Ref: PFPB.1

Project Title: How does lumpy skin disease virus exit from the cell?

Supervisors: Petra Fay & Pip Beard  
Research group: Large DNA Viruses

Project Summary:
Lumpy skin disease (LSD) is a severe poxviral disease affecting cattle. It has spread from Africa and the Middle East into Europe and Asia in the past 5 years and is viewed as a rapidly emerging disease of high concern. LSD causes substantial losses to rural communities, particularly impacting subsistence farmers. LSD is caused by infection with the poxvirus lumpy skin disease virus (LSDV), a member of the capripoxvirus (CPPV) genus. This project will examine how LSDV forms virions (morphogenesis), and how the virions exit an infected cell. The project will be based in the high containment laboratories at the Pirbright Institute.

Poxviruses produce four distinct types of virions during their replication cycle. They are intracellular mature virions (IMVs), intracellular enveloped virions (IEVs), cell associated enveloped virions (CEVs) and extracellular enveloped virions (EEVs). Electron microscopic analysis of cells infected with LSDV has revealed all four virion types present either within cells or in the extracellular space, however little is known about the mechanisms and pathways involved in virion morphogenesis and exit. Studies on vaccinia virus have shown that EEVs and IMVs are crucial for raising a targeted neutralising antibody response and recent publications have shown that using a combination of recombinant IMV and EEV membrane proteins to vaccinate mice generate the strongest antibody responses that are protective.

This project will characterise LSDV virion morphogenesis and exit. The knowledge from this project will promote the development of efficacious vaccines to control the spread of LSD thus improving animal welfare and minimising the economic the impact of the disease. This project will support the H2020 DEFEND programme of work, specifically work package 11 (WP11) which aims to develop novel vaccines against lumpy skin disease virus. The student will be directly supervised by Dr Petra Fay and Dr Pip Beard and will attend the relevant DEFEND project team meetings. They will also be supported by the rest of the Large DNA Viruses team, which consists of ten scientists.

Details:
Depending on progress, the successful student may undertake the following in the duration of the research project:

Assess the effect of different chemical inhibitors on LSDV replication and morphogenesis. Chemical inhibitors that target particularly cellular pathways or processes will be added to LSDV-infected cells, and their impact on LSDV replication measured over time. This objective will use a LSDV strains tagged with an enhanced green fluorescent protein (eGFP) and an IncuCyte live cell analysis system to facilitate high throughput analyses.

Characterise the effect of different chemical inhibitors on LSDV replication. Chemical inhibitors identified will be examined in more detail using virological techniques such as single-step and multistep growth curves, and plaque morphology comparisons. Alterations in the location of virions in infected cells treated with chemical inhibitors will be studied using immunofluorescent confocal microscopy.

Identify mechanisms by which LSDV manipulates cellular pathways to produce virions and exit the cell. Examine in detail the interactions between the virus and host cell that are required for virion morphogenesis and exit using deletion mutant LSDVs and LSDV monoclonal antibodies.
References for Suggested Reading:


To Apply:

Please email your CV (no more than two sides of A4) and a covering letter detailing why you would like to undertake the placement and the knowledge and skills that you will bring to the Institute to lucy.drudge@pirbright.ac.uk

Closing date to apply: 01.02.21