Ref: 2024/03
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Project Title: Understanding essential host factors for FMDV replication in pigs and cows: Towards gene edited FMD resistant livestock.

Supervisors: Dr James Kelly, Dr Stephen Berryman, Dr Toby Tuthill, Dr Soumendu Chakravarti
Research group: Picornavirus Molecular Biology

About The Pirbright Institute

The Pirbright Institute delivers world-leading research to understand, predict, detect and respond to viral disease outbreaks. We study viruses of livestock that are endemic and exotic to the UK, including zoonotic viruses, by using the most advanced tools and technologies to understand host-pathogen interactions in animals and arthropod vectors. Our Institute is made up of a dynamic and vibrant community of employees covering a diverse set of chosen fields, backgrounds and experience. Our outlook is always balanced by our strong sense of purpose, values and behaviours, and an unwavering commitment to a 'one Institute' approach.

Project Summary:

Foot-and-mouth disease virus (FMDV) is the causative agent of foot-and-mouth disease (FMD). This is a highly infectious virus that causes blisters on the feet and mouth of cloven hooved animals such as pigs and cattle. It also reduces the lifetime productivity of the infected animals. FMDV outbreaks impose a significant cost on the global pig and cattle industry, which together are worth £700 billion annually.

As part of an ongoing project, we are investigating on how to create gene edited livestock with resistance to FMDV, as a method to prevent outbreaks of the disease. In this project, we have identified several host genes essential for FMDV replication in porcine cells, reducing the expression of these genes in porcine cells completely prevented viral replication and making the cells resistant to infection with FMDV. This area of research has reached an exciting stage. The internship will contribute to the project by generating FMD resistant cell lines and characterizing the function of these target genes during FMDV infection.

In the first part of the study, the intern will support ongoing work in the group to generate and characterise porcine and bovine gene Knock Out (KO) cell lines. You will then confirm gene KO by sequencing and characterise the effect of gene KO on FMDV by comparing virus replication in KO and normal cells. As part of the project, you will also attempt to grow FMDV in resistant cell lines to assess if the virus can evolve to recover infectivity through adaptation. In addition to this, you will also determine the susceptibility of the KO cells to a panel of other livestock viruses.

In the second part of the project, you will have the opportunity to study how the proteins encoded by these target genes are required during FMDV infection. This part of the project will be driven more by the intern and will involve the use of confocal microscopy to assess where the proteins are localizing in the cell in relation to viral proteins and will also involve creating mutated versions of the proteins to identify functional domains. This will help understand the role these genes play in FMDV replication and how they interact with the virus.

Further Details:

As part of this project the intern will use and learn the following techniques:

- Mammalian cell culture
- Working safely with viruses in high containment laboratories
- Virology techniques including virus infection of cells and measurement of virus growth using a live cell imaging system and infectivity titrations.
- Molecular biology techniques including DNA cloning, mutagenesis, PCR and sequencing. Transfection of cells, recombinant protein expression, electrophoresis and western blotting.
- Immunofluorescence and high performance confocal microscopy to understand how viral and cellular proteins co-localise during infection

During this project you will report at regular group meetings and have the opportunity to present at the Pirbright Institute student day and the Microbiology Society annual meeting. This will give you the opportunity to develop communication, presentation, and networking skills. The internship will be line managed and closely supported by Dr James Kelly, with additional support provided by other members of the supervisory team and the Picornavirus Molecular Biology research group.

References for Suggested Reading:

Pannhorst, K., Carlson, J., Hölper, J.E., Grey, F., Baillie, J.K., Höper, D., Wöhnke, E., Franzke, K., Karger, A., Fuchs, W. and Mettenleiter, T.C., 2023. The non-classical major histocompatibility complex II protein SLA-DM is crucial for African swine fever virus replication. Scientific Reports, 13(1), p.10342.

Hölper, J.E., Grey, F., Baillie, J.K., Regan, T., Parkinson, N.J., Höper, D., Thamamongood, T., Schwemmle, M., Pannhorst, K., Wendt, L. and Mettenleiter, T.C., 2021. A Genome-Wide CRISPR/Cas9 Screen Reveals the Requirement of Host Sphingomyelin Synthase 1 for Infection with Pseudorabies Virus Mutant gD–Pass. Viruses, 13(8), p.1574.

Sun, L., Zhao, C., Fu, Z., Fu, Y., Su, Z., Li, Y., Zhou, Y., Tan, Y., Li, J., Xiang, Y. and Nie, X., 2021. Genome-scale CRISPR screen identifies TMEM41B as a multi-function host factor required for coronavirus replication. PLoS Pathogens, 17(12), p.e1010113.

Kelly JT, Swanson J, Newman J, Groppelli E, Stonehouse NJ, Tuthill TJ. Membrane Interactions and Uncoating of Aichi Virus, a Picornavirus That Lacks a VP4. J Virol. 2022 Apr 13;96(7):e0008222.

To Apply: See our website for details.
Closing date to apply: 26.02.24