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

PART A: PROJECT PROPOSAL	
Division	Virology
Supervisor	Valeria Lulla
Second supervisor (If supervisor's contract ends before October 2025)	
Project title	The molecular signatures of enteric viruses
Project abstract for advert (Max 100 words)	Enteric viruses are a major cause of mortality and morbidity in the young, elderly, and immunocompromised. This project will engage a range of cutting-edge molecular virology, next generation sequencing, and human intestinal organoid techniques to address outstanding questions in the molecular biology of human astrovirus replication, including host-pathogen interactions and molecular deteminants of gut-specific virus infection with a specific focus on poorly characterised membrane-bound astrovirus proteins and their precursors. Understanding the dynamics of the molecular mechanisms of virus replication will advance the development of accurate models and therapeutic approaches.
Keywords Please provide up to five	RNA viruses, virus replication, human intestinal organoids, virus-host interactions
Full details (Max 250 words) **Will be published on Departmental website; please do not include confidential information**	Enteric viruses are the commonest causes of gastroenteritis worldwide. Several virus families cause human enteric diseases, resulting in severe diarrhoea with various potential complications, including spread to the central nervous system. Our laboratory is using enteroviruses and astroviruses as model systems to understand the molecular mechanisms underlying the disease outcomes. This project will engage a range of cutting-edge molecular virology techniques to understand gut-specific components of astrovirus infection. Specifically, we will look at astrovirus- and host-derived components of infection processes using replicon, reverse

	genetics, and virus evolution approaches, focusing on poorly characterised membrane-bound astrovirus proteins and their precursors. The identified astrovirus-specific determinants will be assessed in the infected human intestinal organoid system – a multicellular, nontransformed and physiologically relevant cellular platform. We expect this work to also inform on potential targets for the future generation of new antiviral therapies. Besides myself, our group consists of two postdocs and one PhD student investigating various aspects of enteric virus infection. We seek a creative and enthusiastic PhD student to work on a project aimed at elucidating molecular aspects of astrovirus infection.
Three of your most important publications in support of the proposed project	• **Lulla V***, Wandel M, Bandyra KJ, Ulferts R, Wu M, Dendooven T, Yang X, Doyle N, Oerum S, Beale R, O'Rourke S, Randow F, Maier H, Scott W*, Ding Y*, Firth AE*, Bloznelyte K*, Luisi B*. (**2021**). Targeting the conserved stem loop 2 motif in the SARS-CoV-2 genome. ***Journal of Virology***. PMID: 33963053 • **Lulla V***, Firth AE* (**2020**). A hidden gene in astroviruses encodes a viroporin. ***Nature Communications***, 11(1):4070. PMID: 32792502 • **Lulla V***, Dinan AM, Hosmillo M, Chaudhry Y, Sherry L, Irigoyen N, Nayak KM, Stonehouse NJ, Zilbauer M, Goodfellow I, Firth AE*. (**2019**). An upstream protein-coding region in enteroviruses modulates virus infection in gut epithelial cells. ***Nature Microbiology***, 4(2):280-292. PMID: 30478287 *corresponding authors