Institute of Molecular and Cell Biology
A*STAR

SEMINAR ANNOUNCEMENT

We would like to invite you to attend this seminar hosted by A/Prof Edward Manser:

Date: 26 June 2019, Wednesday
Time: **3:00PM – 4:00PM**
Venue: Level 3, IMCB Seminar Room 3-46, Proteos, Biopolis

Speaker: Dr Helen Mott, Senior Lecturer, Department of Biochemistry, University of Cambridge, United Kingdom
Title: The Ral small G proteins and their interactions with other proteins and membranes: possibilities for cancer therapeutics

The Ral proteins, RalA and RalB, lie downstream of Ras and are involved in a number of processes including exocytosis, endocytosis and transcriptional regulation. The Ras-Ral signalling axis is one of the important pathways for Ras-driven tumourigenesis. Our structure of RalB in complex with the Ral-binding domain of one Ral effector, RLIP76, led us to the design of stapled α-helical peptides that inhibit Ral signalling. In this talk I will describe the latest generation peptides that we have developed with improved properties. RalA and RalB, despite having similar sequences, have different roles in normal and cancer cells. We are trying to understand the structural and biochemical basis for these differences. Both Ral proteins are modified post-translationally with an isoprenyl group at their C-termini. I will describe our work investigating RalA in membrane nanodiscs, where we have used NMR to determine which regions of RalA interact with the membrane. I will also describe the interaction of RalA with Calmodulin, which can remove RalA from membranes by binding to the isoprenyl moiety as well as the RalA C-terminus.

Biography:
Our laboratory uses NMR as our primary structural biology tool, although we also employ crystallization when appropriate. We are very interested in protein-protein interactions and how a detailed knowledge of interfaces and their thermodynamics can be used both for inhibitor design and to understand specificity. We have a continuing interest in the Rho family and their downstream effectors such as the PRK family and the ACK tyrosine kinase. We also have a major interest in Ral signalling and our effort has been geared towards understanding the structure and function of the Ral effector RLIP76 and the structural basis for the difference between RalA and RalB. We have used stapled peptides based on RLIP76 to inhibit Ral signalling and are working on improving our first generation peptides. We are also investigating interactions of small G protein and their effectors with membranes.

ALL ARE WELCOME *(No registration required)*

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Thank you.