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

Division	Microbiology & Parasitology
Supervisor	Dr Richard Hayward
Second supervisor (If supervisor's contract ends before October 2024)	
Project title	Dissecting inclusion biogenesis – the specialised intracellular replicative compartment of Chlamydia trachomatis
Project abstract for advert (Max 100 words)	Chlamydia trachomatis is the principal bacterial cause of sexually transmitted infections worldwide and ocular infections cause 'trachoma' a form of blindness in Developing nations, designated as a neglected tropical disease. Chlamydiae replicate within a specialised intracellular compartment termed an inclusion, which selectively engages host organelles but remains segregated from the endo-lysosomal system. Chlamydial virulence effector proteins are translocated into the host cell, but in most cases how they promote inclusion biogenesis remains poorly understood. This project will apply a multidisciplinary approach spanning biochemistry, cell biology, bioimaging and emerging genetic techniques in Chlamydia to further understand effector structure and function.
Keywords Please provide up to five	Chlamydia, intracellular trafficking, organelle, type III secretion, cytoskeleton
Full details (Max 250 words. Will be published on Departmental website; do not include confidential information)	Chlamydia trachomatis remains the principal bacterial cause of sexually transmitted infections worldwide. In Developing nations, ocular infections cause trachoma, a form of blindness, which is designated by the World Health Organisation as a neglected tropical disease. Chlamydiae are obligate intracellular bacteria that adopt two distinct developmental forms, infectious elementary bodies (EB) force their own actin-dependent uptake into epithelial cells. Once internalised EB differentiate to form reticulate bodies (RB) that survive and replicate within a specialised intracellular compartment called an inclusion. RB re-differentiate into EB and induce inclusion egress or cell lysis to continue the lifecycle. Bacterial virulence effector proteins that are translocated into the host cell control inclusion biogenesis. These effectors integrate into the inclusion membrane, and disseminate into the cytosol and nucleus of the infected cell, where they hijack key host processes including intracellular trafficking, antigen presentation, cytoskeletal architecture, organelle interactions and host gene expression. This project will apply a multidisciplinary approach to investigate the structure and function of chlamydial effectors, involving protein biochemistry, cell biology and infection models in cultured cells, bioimaging and the application of genetic techniques that have only recently been developed in the field. The aim is to identify targets of effectors of unknown function, and to understand the role of the targetted host processes in inclusion biogenesis and disease. In parallel, the project will involve the characterisation of novel host targets we have already identified in ongoing work. Since little is known about the biogenesis of the inclusion this work not only provides training in a wide variety of techniques but also the opportunity to study new aspects of host cell biology.
Three of your most important publications in	Ford C, Nans A, Boucrot E, Hayward RD (2018) Chlamydia exploits filopodial capture and a macropinocytosis-like pathway for host cell entry.

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support of the proposed project	PLoS Pathogens 14:e1007051 Nans A, Kudryashev M, Saibil HR, Hayward RD (2015) Structure of a bacterial type III secretion system in contact with a host membrane in situ. Nature Communications 6:10114 Dumoux M, Menny A, Delacour D, Hayward RD (2015) A Chlamydia effector recruits CEP170 to reprogram host microtubule organization. Journal of Cell Science 128:3420-3434