Department of Pathology fully-funded PhD studentships: project proposal form

To be completed and returned to your Head of Division by Friday 21st September 2018

Division	Microbiology and Parasitology
Supervisor	Dr Betty Chung
Project title	Early PI3-mediated translation response during intracellular bacterial and viral infection
Project abstract for advert (Max 100 words)	Biotic stresses often occur on short timescales, making rapid response crucial for survival of both host and pathogen. Cells respond to stress by regulating gene expression at multiple steps but especially transcription, translation and protein turnover. Transcriptional regulation is generally more versatile; however translational regulation of pre-existing mRNA is faster and more efficient, as it circumvents *de novo* mRNA transcription, processing and transport to the cytoplasm. This project aims toward understanding the complex interplay of host- pathogen gene regulation at the translational levels, and their ultimate effect of the major immune cell for innate immunity in response to biotic stress.
Full details (Max 250 words. Will be published on Departmental website; do not include confidential information)	Understanding the role of translational control in host response to pathogen infection is critical for developing intervention strategies as protein synthesis is a central process in all cells. However, currently most global studies are at the level of transcript abundance (RNA-Seq). Analysing genome-wide responses at the level of protein synthesis has only recently become possible due to the development of ribosome profiling. We are most interested in responses of macrophages – the primary immune cell for innate immunity, in particular with respect to the pathway of phosphoinositide 3-kinase (PI3K). Cells respond to stress by regulating gene expression at multiple steps but especially transcription, translation and protein turnover. Transcriptional regulation is generally more versatile; however translational regulation of pre-existing mRNA is faster and more efficient, as it circumvents *de novo* mRNA transcription, processing and transport to the cytoplasm. We have growing evidence that PI3K in the macrophage plays a major role in early bacterial infection [unpublished data, Okkenhaug laboratory]. However, details of this rapid and early response remains elusive. In collaboration with both Smith and Okkenhaug laboratory, this project will utilize both intracellular bacteria and viruses to stimulate primary macrophages from either wild-type of PI3K-knocked-out mouse strains. Comparison between two drastically intracellular pathogens will allow identification of common anti-pathogen pathways besides host responses specific for each pathogen.
Image(s) related to project (For use in adverts and	

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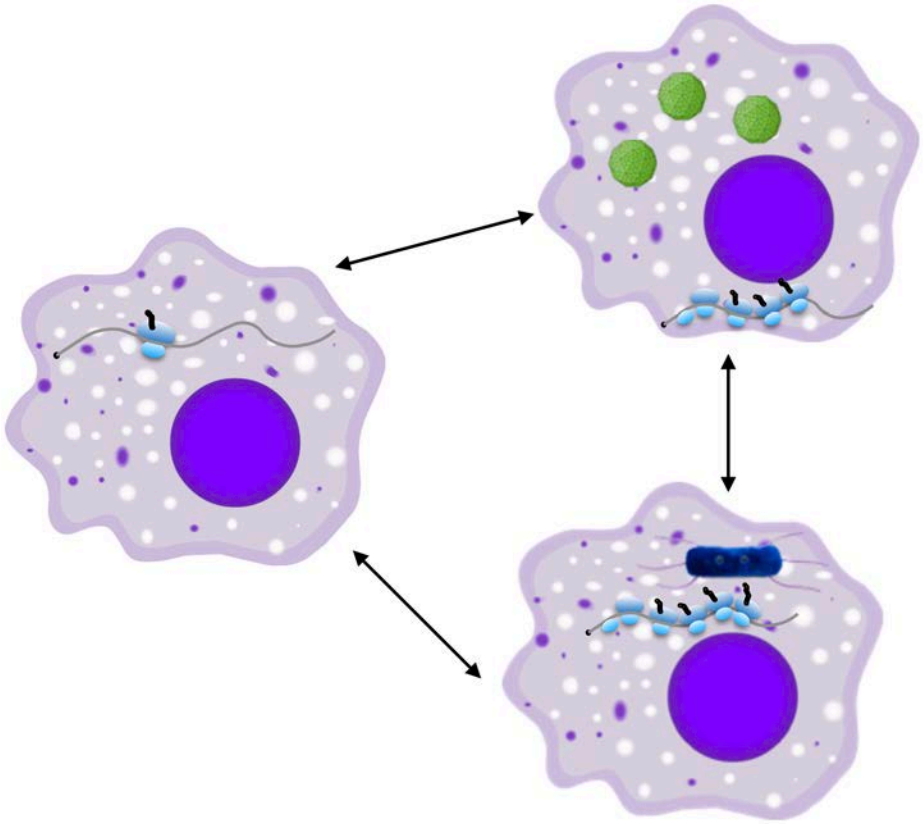
on Departmental website)	
5 recent publications	**Chung, B. (co-corresponding author)**, Deery, M., Groen, A., Howard, J., and Baulcombe, D. (2017) Endogeneous miRNA in the green alga *Chlamydomonas*regulate translation repression through CDS-targeting. ***Nature Plants.*** Oct; 3(10):787-794 DOI:10.1038/s41477-017-0024-6 October issue with an accompanying News and Views highlight **Chung, B. (co-corresponding author)**, Hardcastle, T., Jones, J., Irigoyen, N., Firth, A., Baulcombe, D., and Brierley, I. (2015) The use of duplex-specific nuclease in ribosome profiling and a user-friendly software package for Ribo-Seq data analysis. ***RNA***, 21: 1731-1745, DOI: 10.1261/rna.052548.115 Olspert, A., **Chung, B.**, Carr, J., and Firth, A. (2015) Transcriptional slippage in the positive-sense RNA virus family Potyviridae. ***EMBO Rep***, 16: 995-1004,with an accompanying News and Views highlight DOI: 10.15252/embr.201540509 Cook, A., **Chung, B. (joint first author)**, Bass, D., Moureau, G., Mcalister, E., Culverwell, L., Glucksman, E., Wang, H., Brown, T., Gould, E., Harbach, R., De Lamballerie, X. and Firth, A. (2013)Novel virus discovery and genome reconstruction from field RNA samples reveals highly divergent viruses in dipteran hosts. ***PLoS ONE***, 8: e80720, DOI:

	10.1371/journal.pone.0080720 **Chung, B.**, Firth, A. and Atkins, J. (2010) Frameshifting in Alphaviruses: a diversity of 3′ stimulatory structures. ***J Mol Biol***, 397: 448-456**.** DOI:10.1016/j.jmb.2010.01.044