

Ref: 01/SG

Project Title: Characterisation of self-renewing porcine macrophage cell models and their application to support vaccine development

Supervisors: Simon Graham and Jane Edwards

Research group: PRRS Immunology

Project Summary:

Porcine reproductive and respiratory syndrome viruses (PRRSV) are rapidly evolving RNA viruses responsible for the most economically important disease affecting the global pig industry. There are known to be two species of PRRSV, both of which have evolved to produce several highly pathogenic strains of virus. Commercially available live attenuated vaccines fail to provide broad cross-protection across the plethora of strains that have (and are likely) to emerge and their ability to revert to virulence poses significant challenges to protect livestock. There is, therefore, an urgent requirement to explore alternative approaches to vaccine development to combat the PRRSV panzootic. Working with collaborators, The Pirbright Institute's PRRS Immunology Group are pursuing ambitious complimentary approaches to develop improved PRRS vaccines.

One of the challenges of working with PRRSV is their strict tropism for macrophages. This means that many strains require the isolation of fresh alveolar macrophages from pig lungs for successful virus characterisation. These macrophages do not proliferate and there is therefore a requirement of post mortem animals to advance the assays required for vaccine development. Additionally, significant donor animal variability exists in PRRSV susceptibility, which poses challenges for establishing sensitive and reproducible assays, such as virus neutralisation assays. Our collaborators at the University of Plymouth have established a simple method yielding self-renewing macrophages from mouse foetal liver which reproduce alveolar macrophage specific responses to respiratory pathogens. We have now established self-renewing macrophages from pig embryonic liver and spleen and a pilot experiment has shown that PRRSV strains efficiently infect these cells. We wish to now exploit this important new finding to support our PRRSV vaccine research.

Details:

The initial phase of the project will involve characterising the self-renewing porcine macrophage lines and their susceptibility to a range of attenuated and virulent PRRSV strains. Clonal cell lines will then be established based on expression of PRRSV entry receptors CD163 and CD169 and these will be screened for their susceptibility to infection. Highly susceptible cells lines will then be used to adapt and optimise a PRRSV neutralisation assay. The final stage of the project will be to deploy this assay, incorporating a panel of diverse PRRSV-1 and PRRSV-2 strains, to characterise the breadth and titre of neutralisation by monoclonal antibodies isolated from hyperimmune pigs and serum from pigs immunised with vaccines under development.

The successful applicant will be embedded in the PRRS Immunology Group and will receive support and guidance from the group leader Dr Simon Graham and senior post-doctoral scientist Dr Jane Edwards. Additional support will be provided by other postdocs and students in the group.

This exciting new project is well suited to students with interests in immunology, virology, cellular biotechnology and vaccines.

References for Suggested Reading:

1. www.pirbright.ac.uk/viruses/prrsv
2. www.pirbright.ac.uk/our-science/livestock-viral-diseases/porcine-reproductive-and-respiratory-syndrome-prrs-immunology
3. Fejer G, Sharma S, Gyory I. 2015. Self-renewing macrophages--a new line of enquiries in mononuclear phagocytes. *Immunobiology*. 220(2):169-74.
4. Lunney JK, Fang Y, Ladinig A, Chen N, Li Y, Rowland B, Renukaradhya GJ. 2016. Porcine Reproductive and Respiratory Syndrome Virus (PRRSV): Pathogenesis and Interaction with the Immune System. *Annu Rev Anim Biosci*. 4:129-54.
5. Vu HLX, Pattnaik AK, Osorio FA. Strategies to broaden the cross-protective efficacy of vaccines against porcine reproductive and respiratory syndrome virus. *Vet Microbiol*. 206:29-34

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 yvonne.walsh@pirbright.ac.uk.

Closing date to apply: 31.01.20