

presents the seminar series in
Cancer Biology, Biotherapy and Nanomedicine

**Target the virus replication process for specific
antivirals against Dengue and Zika viruses**

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Date : 30 Aug 2019 (Fri)
Time : 10:00 - 11:00
Venue : TYB-1B-G04, To Yuen Building

Abstract

Accumulation of H3K4me3 epigenetic marks on multiple immune gene promoters underlie robust transcriptional responses during trained immune responses. However, the molecular basis for this remains unknown. Here we show 3D chromatin topology enables H3K4me3-primed immune genes to engage in chromosomal contacts with a newly identified class of lncRNAs (IP-lncRNAs). We mechanistically characterise UMLILO, a prototypical IPL that regulates the robust transcription of the CXCL chemokines. Pre-formed 3D chromatin topology brings UMLILO proximal to the chemokine genes, prior to their transcriptional activation. We show, that acting in cis, UMLILO directs the WDR5/MLL1 complex across the chemokine promoters facilitating their H3K4me3 epigenetic priming. This mechanism appears shared amongst other trained immune genes. We show that β -glucan, a classic inducer of trained immunity, epigenetically reprograms immune genes by upregulating IPLs in an NFAT-dependent manner. This provides strong evidence that IPL-mediated changes to the epigenetic status of immune gene promoters permit the enhanced pro-inflammatory response observed in trained monocytes. This creates a new paradigm for how nuclear architecture and lncRNA regulation may orchestrate H3K4me3 promoter priming and the robust transcription of innate immune genes.

About the Speaker

Musa M. Mhlanga (USA citizen), American-born male cell biologist, holds a PhD in cell biology & molecular genetics from New York University School of Medicine (2003). He began his PhD at the Rockefeller University in the laboratory of David Ho where he worked on spectral genotyping of human alleles. He then went on to work on the development of in vitro and in vivo applications of molecular beacons for their use in visualizing RNA in living cells with Fred Russell Kramer and Sanjay Tyagi at New York University School of Medicine. Upon completion of his doctoral work he was awarded a U.S. National Science Foundation post-doctoral fellowship at the Institut Pasteur in Paris, France to work in the laboratory of nuclear cell biology. There he worked on RNA transport and single molecule visualization and tracking of RNA in living cells. In late 2008 he moved his lab to South Africa to join the Council of Scientific and Industrial Research as the Research Leader of the Synthetic Biology Emerging Research Area. He heads the Laboratory for Gene Expression & Biophysics and holds a joint appointment to the Institute of Molecular Medicine in Lisbon, Portugal. His laboratory now at the University of Cape Town Medical School, works on gene regulation, host-pathogen interactions, single molecule imaging of gene expression and the development of cell-based visual high-throughput biology techniques for screening in basic and clinical biology.

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All are welcome!