

**Project Title:** Investigating the use of modified glycan receptors by avian influenza viruses.

**Supervisors:** Dr Thomas Peacock

**Research group:** Zoonotic Influenza Viruses

### ***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 employee's 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.

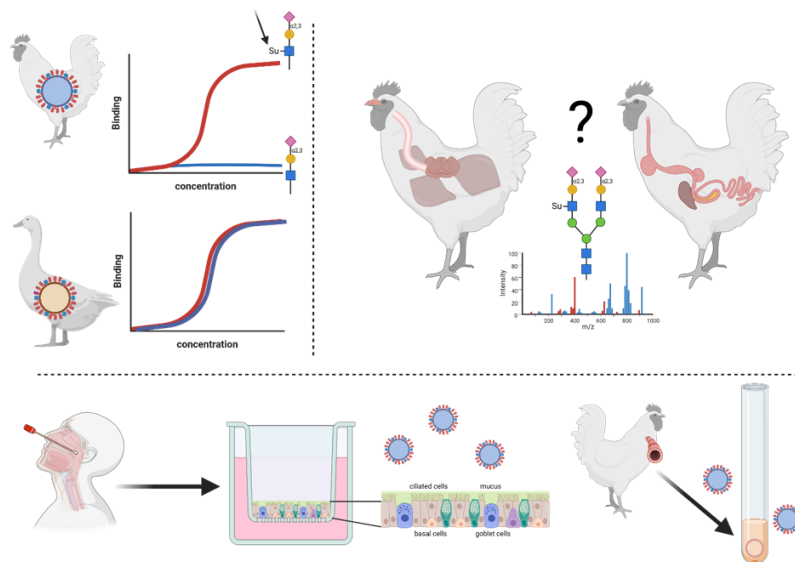
### **Project Summary:**

Avian influenza viruses (AIVs) have caused three of the last five respiratory virus pandemics. However, AIVs replicate very poorly in humans and must substantially mutate and adapt to efficiently infect and transmit between humans. Influenza viruses use glycan receptors to enter host cells (specifically glycans with the terminal sugar sialic acid, called sialylated glycans). The type and distribution of these sialylated glycan receptors differ between birds and humans. AIVs must learn to use the human-like receptors to go pandemic.

We have recently found that several chicken-adapted AIVs are considered to have pandemic potential do not bind the typical avian-like sialylated glycan receptors and instead only bind these receptors when they are modified through addition of a sulphate side chain. It appears this property has evolved multiple times in highly chicken-adapted AIVs, but not seen in ducks; which are thought to be the natural reservoir of AIVs. This research suggests that this is the preferred sulphate, sialylated glycan and gives a fitness advantage in a chicken host.

We hypothesise that the change in receptor preference may be due to either changes in the host (from waterfowl to chickens) or due to changes in virus tropism (from gastrointestinal tropism in waterfowl to respiratory tropism in chickens). The distribution and abundance of this modified receptor is not described in chickens and humans, and it is unclear if this adaptation to chickens enhances or decreases the chance of these viruses spilling over into humans and causing zoonotic infections, or even a future pandemic.

In this project the student will study the distribution and biological relevance of these modified sulphated, sialylated glycan receptors in chickens and humans, determining how widespread this property is in diverse AIV subtypes, and what impact this change in receptor use has on zoonotic and pandemic potential of AIVs.



### Further Details:

This project is a great opportunity for students that are interested in both human and veterinary microbiology, as well as those with an interest within pandemic preparedness and risk assessment. The student will join the recently established [zoonotic influenza viruses](#) group at Pirbright, which is led by [Dr Thomas Peacock](#).

The zoonotic influenza viruses group investigates influenza and coronavirus cross-species transmission and evolution with a focus on viruses with pandemic, zoonotic and panzootic potential.

This project will involve a range of diverse interdisciplinary techniques including classical virology, bioinformatics and phylogenetics as well as virus reverse genetics, biophysical protein-glycan binding assays, molecular cloning, cell culture and cell line engineering, use of primary cells and ex vivo organ cultures.

This project is part of an ongoing collaboration with the Liu and Haslam groups at Imperial College London. As part of this project the student will have the opportunity to be hosted by these groups for a few weeks to gain experience performing mass-spectrometry based glycomics (at the Haslam lab at the South Kensington Campus) or glycan microarrays (at the Liu lab at the Hammersmith Hospital campus).

### References for Suggested Reading:

Long et al, Host and viral determinants of influenza A virus species specificity, Nature reviews Microbiology, 2019 <https://doi.org/10.1038/s41579-018-0115-z>

Peacock et al, Variability in H9N2 haemagglutinin receptor-binding preference and the pH of fusion, Emerging Microbes and Infection, 2017 <https://doi.org/10.1038/emi.2016.139>

Peacock et al, Genetic Determinants of Receptor-Binding Preference and Zoonotic Potential of H9N2 Avian Influenza Viruses, JVI, 2021 [https://doi.org/10.1128/jvi.01651-](https://doi.org/10.1128/jvi.01651-21)

de Vries et al, A single mutation in Taiwanese H6N1 influenza hemagglutinin switches binding to human-type receptors, Embo Mol Med, 2017 <https://doi.org/10.15252/emmm.201707726>

**To Apply:** See [our website](#) for details.

**Closing date to apply:** 26.02.24