analogues as antibacterial agents.	**U.S. Patent 12221450**, issued **11/2/2025**.	Granted
6.	(E)-1-(2-(4-substitutedphenyl)-2-oxoethyl)-4-((hydroxyimino) methyl) pyridinium bromides as antitubercular agents.	**U.S. Patent 12215082**, issued **4/02/2025**.	Granted
7.	5-(Substitutedphenyl)-7-Imino-7,8-Dihydropyrimido[4,5-*d*]pyrimidine-2,4(1*H*,3*H*)-dione analogues as anti-inflammatory agents.	**U.S. Patent 12187733**, issued **07/01/2025**.	Granted
8.	(E)-2-(3-Cyano-4-isobutoxyphenyl)-N′-(substituted benzylidene)-4-methylthiazole-5-carbohydrazides as anti-tubercular agents.	**U.S. Patent 12172973**, issued **24/12/2024**.	Granted
9.	(E)-2-(3-cyano-4-isobutoxyphenyl)-n′-(substituted benzylidene)-4-methylthiazole-5-carbohydrazides as anti-tubercular agents.	**U.S. Patent 12,145,915**, issued **19/11/2024**.	Granted
10.	Substituted 1,3,4-oxadiazole derivatives as anti-tubercular agents.	**U.S. Patent 11998532B1**, issued **04/06/2024**.	Granted
11.	3-Cyano 4,5-diphenyl furan-2-carboxamides as potential antitubercular agents.	**U.S. Patent 11987563B1**, issued **21/05/2024**.	Granted
12.	(6-Methyl-4-substitutedphenyl-2-oxo/thioxo-1,2,3,4-tetrahydropyrimidin-5-yl)(piperidin-1-yl)methanones as anti-tubercular agents.	**U.S. Patent 11986476B1,** issued **21/05/2024**.	Granted
13.	7-isopropyl 1, 2-dimethyl 3-(substituted benzoyl) indolizine-1, 2, 7 tricarboxylates as adenosine receptor active compounds.	**U.S. Patent 11981673B1**, issued **14/05/2024**.	Granted
14.	Oxoimidazolidine derivatives as anti-tubercular agents.	**U.S. Patent 11981643B1**, issued **14/05/2024**.	Granted
15.	7-isopropyl 1-ethyl/methyl 3-(substituted benzoyl)-2-substituted indolizine-1, 7-dicarboxylates as larvicidal agents.	**U.S. Patent 11981674B1**, issued **14/05/2024**.	Granted
16.	Substituted 7-amino-3-(substituted benzoyl) indolizine-1-carboxylates as anti-tubercular agents.	**U.S. Patent 11976066B1**, issued **07/05/2024**.	Granted
17.	Adenosine receptor activity of methyl/ethyl 3-(substituted benzoyl)-6, 8-dimethylindolizine-2-substituted-1-carboxylates.	**U.S. Patent 11974991B1**, issued **07/05/2024**.	Granted
18.	{5-chloro-2-(2-(3-(substitutedphenyl)-1,2,4-oxadiazol-5-yl)ethyl)phenyl}(phenyl) methanones as larvicidal agents.	**U.S. Patent 11970470B1**, issued **30/04/2024**.	Granted
19.	4-[(substituted-1*H*-benzimidazol-2-ylsulfanyl)methyl]-6-substituted-2*H*-chromen-2-ones as larvicidal agents.	**U.S. Patent 11970489B1**, issued **30/04/2024**.	Granted
20.	5-(3-substitutedphenyl)-pyrimido[4,5-*d*]pyrimidine-2,4,7(1*H*,3*H*,8*H*)-trione derivatives as anticancer agents.	**U.S. Patent 11964982B1**, issued **23/04/2024**.	Granted
21.	Dimethyl 7-bromo-1-(4-substituted benzoyl)pyrrolo[1,2-*a*]quinoline-2,3-dicarboxylates as anti-inflammatory agents.	**U.S. Patent 11945819B1**, issued **02/04/2024**.	Granted
22.	Ethyl 2-substituted-1-(substitutedbenzoyl)-7-methylpyrrolo[1,2-a]quinoline-3-carboxylate derivatives as anti-tubercular agents.	**U.S. Patent 11938120B1**, issued **26/03/2024**.	Granted
23.	Substituted 1,4-dihydropyrimidines as antitubercular agents.	**U.S. Patent 11932609B1**, issued **19/03/2024**.	Granted
24.	Thieno [2,3-*d*]pyrimidines as COX-2 inhibitors.	**U.S. Patent 11932656B1**, issued **19/03/2024**.	Granted
25.	5-(3-substitutedphenyl)-pyrimido[4,5-*d*]pyrimidine-2,4,7(1H,3H,8H)-trione derivatives as anticancer agents.	**U.S. Patent 11932649B1**, issued **19/03/2024**.	Granted
26.	Substituted 7-methyl quinoline derivatives as antitubercular agents.	**U.S. Patent 11926627B1**, issued **12/03/2024**.	Granted

