Cancer Science Institute of Singapore

SEMINAR ANNOUNCEMENT

Uttiya Basu

Associate Professor,
Department of Microbiology and Immunology
Columbia University, New York

Noncoding RNA Regulation in B Cell Immunity and Cancer

Date: Wednesday, 23 August 2017
Time: 10.30am – 11.30am
Venue: Auditorium, Clinical Research Centre (MD11) (10 Medical Drive, Singapore 117597)
Chair: Dr Melissa Fullwood

Abstract:

The immune system responds to a universe of pathogenic organisms and non-self molecules by generating antibodies with almost infinite diversity. B-lymphocytes accomplish this task by carrying out three remarkable DNA alteration processes: VDJ recombination, somatic hypermutation (SHM), and class switch recombination (CSR). V(D)J recombination on immature B lymphocytes in the bone marrow dramatically increases the immunoglobulin (Ig) repertoire; subsequently, B cells migrate to secondary lymphoid organs where they undergo SHM, increasing the affinity of an immunoglobulin for cognate epitopes, and CSR, tailoring the effector function triggered by a specific antigen-recognizing antibody. These last two genetic alterations depend on the single stranded (ss)DNA cytidine deaminase, AID. The DNA mutator AID catalyzes both CSR--by initiating the generation of DNA double strand breaks in the immunoglobulin heavy chain locus (IgH) switch sequences (IgS)—and SHM (by incorporating point mutations in the immunoglobulin variable region genes). However, AID can also accidentally create DNA lesions in the B cell genome, potentially causing B cell malignancies. AID's activity is regulated, among other factors, by the cellular non-coding RNA processing pathway complex RNA exosome. Using a mouse model in which RNA exosome activity can be conditionally deleted, we have found that genomic regions targeted by AID express a subset of antisense non-coding RNAs and that these regions demonstrate divergent transcription. In addition, we have also identified regions in the B cell genome that express various long non-coding RNAs including enhancer RNAs (eRNAs) and these AID target DNA sequences are hypermutated by AID. In sum, our laboratory investigates how transcription of non-coding RNAs may influence AID-induced B cell genome mutagenesis that ultimately leads to B cell lymphomagenesis. Our work has implications in the fields of B cell mediated immunity, B cell oncogenesis, and regulation of the non-coding RNA transcriptome.

Biosketch:

Uttiya Basu received his PhD in molecular biology from Albert Einstein College of Medicine. After finishing his postdoctoral training which focused on molecular immunology at Harvard Medical School, he joined Columbia University as an assistant professor in the Department of Microbiology and Immunology. His laboratory utilizes technologies involving genome engineering, genomics, biochemistry and in vivo imaging. His research is focused on the various mechanisms by which non-coding RNA transcription controls genome architecture and somatic mutagenesis processes in mammalian cells, especially those of lymphocyte origin. Dr. Basu has been recognized with the Irvington Institute (CRI) fellowship, the Leukemia and Lymphoma Society of America Scholar award, the Leukemia Research Foundation New Investigator award, the Irma Hirschl Fellowship, and the NIH Director's program Innovator award. In 2016, he was awarded tenure at Columbia University in the City of New York and promoted to Associate Professor.