



STEM CELL SOCIETY
SINGAPORE

STEM CELL SOCIETY SEMINAR ANNOUNCEMENT

12 March 2013, Tuesday, Aspiration Theatre, Matrix Building Level 2M
30 Biopolis Street, Singapore 138671

PROGRAMME

4.30 - 5.30pm

Ramanuj DASGUPTA

Assoc Prof, NYU School of Medicine/Cancer Institute

"Exploring the TCF-dependent versus independent functions of b-catenin in stem cell regulation: lessons from *Drosophila* germ cells to mouse embryonic stem cells (mESCs)"

5.30pm onwards

Networking (brought to you by Stem Cell Society Singapore)

Hosted by

Huck Hui NG

President, Stem Cell Society and ED, Genome Institute of Singapore



SPEAKER

Dr. Ramanuj DasGupta, NYU School of Medicine

Exploring the TCF-dependent versus independent functions of b-catenin in stem cell regulation: lessons from *Drosophila* germ cells to mouse embryonic stem cells (mESCs)

Abstract

miRNAs are regulators of global gene expression, and function in a broad range of biological processes. Recent studies have suggested that miRNAs can function in the regulation of stem cells by modulating expression/activity of known pluripotency or differentiation promoting factors. Functional studies have also implicated miRNAs in cancer where they can serve as tumor-suppressors or oncogenes by modulating activities of evolutionarily conserved signaling pathways that are commonly dysregulated in cancer. We report the identification of the miR-310/13 cluster as a novel antagonist of Wnt/*wingless* (*wg*) pathway activity in a functional screen for *Drosophila* miRNAs. We demonstrate that the miR-310/13 cluster can modulate β -catenin (β -cat)/Armadillo (*arm*) expression and activity by directly targeting the 3'-UTRs of *arm* and dTCF *in vivo*. Interestingly, flies deficient for miR-310/13 function exhibit a striking phenotype in the male germline where they exhibit accumulation of large, abnormal clusters of undifferentiated early germ, and somatic progenitor cells. While this phenotype can be significantly rescued by the reduction of Arm protein levels/activity, we find that reducing dTCF activity does not completely rescue the

phenotype, thereby raising questions regarding TCF-dependent versus -independent functions of β -cat in the regulation of germ cell differentiation. Surprisingly a pilot unbiased RNAi screen (*Chatterjee et al., 2013 unpublished*) to identify novel cell-signaling regulators in mouse embryonic stem cell (mESC) homeostasis also revealed similar observations, and insights into the molecular function of TCF- β -catenin in the maintenance/differentiation of mESCs. Taken together, our results implicate a previously unrecognized function for miRNA-mediated regulation of nuclear- and membrane-associated β -catenin/Arm in early somatic and germline progenitor cell differentiation in *Drosophila*. Moreover, these studies have also revealed interesting aspects of TCF function in the regulation of β -catenin activity in stem cell maintenance and differentiation both in *Drosophila* and mESCs.

Biography

Dr. DasGupta was trained as a synthetic organic chemist at Delhi University. Then he switched to Developmental Genetics at Cambridge University, UK.

In Dr. Daniel St. Johnston's he investigated the function of the *mago nashi* gene in the localization of polarity-determining mRNAs such as *oskar*, which have critical functions in the establishment of the anterior-posterior axis in the *Drosophila* egg chamber.

For his graduate studies he worked with Dr. Elaine Fuchs. His work was the first to describe the function of β -catenin-dependent Wnt signaling in the determination of the hair follicle versus epidermal cell fates during epidermal morphogenesis, and the activation/regulation of epithelial "bulge" stem cells during hair regeneration/cycling.

In Dr. Norbert Perrimon's lab at the Harvard Medical School (2002-2005), Dr. DasGupta was part of the team that established some of the first RNAi-based high-throughput screens (HTS) for cell signaling pathways, using *Drosophila* cell-based assays. He established his independent research program at the NYU School of Medicine/Cancer Institute in early 2006, where he has been ever since. He also established the NYU-RNAi screening center (as its Scientific Director). Dr. DasGupta has been the recipient of the Concept Award from the Breast Cancer Research Foundation (USA), the NYSTEM Idea Award (New York State), an ACS Research Scholar Award (USA), the March of Dimes Research Grant, and the NYC BioAccelerate Prize, amongst others.