NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

SEMINAR

Wed, 4 April 2018 | 2pm | DBS Conference Room 1

Hosted by Prof Jayaraman Sivaraman

Regulation of genome expression by heterochromatin

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My lab is interested in fidelity of heterochromatin formation and structural changes in chromatin that lead to heterochromatic silencing. To understand this processes we apply various methods ranging from genetic and genomics to biochemistry and cryo-EM.

We have contributed to the understanding of fundamental process of how genomes recognize repetitive and transposable elements and target them into heterochromatin formation (Halic, Cell, 2010; Marasovic, Mol Cell, 2013). To achieve this, the host cells generate Dicer-independent small RNAs that scan the transcriptome to distinguish self from non-self (Marasovic et al, Mol Cell, 2013). We have also shown that degradation of Argonaute-bound small RNAs is essential in providing fidelity in RNAi mediated silencing (Pisacane and Halic, Nature Communications, 2017) and that retention of lncRNAs on chromatin perturbs heterochromatin organization and silencing (Broenner et al, Genome Research, 2017).

We use structural methods to understand mechanisms of RNAi and heterochromatin formation. We have solved structure of a chromodomain, a reader of H3K9 methylation mark, bound to a H3K9-methylated nucleosome (Zocco et al, Cell Discovery, 2016). In our recent work we have solved several structures that show how nucleosomes open and unwind DNA and how histone octamer adapts to DNA unwinding (Bilokapic et al, NSMB, 2017). Our latest nucleosome structures reveal how histone octamer core rearranges and deforms the nucleosome to translocate the DNA. These structures unveil first mechanistic insights into nucleosome remodeling. Nucleosome plasticity observed in our structures is likely exploited by other chromatin machineries beyond chromatin remodeling (Bilokapic et al, in review). Recently, we have also solved a structure of histone H1 chaperone-import complex that shows how the complex of two importins shields and chaperons histone H1 in transport to the nucleus and chromatin (Ivic et al, in review).

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