TIFR Centre for Interdisciplinary Sciences
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# Seminar

## Post-transcriptional Gene Silencing Mediated by RNA-Binding Proteins

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How do RNA-binding proteins effect post-transcriptional gene regulation? Our group explores the role of regulatory proteins which bind to a variety of RNA molecules and effect post-transcriptional gene regulation.

In prokaryotes, the gene regulation is manifested by a set of long non-coding RNA which are globally regulated by Hfq and specifically controlled by Crc, proQ, RapZ etc. Our lab has derived the solution structure of Crc (~ 32 kDa) using solution NMR technique. We find that Crc is divergently evolved from AP endonucleases and regulates lncRNA using a non-canonical surface.

In higher eukaryotes, the RNA interference (RNAi) uses two key enzymes, Dicer and Argonaute, which are assisted by a variety of multiple dsRNA binding domains (dsRBDs) containing proteins (dsRBPs) to regulate RNA mediated gene silencing. A seemingly conserved pathway of RNAi exhibits significant heterogeneity across organisms, e. g., in C. elegans and H. Sapiens, only one Dicer and one or two dsRBDs are found to dictate both siRNA and miRNA biogenesis. Whereas, organisms like D. melanogaster have two separate sets of Dicer : dsRBPs for executing siRNA and miRNA pathway. On the contrary, A. thaliana requires four Dicers and four dsRBPs to accomplish the small RNA pathway in a unique and highly controlled fashion. Sequence analysis of Dicer and dsRBPs show a variety of differences, e. g., the linker between RDE-4 dsRBDs (C. elegans) is composed of ~ 70 amino acids, whereas, DRB4 (A. thaliana) contain linker of 8 amino acids. Additionally, several prominent changes in the key features of dsRBDs, C-terminal regions, dimerization etc. can be further noticed. To understand the origin and necessity of the evolutionary divergence in RNAi, we have defined the functional roles of RDE-4 (C. elegans) as well as DRB4 and DRB2 (A. thaliana) using solution structures and complementary assays. Further, $^{15}N$ backbone relaxation and CPMG experiments are used to probe functionally relevant dynamics in dsRBDs. Moreover, relative inter-domain orientation determined through PREs and SAXS provides a vivid picture on the role of dsRBPs in the RNAi initiation.

***Thursday, Oct 6th 2016***

***4:00 PM (Tea/Coffee at 3:45 PM)***

***Seminar Hall, TCIS***