Research Projects:

Title	Role (PI/ Co-PI)	Funding Agency	Amount (in Lacs)	Duration
Anticancer Drug Discovery Targeting A_{2A} Adenosine Receptor by Optimizing 2/4-Amino-5,6-substituted-thieno[2,3-*d*]pyrimidine Scaffold	PI	Birla Institute of Technology (BIT), Mesra, Ranchi, Seed Money Scheme (Grant Number BIT/DRIE/SMS/2024-25/1877).	5	2 Years (2024-2025)
Design, Synthesis and Evaluation of Novel Hetero-fused Bicyclic and Tricyclic Thienopyrimidines as Possible Adenosine Receptor Antagonists	PI	Scientific Research Fund, Ministry of Jordan. (MPH/1/33/2018)	70	3 Years (2019-2022)
Lead optimization of 2-(4-methoxyphenyl)-3,5,6,7-tetrahydro-4*H*-cyclopenta[4,5]thieno[2,3-*d*]pyrimidine-4-one: Synthesis, & Evaluation of New Derivatives as Possible Inhibitors of Cyclooxygenase Isoenzyme 2 (COX-2)	PI	Philadelphia University Research Grant, Jordan, Project ID: 46/34/100PU	15	2 Years (2017-2019)
Hit to Lead Optimisation: Synthesis and Biological Evaluation of New Thienopyrimidine Derivatives as Potential Antagonists of Adenosine A_3 Receptor, A Promising Target for the Treatment of Asthma.	PI	Ministry of Science, Technology and Innovation Malaysia, Project ID: 06-02-09-SF0048 (IMU R 164/2015)	35	3 Years (2015-2017)
Design, synthesis, and Evaluation of some Novel Thienopyrimidine Derivatives as Possible A3 Adenosine Receptor Antagonists.	PI	International Medical University, Malaysia (IMU 293/2013)	10	2 Years (2013-2015)

Project 1: Anticancer Drug Discovery Targetting Adenosine Receptors and COX-2 Enzyme

Problem Statement:

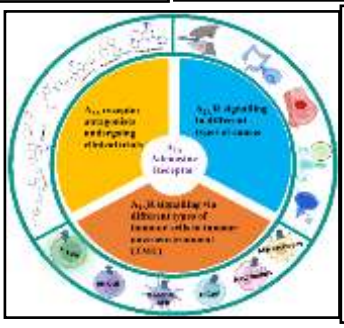
- Tumor microenvironment (TME) overexpresses A2AAR on cytotoxic immune cells, where adenosine binding to A2A AR & inhibits T-cell activation, suppresses cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells, promotes regulatory T cells (Tregs), and impairs antigen-presenting cells (APCs). A2AAR antagonists work synergistically with immune checkpoint inhibitors (ICIs), radiotherapy, and chemotherapy, counteracting adenosine-induced immunosuppression.
- The COX-2 enzyme plays a key role in cancer development by promoting angiogenesis, proliferation, metastasis, evasion of

Applications:

- Adenosine A_2A receptor antagonists can be used either as a standalone therapy or as an adjuvant to enhance anti-tumor responses and improve the efficacy of cancer immunotherapy by restoring immune function, activating $CD8^+$ T cells, increasing NK cell cytotoxicity, reducing Treg-mediated immune suppression, and improving antigen presentation.
- COX-2 selective inhibitors hold potential not only for the safe treatment of chronic pain and inflammation but also for providing therapeutic benefits in various cancers, including

