Project Title: Activation-induced markers to identify T cells associated with protection against ASFV

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Research group: African Swine Fever Vaccinology & T-cell Biology

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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:

CD4 T-helper cells play a pivotal role in steering adaptive immune responses, particularly in safeguarding against viral infections. Their significance becomes even more pronounced in the defence against African swine fever (ASF), a disease caused by the complex ASF virus (ASFV) that has triggered numerous outbreaks across the globe. ASFV poses a severe threat, inducing a contagious and often fatal disease affecting both domestic and wild pigs. Given the absence of a widely licensed vaccine, disease control relies on drastic measures such as quarantine and culling of infected and exposed animals.

Recent findings suggest a link between vaccine efficacy against ASF and the activity of CD4 T-helper cells. Despite this correlation, the specific characteristics and contributions of individual CD4 T-cell subsets remain elusive. The T-cell biology group has devised an Activation-Induced Marker (AIM) assay utilising multi-parameter flow cytometry tailored to porcine T cells. AIM assays offer the advantage of detecting antigen-specific T cells in live samples, distinguishing them from conventional methods that necessitate fixation for intracellular staining of cytokines. This project will mainly focus on adapting the AIM assay to identify ASFV-primed T cells. This would facilitate a nuanced exploration of the heterogeneous responses orchestrated by CD4 T cells, shedding light on their intricate contributions to protection against ASF.

We possess an extensive repository of banked samples from prior ASF and vaccine studies, supplemented by ongoing vaccine development work. The student involved in this project will conduct the following assays on these samples:

1. High resolution analysis of systemic T cell responses using the optimised AIM assays and functional assays, including cytokine production in T cells
2. Optimisation of the AIM assay for fluorescence-activated cell sorting and expansion of the assay to include more activation markers in ASFV-primed cells
3. Generate a method to block CD40-CD40L interaction between antigen presenting cells and T cells using recombinant protein expression to increase extracellular expression of this key activation marker

Further Details:

Once established, the AIM assays will allow the identification and isolation of rare ASFV-specific T cells for future transcriptomic analyses to unravel molecular profiles associated with protection. This project will lay the basis for deeper insights into the intricate mechanisms underpinning protection against ASFV, offering valuable contributions to understanding fundamental processes in ASFV protection. This work will also broaden the AIM assay's utility for other porcine diseases. The student will be working with both the ASF Vaccinology and T-Cell Biology groups and will acquire expertise in areas such as: working in high containment, isolation of peripheral blood mononuclear cells, cell culture, expression of recombinant proteins, high parameter flow cytometry techniques and data analysis. This immersive experience will expose the student to the unique scientific environment at Pirbright, fostering a comprehensive skill set and contributing to advancements in porcine disease research.

References for Suggested Reading:

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Frentsch, M., Arbach, O., Kirchhoff, D. et al. Direct access to CD4+ T cells specific for defined antigens according to CD154 expression. Nat Med 11, 1118–1124 (2005). https://doi.org/10.1038/nm1292

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