Azadi Ka Amrit Mahotsav

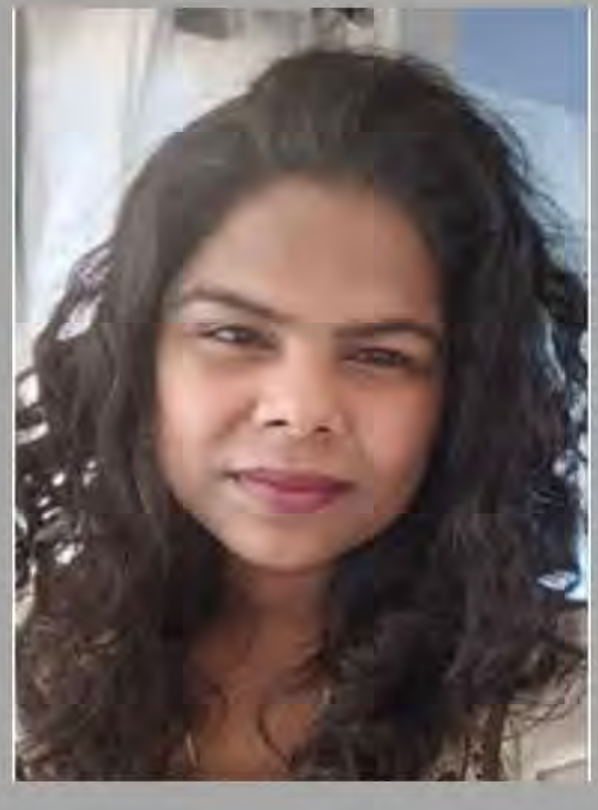
सत्यमेव जयते

राष्ट्रीय प्रतिरक्षाविज्ञान संस्थान

National Institute of Immunology

GRADUATE STUDENT SEMINAR

ANALYZING MUTATION-INDUCED CONFORMATIONAL CHANGES IN EGFR KINASE AND THE DEVELOPMENT OF SMALL MOLECULE DRUGS USING MACHINE-LEARNING BASED METHODS



SAPNA PAL

BIOINFORMATICS CENTRE

EGFR kinases have been selected as drug targets for several cancer types and various computational methods have been used to design kinase inhibitors. While the majority of earlier efforts utilized either ligand-based (QSAR or pharmacophore type) approach, or structure-based approaches like docking/simulations, in recent years machine learning (ML) has been increasingly used and they are known to be much less compute intensive. Ranking compounds as per their experimental binding affinity has also remained a significant challenge. Therefore, it is necessary to develop ML-based scoring functions (SF) for predicting the binding affinity of drugs for the EGFR kinase domain and such methods also have to be standardized on available datasets for other kinases as well as other drug targets with known binding affinities for large compound libraries. The discovery of increasing drug resistance mutations in the EGFR kinase domain also necessitates deciphering the structural basis of drug resistance by conducting MD simulations on native and mutant kinases. Understanding the resistance mechanism will help us to develop better drugs against drug resistance kinases.

25 MAY 2023, 4.00 PM

GP TALWAR AUDITORIUM, NII

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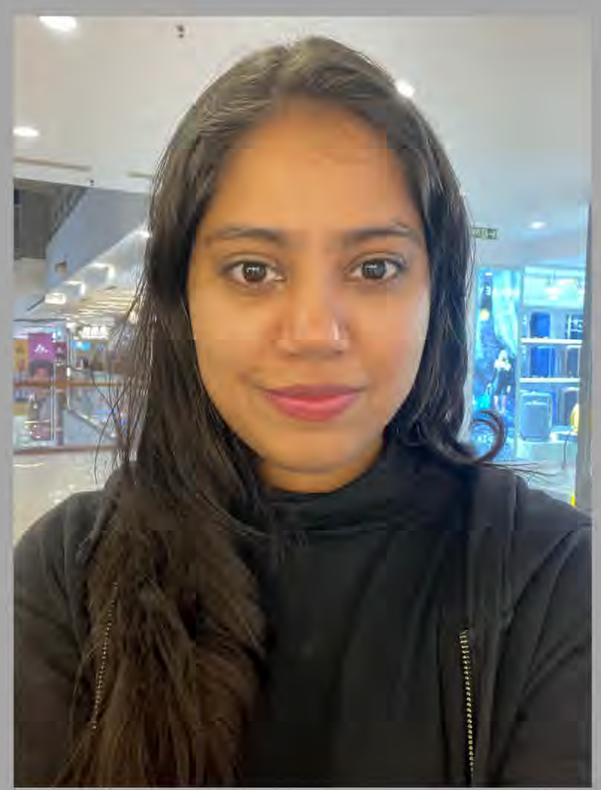
GRADUATE STUDENT SEMINAR

ELUCIDATING THE UNDERLYING BASIS FOR STRUCTURAL STABILITY OF HUMAN ARGINASE-I: A THERAPEUTICALLY IMPORTANT ENZYME



ANJALI KALIA

PROTEIN ENGINEERING LABORATORY

Arginase (EC 3.5.3.1) is a bimetallic enzyme that hydrolyses L-arginine into L-ornithine and urea. Previous studies indicated the therapeutic potential of the Co^{2+}-reconstituted human arginase-I (hArg-I) for the treatment of hyperargininemia and L-arginine auxotrophic cancers due to its high catalytic efficiency. Recent reports also indicated the importance of the structural stability of this protein in its therapeutic application. In this study, we aim to investigate the underlying basis for the structural stability of this enzyme. Using combined approaches, we found certain conserved residues at the core that play a vital role in protein stability. Interestingly, these residues also have a long-range effect in the regulation of activity. Furthermore, we found that protein oligomer formation plays a role in the stability. These findings may be helpful to develop strategies for its better therapeutic potential.

25 MAY 2023, 4.30 PM

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