CANCER SCIENCE INSTITUTE OF SINGAPORE

SEMINAR ANNOUNCEMENT

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Structural Biology of Small RNA-mediated Gene Regulation and Methylation-mediated Epigenetic Regulation

Date: **Wednesday, 18 July 2012**
Time: **11am – 12pm**
Venue: **LT 36, Level 3, Centre for Translational Medicine (CeTM)**
14 Medical Drive, MD 6, Singapore 117599

Abstract:

The RNA segment of the lecture will focus on the structural biology of riboswitches, mRNA elements consisting of a sensing domain and an expression platform, that undergo conformational changes on metabolite binding, and utilize on-off switches to control gene expression. This segment will be followed by our recent research on the structural biology of Argonaute and Dicer proteins and emerging mechanistic insights into cleavage events associated with RNA silencing.

The chromatin segment of the lecture will describe recently determined structures of productive and autoinhibitory DNMT1-DNA complexes, thereby formulating a two-state model of eukaryotic maintenance DNA methylation. Finally, we shall outline our structural studies of readers and erasers of histone marks and the impact of small molecules that perturb these epigenetic regulation processes.

Biography:

Dr. Dinshaw Patel's structural biology research program is centered on an understanding of molecular processes controlling gene regulation, with recent emphasis on projects involving RNA silencing-based suppression of genes and the role of DNA's packaging proteins in spatial and temporal regulation of gene function. His group's research has profoundly impacted on the RNA silencing field through definitive structural characterization of recognition events associated with targeting duplex length, 5'-phosphate and 3'-overhang ends of small interfering RNAs. His research has also provided a mechanistic framework for argonaute-mediated site-specific cleavage of messenger RNA through systematic studies of argonaute complexes with bound guide strand and added target strand, thereby identifying the nucleic acid-binding channel, the base pairing within the seed segment, the alignment at the catalytic cleavage site, and the conformational transitions on binary and ternary complex formation.

His group's structure-function studies on epigenetic regulation have provided mechanistic insights into recognition by writers, readers, and erasers of site-specific lysine modification marks on histones and methylation marks on DNA and their contribution to the establishment and maintenance of chromatin-mediated epigenetic ON/OFF states. In particular, his research has addressed how post-translational modifications of nucleosomal histones regulate access to the underlying DNA by modulating local chromatin structure.