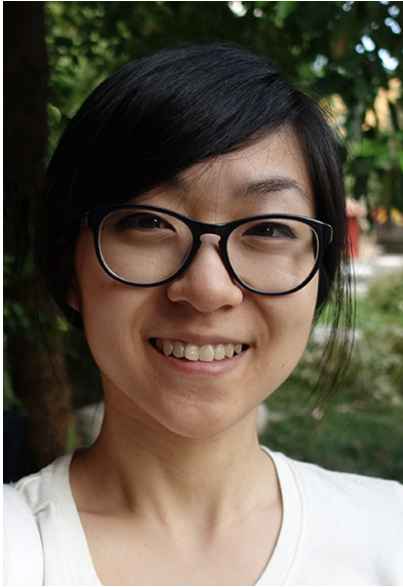


2018 Seminar Series – PhD Oration



Wednesday 2nd of May
12-1pm

Bio21 Institute Auditorium
30 Flemington Road, Parkville

Haiyin Liu

Mintern & Villadangos Laboratories,
Department of Biochemistry and Molecular
Biology. University of Melbourne.

The MARCH for your immune system: how ubiquitin controls membrane receptors

Membrane associated RING-CH (MARCH)1 is a RING-type E3 ubiquitin ligase that downregulates the cell surface abundance of several key immunoreceptors, such as CD86 and major histocompatibility complex class II (MHC II). Expression of MHC II on the surface of antigen presenting cells is crucial for the development and activation of CD4⁺ T cells. Although existing studies have addressed the physiological functions of MHC II ubiquitination by MARCH1, much about the mechanisms of its activity are still unclear.

Here we have utilised a multi-pronged approach to investigate the nature, machinery and physiological relevance of MARCH-mediated MHC II ubiquitination. Using mass spectrometry, we have characterised the “ubiquitin code” associated with MHC II in primary immune cells. Additionally, we employed a genome wide CRISPR KO library screen to identify a new component of the MARCH1-MHC II ubiquitination machinery. Finally, we used transgenic mice to demonstrate differential roles for MARCH E3 ligases across different immune cells, including critical implications for CD4 T cell development.

Altogether, our findings offer new insights into MARCH-mediated ubiquitin control of immunoreceptors, and could advance current understanding of the mechanisms and biological functions of membrane protein ubiquitination.