UNIVERSITY OF CAMBRIDGE

Fully funded PhD studentship in virus:host interactions

Project title:

Targeting protein phosphorylation to prevent herpesvirus spread

Supervisor:

Professor Stephen Graham, Department of Pathology, University of Cambridge

Project:

Herpes simplex virus (HSV) infects approximately two-thirds of the adult population, causing cold sores and genital herpes. There are no licensed medicines to prevent or cure HSV infection, which persists for life. HSV is expert at reprogramming the machinery of infected human cells to turn them into virus production and dissemination factories; understanding how the virus achieves this this will allow us to pinpoint key steps that could be inhibited with antiviral drugs or modified for rational vaccine design. One key control mechanism within cells is protein phosphorylation, a molecular 'on/off switch' that helps regulate most processes within the human cell. This switch is flipped by enzymes that add or remove phosphorylation marks from proteins, called 'kinases' (addition) or 'phosphatases' (removal). We identified that the HSV protein pUL21 has the unexpected ability to flip the phosphorylation state of cellular and viral proteins by hijacking the activity of a cellular phosphatase, and this activity is required for efficient virus cell-to-cell spread. We will define how HSV regulates protein phosphorylation within infected cells, how this promotes virus spread, and how this could be targeted to treat or prevent herpesvirus infection. The student will obtain training and experience in cell-based infection assays, fluorescence microscopy, quantitative proteomics, protein biochemistry and structural biology.

Key references:

1. T.H. Benedyk, et *al*. (2022) Herpes simplex virus 1 protein pUL21 alters ceramide metabolism by activating the inter-organelle transport protein CERT. *J. Biol. Chem*, 298: 102589
2. T.H. Benedyk, et *al*. (2021) pUL21 is a viral phosphatase adaptor that promotes herpes simplex virus replication and spread. *PLoS Pathog.*, 17: e1009824
3. T.K. Soh, et *al*. (2020) Temporal Proteomic Analysis of Herpes Simplex Virus 1 Infection Reveals Cell-Surface Remodeling via pUL56-Mediated GOPC Degradation. *Cell Rep.*, 33: 108235

Host laboratory:

Prof. Graham and his team investigate how viruses alter the infected-cell environment, particularly the architecture and composition of cellular membranes, and how they achieve this without triggering cellular immune responses. The lab uses a broad range of biochemical, biophysical and cell biology techniques, ranging from cell-based models of infection and proteomics to biophysical analysis and atomic-resolution structures of protein complexes. It is a collaborative lab environment that aims to support the personal and professional development of every member. More details of recent activities can be found on the lab website: http://www.atomicvirology.path.cam.ac.uk/

Further details:

This studentship is available to student who qualify for UK (Home) fees only and has been funded by the British Skin Foundation (https://www.britishskinfoundation.org.uk/). It is anticipated that the successful candidate will commence their studies in Michaelmas term (October) 2023. Funding is available for three years in the first instance, with the possibility of extension in the fourth year, and includes fees plus a tax-free stipend at the RCUK rate (currently £17,668 per year).

Application deadline:

16th May

Apply:

https://www.postgraduate.study.cam.ac.uk/courses/directory/blpapdpth