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THE HONG KONG UNIVERSITY OF SCIENCE & TECHNOLOGY

Division of Life Science

LIFS Seminar Series

Noncoding RNA transcription and genome organization during immunity and cancer

by

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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.

Date : 25 August 2017 (Friday)

Time : 4:00 p.m.

Venue : Lecture Theatre F
The Hong Kong University of Science & Technology
Clear Water Bay, Kowloon

(Host faculty: Dr. Jiguang Wang)

All are Welcome!!