Project Title: **Pathogenesis, immunity, and control of influenza viruses**

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Research group: Mucosal Immunology

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:

Current vaccine strategies against influenza viruses induce strain specific neutralising antibodies but the rapid emergence of variant strains leads to loss of protection, necessitating frequent updating of vaccines. An alternative approach is to target conserved antigens that induce T cell responses, providing the basis for a universal influenza vaccine. Furthermore, seasonal influenza vaccines are administered intramuscularly, although local immunity in the respiratory tract is important in control of respiratory infections.

The pig is physiologically, anatomically genetically and immunologically more similar to humans than small animals and is a natural host for very similar influenza viruses to humans. Furthermore, the lung structure and morphology closely resemble that in humans, and pig antibody responses to influenza have a very similar specificity to humans. In collaboration with the University of Oxford we have shown that a vaccine consisting of conserved internal proteins of the virus, induces T cell responses in the pig influenza model that prevent viral shedding from the nose and reduce lung pathology and lung viral load. Many banked samples from these influenza vaccine and infection experiments are available and the intern will use them to further investigate the mechanisms of protection, performing the following studies:

1. High resolution analysis of systemic and mucosal T cell immune responses by ELISpot and multi-parameter flow-cytometry to determine the ability of T cells to secrete cytokines following infection or immunisation.
2. Assay neutralisation and binding of antibodies to influenza proteins to establish the role of antibody in serum, nasal and lung tissue.
3. Use plaque assays to measure viral load, viral shedding and transmission.

A broadly cross-protective influenza vaccine could replace seasonal influenza vaccines, providing a high level of protection against any influenza A virus, including new pandemic viruses, even before a new pandemic begins. Data produced in the pig influenza model is crucial for future human studies and clinal trials.

Further Details:

This represents an exciting opportunity to be part of a One Health research project and is suitable for individuals with a keen interest in translational research for human and animal health. The intern will learn immunological and virological techniques well established in Pirbright. They will have the opportunity to further develop the assays, become an expert in mucosal immunology and take a leading role in analysing efficacy of novel vaccines and transmission blockers.

References for Suggested Reading:

Vatzia E *et al*. Immunization with matrix-, nucleoprotein and neuraminidase protects against H3N2 influenza challenge in pH1N1 pre-exposed pigs (2023) **NPJ Vaccines**, 8:19.

Vatzia E *et al*. Respiratory and intramuscular immunization with ChAdOx2 NPM1-NA induces distinct immune responses in H1N1pdm09 pre-exposed pigs (2021). **Frontiers in Immunology** 12:763912.

Martini V *et al.* Simultaneous aerosol and intramuscular immunization induces powerful protective local T cell and systemic antibody immune responses in pigs (2021). *J Immunology* 206(3):652-663.

Tchilian E and B Holzer. Harnessing Local Immunity for an Effective Universal Swine Influenza Vaccine. (2017) *Viruses* 9(5): 98.

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Closing date to apply: 26.02.24