Ref*:* 2024/05
Closing date: 26.02.24

Project Title: Deciphering the mechanism of attenuation of a novel avian coronavirus vaccine candidate.

Supervisors: Dr. Katalin Foldes, Dr Renata Fleith, Dr Sarah Keep & Dr Trevor Sweeney.
Research group: Coronaviruses and Viral Gene Expression

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:

The *Gammacoronavirus* infectious bronchitis virus (IBV) is a highly contagious pathogen of domestic fowl that causes significant production loss across the globe. IBV vaccines are currently generated by serial passage of virulent field isolate through embryonated hens' eggs; the exact mechanism of attenuation is unknown and there is a risk for reversion to virulence. Methods for rational attenuation are therefore highly desirable for future vaccine development. Our previous research showed that specific modifications in the non-structural proteins (nsps) offer a promising avenue for rational attenuation.
These amino acid changes could both result in attenuated and temperature-sensitive replication phenotype, suggesting that the two phenotypes are linked; however, the mechanism of both is unknown.

The aim of this project is to investigate the mechanistic action of the identified amino acid changes and to study the potential for reversion to virulence. The student will engage with two enthusiastic groups of scientists. Within the Viral Gene Expression group, the student will study the mechanistic action of the attenuating mutations evaluating aspects such as RNA capping, translation, and protein thermostability. Within the Coronavirus group, the student will investigate the stability of the mutations and identify possible paths to reversion to virulence.
The project will involve a wide range of both molecular biology and virology techniques including protein expression and purification, *in vitro* transcription, RNA capping, virus propagation and growth kinetic assays both *in vitro* and in *ex vivo* tracheal organ cultures, plaque assays and reverse genetics.

Further Details:

This project offers an opportunity to gain experience in collaborative working and to develop skills in a wide range of both molecular biology and virology techniques. Coronaviruses continue to be a hot topic and this project provides an opportunity to gain experimental experience in the coronavirus field. The student will have the opportunity to attend seminars, to present their research at The Pirbright student day and lab meetings.

References for Suggested Reading:

Keep S, et al (2022). Identification of amino acids within non-structural proteins 10 and 14 of the avian coronavirus infectious bronchitis virus that result in attenuation *in vivo* and *in ovo*.
doi.org/10.1128/jvi.02059-21

Keep S, et al (2022). A Temperature-Sensitive Recombinant of Avian Coronavirus Infectious Bronchitis Virus Provides Complete Protection against Homologous Challenge.
doi: 10.1128/jvi.01100-22.

V'kovski et al (2021). Coronavirus biology and replication: implications for SARS-CoV-2.
doi.org/10.1038/s41579-0200468-6.

To Apply: See How to apply for details.
Closing date to apply: 26.02.24