NANYANG TECHNOLOGICAL UNIVERSITY

School of Biological Sciences

Reg. No. 200604393R

Research Theme: Cryo-EM, Structural Biology, AIRE, autoimmune diseases.

Research Project Title: Comprehending the molecular dynamics of CARD domain driven Nuclear Speckles -- a 'nuclear' approach to understand autoimmune diseases.

Principal Investigator/Supervisor: WU, Bin

Collaborator: Sun HUR (Harvard Medical School)

Project Description

a) Background: To live in a dynamic environment full of micro-organisms surrounding us, the immune system in our body needs to recognize and differentiate various pathogenic threats and respond accordingly. The understanding of pathogen associated molecular pattern (PAMP) recognition has made tremendous progress in the recent two decades, after the successful characterization of dozens of cytosolic and cellular surface receptors, as well as their associated signaling pathways [1-7]. Due to technical difficulties associated with studying large dynamic heterogeneous complexes, immune-regulation events at the transcriptional level, more specifically the formation and dynamics of nuclear speckles are underappreciated and less studied [8]. Considering that immune stimulus/differentiation triggered transcriptional profile shift is a key aspect of immune responses [9–11], **it carries great scientific significance to examine the structure and functions of these nucleus located immuno-granules**. Our central hypothesis is that the molecular knowledge of the human CARD domain containing Nuclear Speckle Protein **(CARD-NSP) oligomeric complexes, including Autoimmune Regulator (AIRE), Speckle Protein 100 (SP100), SP110, SP140, SP140L,** would provide us with better models to understand and modulate transcriptional profiles that are critical for immune cell differentiation and anti-pathogen responses. In particular, one of the CARD-NSP, **AIRE, is found to be one of the most critical transcriptional regulators during T cell development** [12,13]. Our preliminary data include several new cryo-EM complex structures demonstrating how CARD-NSP phase transit from a less compact oligomeric complex into densely packed hydrogel. Furthermore, the reconstituted biochemical platforms we developed along with the structural investigation are conveniently available for screening intrinsic and therapeutic regulators for human promyelocytic leukemia nuclear bodies (PML-NB) formation, which are predominantly regulated by CARD-NSP.

b) Proposed work: To solve the complex structures of all nuclear speckle proteins, and to explore strategies to eliminate chronic viral infections caused by ccc DNA.

c) Preferred skills: Math

Supervisor contact:

If you have questions regarding this project, please email the Principal Investigator:

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SBS contact and how to apply:

Associate Chair-Biological Sciences (Graduate Studies) : AC-SBS-GS@ntu.edu.sg

Please apply at the following:

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Application portal:

https://venus.wis.ntu.edu.sg/GOAL/OnlineApplicationModule/frmOnlineApplication.ASPX

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