PhD Studentship: Development of ex-vivo organ culture methods to assess immune responses to viral antigens in pigs

Project Ref: 2022/02/WG/DW
Anticipated Start Date: October 2022  Duration: 3.5 years full-time
Closing date to apply: 20 March 2022

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 their undergraduate degree, or a Masters degree - subject to university regulations). Other first degrees, eg 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. EU and international applicants are welcome to apply, however international university tuition fees will apply and these are not included in the funding – please 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 Wilhelm Gerner (The Pirbright Institute), Prof Dirk Werling (Royal Veterinary College)
Co-Supervisors: Dr Elma Tchilian, Dr Selma Schmidt (The Pirbright Institute), Dr Rob Noad (Royal Veterinary College)
Research Group: T-cell Biology

Project Details:
For most vaccines that are currently used in humans and animals, antibodies are a strong correlate of protection. Antibodies are produced by B cells. B cells can differentiate via plasmablasts into long-lived plasma cells or develop into memory B cells. For most activated B cells, this differentiation process occurs in germinal centres (GCs) of secondary lymphoid organs (SLOs) like spleen and lymph nodes. B cells in GCs undergo somatic hypermutation, resulting in the selection of B cells that produce antibodies of higher affinity. Somatic hypermutation and B-cell differentiation in SLOs are complex processes, which are controlled by the tissue microenvironment.

Mimicking the GC reaction in vitro would be a major advancement in the process of vaccine candidate testing. In this way antigens and adjuvants could be tested rapidly and efficiently for their capacity to induce antibody responses, reducing the need for experiments with living animals. The project will use cells and tissues from pigs, since vaccination is an important tool for disease control in swine herds. In addition, swine are a large animal model in biomedical research because of their similarity to humans in terms of tissue/organ anatomy and physiology.

The project will investigate two approaches for in vitro B cell GC cultures: organoid cultures from SLO cell preparations and precision cut lymph node slices. Organoid cultures from human tonsil preparations mimicking GC reactions were described recently and the teams of Drs Gerner and Tchilian were able to adopt this approach for porcine lymph node cultures. Precision cut tissue slices (PCTS) are three-dimensional tissue explants, which are cultured ex vivo and retain the anatomical architecture of the organ. Precision cut tissue slices from porcine lymph nodes were recently established by Prof Werling’s team.

The project will be organised according to the following objectives:

1. Establishment of optimised cultivation conditions for re-aggregation of SLO cell suspensions that lead to an effective stimulation of T and B cells for antigen recall (determined by T and B-cell activation as well as antibody and cytokine production).
2. Investigation of changes in T and B cell phenotypes as well as quantitative changes over the time of in vitro stimulation.
3. Comparison of the T/B cell response and antibody production of re-aggregated organoid cultures with PCTS from the same SLO material.
4. Investigations on the induction of primary immune responses, i.e. SLOs from naïve pigs will be used and in vitro stimulated with swIAV live virus but also different types of vaccines and adjuvants. The student will have access to the scientific environments at The Pirbright Institute and the Royal Veterinary College, both offering state of the art equipment and technologies. There will also be the opportunity to present results at national and international scientific meetings.

References for Background Reading:


Registration, Training and Funding:
This is a Pirbright Institute/RVC fully funded studentship. All students are eligible for the full award (stipend and home rated university tuition fees). EU and international students will be liable for tuition fees at the international rate and must be able to fund the difference between “Home” and “Overseas” tuition fees themselves. For Home student eligibility guidelines, please refer to the UKRI Full Eligibility Criteria (Annex One).

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 minimum annual stipend of £16,062 plus a cost of living top-up allowance of £2,200 per annum. Home rated university registration fees will be paid. Highly subsidised 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 20 March 2022.

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.