PhD Studentship: African swine fever virus host-pathogen interactions at the interface between the innate and adaptive immune responses

Project Ref: 2025/08
Anticipated Start Date: October 2025 **Duration:** 3.5 years full-time
Closing date to apply: 15 June 2025

Eligibility:

- This studentship is open to science graduates with, or who anticipate obtaining, at least a 2:1 or equivalent in a relevant biological subject in an undergraduate degree, or with a Masters degree - subject to university regulations**.** Other first degrees, e.g. veterinary science, will be considered. You should be looking for a challenging, interdisciplinary research training environment and have an active interest in the control of infectious diseases.
- This is a 3.5 year fully funded studentship open to UK nationals. International candidates may apply, however funding for this studentship includes university tuition fees at the Home rate only - see funding information below.
- Students without English as a first language must provide evidence that they meet the English language requirement, e.g. with an average IELTS score of 7.0, with no lower than 7.0 in listening/reading and no lower than 6.5 in speaking/writing.

Supervision:

Principal Supervisors: Dr Chris Netherton (The Pirbright Institute), Prof Dirk Werling (Royal Veterinary College)
Co-Supervisor: Dr Priscilla Tng (The Pirbright Institute)
Industrial Partner: Boehringer Ingelheim
Research Group: African Swine Fever Vaccinology

Project Details:

As obligate parasites, viruses have evolved multiple different strategies to evade innate and adaptive immune responses in order to successfully propagate within hosts. Viral factors that facilitate evasion of intrinsic or innate immune responses can be identified through targeted or genome wide functional screens, but the onward relationship of such evasion, if it exists, with the adaptive immune response can be difficult to assess.

African swine fever virus (ASFV) is a large complex dsDNA virus that encodes for more than 200 open reading frames. The virus causes an invariably fatal disease in domestic pigs and wild boar that has spread across the globe in the last twenty years with significant impacts on pig production and food security. Safe and effective vaccines are the principle missing disease control tool against ASFV and developing subunit vaccines against the current panzootic isolate has been particularly problematic.

Cellular immune responses against ASFV are considered particularly important for protection against ASFV and experimental modified live virus (MLV) vaccines and viral vectored subunit vaccines that induce such responses are available in the laboratory. Cellular immunity is typically assessed using *ex vivo* recall assays where peripheral blood mononuclear cells (PBMCs) from immunised animals are restimulated with live virus and the expression of Th1 cytokines, in particular interferon gamma (IFNγ), are used as a readout. Flow cytometry analysis shows that a variety of different cells respond in such assays and a key role for both CD4+CD8α+ and CD4-CD8α+ T-cells has been suggested in this response, however, it is not clear which immune cells are directly responding to viral stimulation. It is also unclear whether there are differences in the immune responses induced by different experimental vaccines.

An additional complicating factor is that different isolates of ASFV appear to have differing levels of immunostimulatory activity and we have recently identified a region of the ASFV genome that suppresses the secretion of IFNγ. Recall assays are clearly artificial and adding live virus to PBMC cultures are likely to induce innate responses as well as secretion of IFNγ. Precision cut tissues slices (PCTS) and lymph node derived cultures (LNDC) represent a model closer to the natural system and an exciting opportunity to study the innate immune

response in naïve animals. Therefore, we will compare LNDCs, PBMCs and macrophage cultures after infection with wild type and ASFV deletion mutants to assess whether viral suppression of T-cell responses is linked to the induction of innate immune responses.

We hypothesise that understanding how ASFV interacts with the cellular immune response will lead to the rational development of effective subunit vaccines against the disease. The aim is to assess the impact of a reduced IFNγ signalling on ASFV – host interaction. To achieve this aim, the overall objectives of this proposal will be to:

1) Understand the role of different T-cell populations in the cellular response to ASFV induced by different experimental vaccines.
2) Identify ASFV genes and mechanism responsible for viral suppression of T-cell responses.
3) Develop lymph node derived cultures as a model to understand the role of the innate immune response in viral suppression of the adaptive immune response.

The successful candidate will be trained to work in the high containment laboratories at The Pirbright Institute under the supervision of Dr Chris Netherton and Dr Priscilla Tng. The student will learn both virological and immunological techniques, including primary cell culture, virus culture and titration, ELISA, ELISpot, making and characterizing recombinant ASFV deletion mutants, fluorescence activated cell sorting, spectral flow cytometry, high parameter analysis and single cell RNA sequencing. The student will also spend time in Professor Dirk Werling's laboratory at the Royal Veterinary College to learn how to generate and culture precision cut tissues, and will have the opportunity for a placement with our industrial partner Boehringer Ingelheim Animal Health.

The student will be supervised by Chris Netherton and Priscilla Tng at the Pirbright Institute and Dirk Werling at the Royal Veterinary College. Chris Netherton and Priscilla Tng have extensive experience of the molecular virology and immunology of African swine fever virus. Dirk Werling is an immunologist with a long track record in veterinary science and has recently been developing precision cut tissues as a method to better understand host-pathogen interactions.

References for Background Reading:

Portugal R, Goldswain H, Moore R, Tully M, Harris K, Corla A, Flannery J, Dixon LK, Netherton CL. (2024) Six adenoviral vectored African swine fever virus genes protect against fatal disease caused by genotype I challenge. *Journal of Virology* 98(7):e0062224. https://doi.org/10.1128/jvi.00622-24

Goatley LC, Nash RH, Andrews C, Hargreaves Z, Tng P, Reis AL, Graham SP, Netherton CL. (2022) Cellular and Humoral Immune Responses after Immunisation with Low Virulent African Swine Fever Virus in the Large White Inbred Babraham Line and Outbred Domestic Pigs. *Viruses*. 14(7):1487. https://doi.org/10.3390/v14071487.

Majorova *et al.*, (2021) Use of Precision-Cut Tissue Slices as a Translational Model to Study Host-Pathogen Interaction *Frontiers in Veterinary Science* 8: https://doi.org/10.3389/fvets.2021.686088.

C.L. Netherton (2021) African swine fever vaccines. In Understanding and combatting African swine fever: A European perspective, 2021 page 161-182. Editors Laura Iacolina, Mary-Louise Penrith, Silvia Bellini, Erika Chenais, Ferran Jori, Maria Montoya, Karl Ståhl and Dolores Gavier-Widén. Published by Wageningen Academic Publishers. https://doi.org/10.3920/978-90-8686-910-7_6.

Registration, Training and Funding:

This is a Pirbright Institute/RVC/Boehringer Ingelheim fully funded studentship. The studentship covers stipend and Home rated university tuition fees. International students will attract tuition fees at the overseas rate and must show evidence at the time of application of their ability to cover the difference between Home fees and Overseas fees for the duration of study.

The student will be based primarily at The Pirbright Institute and registered with the RVC. The student will visit the university to meet with their supervisors and undertake training or complete specific project tasks as required. Eligible students will receive a UKRI-aligned stipend (£20,780 for 2025/26) plus a cost of living allowance of £2,200 per annum. Home rated university tuition fees will be paid. Highly subsidised Pirbright Institute student housing will be offered. A full range of research and transferrable skills training will be made available to the student as appropriate.

Applications:

How to Apply: Closing date 15 June 2025

Essential documents:

- Application Form
- CV
- Two references sent directly by your referees

Please email your application to studentship@pirbright.ac.uk by the closing date.