

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

Division	Immunology
Supervisor	Dr Brian Ferguson
Second supervisor (If supervisor's contract ends before October 2024)	
Project title	How is viral DNA sensed by human cells?
Project abstract for advert (Max 100 words)	The ability of a host to sense and respond to virus infection is largely dependent on the intracellular detection of viral nucleic acids. This project aims to define the molecular mechanisms by which the pattern recognition receptors that sense the presence of viral DNA initiate the anti-viral innate immune response. We will use multiple techniques in primary and immortalised cells to characterise the signalling pathways downstream of DNA-sensing PRRs and the how they impact DNA virus infections.
Keywords Please provide up to five	Innate Immunity Anti-viral response Type-I interferon Nucleic acid sensing Pattern recognition receptors
Full details (Max 250 words. Will be published on Departmental website; do not include confidential information)	The ability of a host to sense and respond to virus infection is largely dependent on the intracellular detection of viral nucleic acids. The DNA-sensing pattern recognition receptors (PRRs) that bind viral DNA and initiate the type-I interferon response are an essential component for mammalian host defence against DNA virus infections. The viral DNA-sensing PRRs cGAS, DNA-PK and IFI16 all function in human cells but how exactly they sense and respond to DNA virus infections is not well understood. This project aims to define the molecular mechanisms by which the pattern recognition receptors that sense the presence of viral DNA function to initiate and anti-viral response. We will use multiple methods in primary and immortalised human cells to characterise the signalling pathways downstream of DNA-sensing PRRs and the how they impact DNA virus infections.
Three of your most important publications in support of the proposed project	Ben J. Trigg, Katharina B. Lauer, Paula Fernandes dos Santos, Heather Coleman, Gabriel Balmus, Daniel S. Mansur and Brian J. Ferguson The Non-Homologous End Joining Protein PAXX Acts to Restrict HSV-1 Infection. <i>Viruses</i> 2018, Volume 9(11) J Zinngrebe, E Rieser, L Taraborrelli, N Peltzer, T Hartwig, H Ren, I Kovács, C Endres, P Draber, M Darding, S von Karstedt, J Lemke, B Dome, M Bergmann, BJ Ferguson*, H Walczak* LUBAC deficiency perturbs TLR3 signaling to cause immunodeficiency and autoinflammation. <i>J Experimental Medicine</i> 2016

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	BJ Ferguson, DS Mansur, NE Peters, H Ren, GL Smith. DNA-PK is a DNA sensor for IRF-3-dependent innate immunity. eLife Sciences, 2012, 1 e00047
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