TIFR Centre for Interdisciplinary Sciences
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Seminar

Structural Biochemistry: Insights into Biological Reactions

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Here we discuss select systems where a combination of X-ray crystallographic and biochemical techniques has been employed to develop insights into mechanism of catalysis, structure-function relationship, protein-protein interactions in enzymes and protein-DNA regulation. The three-dimensional structure enables one to visualize protein structures at the atomic level and enhances our understanding of protein function and combined with other tools can facilitate understanding of the allosteric changes necessary for catalysis. In this talk we discuss two enzyme systems: the first problem deals with deciphering the structure-activity and evolutionary relationships of enzymes involved in nucleobase deamination. The enzyme under investigation, NE0047 was established to be a guanine deaminase with moonlighting activity towards ammeline. Subsequently, the allosteric mechanism of action and structural basis of substrate specificity was determined. By utilizing the information obtained, the enzyme was further engineered so that it can function either exclusively as a guanine deaminase or serve as a specific ammeline deaminase with no cross reactivity.

The second work deals with understanding the mechanism of antibiotic regulation and resistance in Streptomyces. Streptomyces species contribute to two-third of naturally occurring antibiotics. Production of antibiotics and resistance pathways in these species are dictated by interplay of transcriptional regulatory proteins. These proteins belong to the tetracycline family of efflux pump regulators and possess a ligand binding site and a DNA binding site, both of which remain elusive. To decipher the structural mechanism of action here we present the crystal structure of CprB (a putative regulator) in complex with its consensus DNA element. The binding of the DNA induces the restructuring of the CprB dimeric interface, thereby inducing a pendulum like motion, which facilitates transcription regulation via conformationally switching of the protein to the repressed form. Furthermore, it was established that CprB is a pleotropic regulator that also autoregulates it own expression. The identity of the ligand that induces transcriptional activation of CprB was additionally investigated and it was concluded that CprB plays a dual role and may be induced by quorum sensing molecules in early stages of growth and antibiotic intermediates in late growth phase

Thursday, September 11th 2014

11:30 AM (Tea/Coffee at 11:15 AM)

Seminar Hall, TCIS