

Medicine, Nursing and Health Sciences

Biomedicine Discovery Seminar

Monash Biomedicine Discovery Institute



DOGmas, CAT tails, and a Structural Surprise: New Concepts in Protein Quality Control and Neurodegeneration

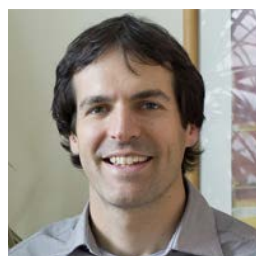
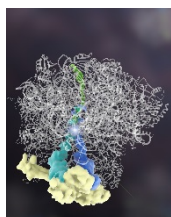
 Tuesday 22 November 2016

 12:00 – 1:00pm

 Level 3 Seminar Room
15 Innovation Walk
Clayton campus

About the presenter

Adam Frost earned his MD and PhD degrees from Yale University in 2009, where he worked with Pietro De Camilli and Vinzenz Unger to resolve how membrane-binding proteins of the BAR domain family and the Dynamin GTPase family remodel cellular membranes. He was then a post-doctoral scholar with Jonathan S. Weissman at UCSF until 2011, where he mapped both conserved and repurposed genetic interaction networks in order to discover novel quality control and homeostasis pathways. He joined the faculty of the biochemistry department at the University of Utah in 2011, before returning to UCSF as the Herbert Boyer Junior Faculty endowed chair in 2014.



Presenter

Dr Adam Frost

MD, PhD

Biochemistry and Biophysics and the
Macromolecular Structure Group, University
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Abstract

In Eukarya, stalled translation induces 40S dissociation and recruitment of the ribosome quality control complex (RQC) to the 60S subunit, which mediates nascent chain degradation. We used cryo-electron microscopy to reveal that the RQC components Rqc2 and Ltn1 bind to the 60S subunit at sites exposed after 40S dissociation, placing the Ltn1p RING ubiquitin ligase domain near the exit channel and Rqc2p over the P-site transfer RNA (tRNA). We further demonstrated that Rqc2p recruits alanine- and threonine-charged tRNA molecules to the A-site to direct elongation of nascent chains independently of mRNA or 40S subunits. Our work uncovers an unexpected mechanism of protein synthesis, in which a protein—not an mRNA—determines tRNA recruitment and the tagging of nascent chains with carboxy-terminal Ala and Thr extensions ("CAT tails"). In this seminar I will discuss the discovery of the CAT tail, our very recent work on the mechanisms of CAT tail synthesis, and the role of CAT tails in protein quality control and stress signaling.

This image was created by Janet Iwasa and illustrates the protein Rqc2 (yellow) coordinating two tRNA molecules (green and blue) in the PTC of the 60S ribosome without a genetic template. Janet Iwasa's art was featured in a remarkable number of news outlets highlighting our surprising discovery.



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