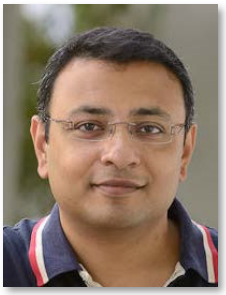
DukeNUS Medical School | National Cancer Centre Singapore, SingHealth | CSCB Cancer and Stem Cell Biology

Seminar Series

Tumor evolution: through the looking glass of a single cell

Abstract:

Intra-tumor heterogeneity (ITH) generates distinct cell-populations with specific functions in tumor maintenance, metastasis, and drug-resistance. How intra-tumor 'phenotypic-heterogeneity' contributes to their evolution under the selection pressure of drug treatment and metastasis remains largely underexplored. We utilized the power of single cell RNA-sequencing (scRNA-seq) combined with functional genomics to investigate the mechanism(s) of survival exhibited by distinctly heterogeneous patient-derived tumor models under a wide variety of selective stress, including chemotherapeutic drugs and metastasis. We demonstrated that tumor cell populations (squamous cell carcinomas) can adopt divergent modes of evolution when treated with cisplatin, a commonly used chemotherapy drug. While some populations undergo 'Darwinian-selection' based on their pre-determined 'resistant' states, others utilize cellular reprogramming mechanisms that result in the appearance of novel traits as an 'adaptive' mechanism to drive the emergence of *de novo* resistant cell-states. Mechanistically, we demonstrated that cellular-reprogramming is associated with a stem cell-switch that modulates epigenetic plasticity, and expression of resistance-associated poised promoters. Ongoing studies continue to expand on the initial work to explore how tumors evolve under different selection pressures by modulating gene regulatory networks (GRN) that drive the expression of selection-specific transcriptomes. We are also exploring the role of the tumor microenvironment (TME) in modulating tumor evolution, both in the context of tumorigenesis as well as progression into treatment refractory states. Altogether we hope to provide novel mechanistic insights into the modes of tumor evolution and its implication in targeting resistant, metastatic disease.



Speaker:

Dr. Ramanuj DasGupta

Group Leader/Senior Investigator
Genome Institute of Singapore, A*STAR
Cancer Therapeutics & Stratified Oncology
Singapore

Dr. DasGupta is a Senior Investigator at the Genome Institute of Singapore (Cancer Therapeutics and Stratified Oncology), and holds an adjunct Associate Professor position at CSI-NUS. He also holds an adjunct Associate Professor position at the New York University Cancer Institute, New York. The major focus in the DasGupta laboratory is to implement "Phenotype-driven Precision Oncology" in the clinic by establishing the next-generation of HTS-amenable patient-personalized cancer models to identify novel therapeutic opportunities, and biomarkers. The overall research goal is to define the impact of intra-tumor heterogeneity (ITH) and the tumor microenvironment (TME) on tumor evolution during the emergence of treatment resistant, metastatic disease. A wide variety of functional genomic approaches are employed including single-cell/bulk transcriptomics, epigenomics, and exome-seq to address questions related to how individual cells evolve/acquire metastatic and resistant phenotypes. In addition, the DasGupta lab is also interested in the identification and functional characterization of non-coding RNAs (ncRNAs), and associated RNA-binding proteins (RNPs) in the regulation of oncogenic signaling pathways, as well as in defining specific developmental cell-states both in normal and cancer stem cells (CSCs).

Date:

15 February 2019 (Friday)

Venue:

Amphitheatre, Level 2
Duke-NUS Medical School
8 College Road,
Singapore 169857

Time:

12:00 -1:00 p.m.

Host:

Dr. Koji ITAHANA
Associate Professor
Laboratory of Tumor Suppression
Programme in Cancer & Stem Cell Biology

No registration is required. All are welcome.
Any enquiries, please contact:
Lilian Poon (6601 3779)