Strategy/ Approach/ Technique/ Experiments used to solve

- *In silico* computer-aided drug design (CADD) of Novel Chemical Entities (NCEs).
- Synthesis, purification and characterization of designed Novel Chemical Entities (NCEs).
- *In vitro* adenosine receptors & COX-2 binding studies of NCEs.
- *In vitro* anticancer studies.
- *In vivo* toxicity profiling of the potent



Publication/patent:

1. *RSC advances*. **2025**;15(26):20418-20445.
2. *ACS Pharmacology & Translational Science*. **2025**;8(6):1498.
3. *J. Molecular Structure* **2025**:142907.
4. RSC *CrystEngComm*. **2025**, 27,2070.
5. *Pharmaceuticals*, **2024;** 17, 1645.
6. **U.S.Patent**11932656B1,Granted 18/2/**2025**
7. **U.S.Patent**11932656B1,Granted 07/1/**2025**

Project 2: Discovery of Anti-TB Agents Targeting InhA Enzyme

Problem Statement:

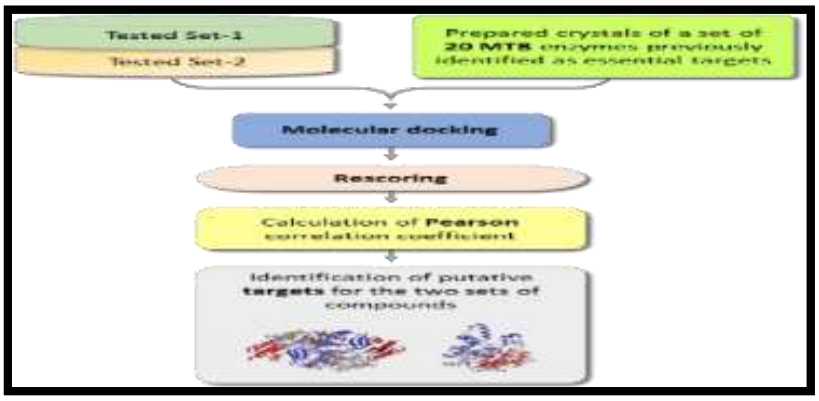
- Tuberculosis (TB) has been known to affect human beings for millennia with a high mortality rate, and the control of TB remains one of the largest endeavors of public health authorities.
- Although predominantly a pulmonary pathogen, TB can spread throughout the body and remains a major global public health burden, responsible for 1.4 million deaths & 10 million infections worldwide in 2019. Our research efforts are focused towards the development of novel compounds with different

Applications:

- Isoniazid (INH), the primary drug for treating tuberculosis, functions by inhibiting Enoyl-ACP reductase (InhA). However, mutations in either InhA itself or, more commonly, in KatG catalase-peroxidase, which activates the INH prodrug, can reduce the effectiveness of isoniazid.
- Therefore, the discovery of inhibitors that directly target InhA, bypassing the need for activation by KatG (known as direct InhA inhibitors), could offer a promising approach to overcome isoniazid resistance

Strategy/ Approach/ Technique/ Experiments used to solve

- *In silico* design (CADD) of Novel Chemical Entities (NCEs) and to identify the putative drug target(s) and, consequently, uderstand their mechanism of action.
- Synthesis, purification and characterization of designed Novel Chemical Entities (NCEs).
- *In vitro* anti-TB assay of designed NCEs against drug Susceptible (H37Rv), multi-drug resistant (MDR) and extremely-drug resistant (XDR-TB) strains of M. tuberculosis.
- *In vitro* & *In vivo* InhA enzyme inhibition study.



Publication/patent:

1. RSC CrystEngComm. **2025**, 27:1707-1721.
2. *International Journal of Biological Macromolecules* **2024**, 133285.
3. *Journal of Enzyme Inhibition and Medicinal Chemistry.* **2021**, 36 (1), 869-884.
4. *Journal of Enzyme Inhibition and Medicinal Chemistry.* **2021,** 36(1), 1472-87.
5. **U.S. Patent 12,297,204**, Granted 13/5/**2025**
6. **U.S. Patent** 12,227,480, Granted 18/2/**2025**
7. **U.S. Patent** 12215082, Granted 04/02/**2025**
8. **U.S. Patent** 12172973, Granted 24/12/**2024**