PhD Studentship: Rational development of the next generation of vaccines for Infectious Bronchitis Virus

Project Ref: 2024/01
Anticipated Start Date: October 2024 **Duration:** 4 years full-time
Closing date to apply: 19.02.24

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, 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 4 year fully funded studentship open to UK nationals (or those with settled status or unlimited leave to remain in the UK).
- Students without English as a first language must provide evidence that they meet the English language requirement, ie 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, or equivalent.

SUPERVISION:

Principal Supervisors: [1]Dr Sarah Keep, [2]Prof Andrew Davidson

Co-Supervisors: [1]Dr Thomas Peacock, [1]Dr Erica Bickerton, [2]Dr Isobel Webb

[1]The Pirbright Institute [2]University of Bristol

Research Group: Coronavirus

PROJECT DETAILS:

The *gammacoronavirus* Infectious Bronchitis Virus (IBV) causes Infectious Bronchitis, an acute, economically important respiratory disease of chickens. There are several genetically distinct co-circulating strains that are categorised by serotype, genotype and protectotype with new strains constantly emerging. Vaccination uses live attenuated vaccines generated via serial passage of a virulent field isolate through embryonated hens' eggs, typically ~100 times. The process of vaccine generation is slow, does not allow for rapid reaction to emerging strains and is dependent on the supply of eggs. Next generation vaccines are therefore required, in which the vaccine viruses are 1) rationally attenuated, and 2) can be manufactured in cell culture. The Spike (S) protein is the major antigen, attachment and entry protein of IBV. Most IBV strains cannot replicate in cell culture, but our previous research demonstrated the S protein, specifically the S2 subunit, from the attenuated lab adapted Beaudette strain confers Beaudette's unique ability to replicate in Vero cells, a cell line used for vaccine manufacturing.

This project will build on our previous research to identify amino acids that enable replication in Vero cells and investigate host proteases to further boost replication. This knowledge will be combined to generate a system for enhanced and universal IBV replication in Vero cells, a resource that would be highly valuable to vaccine manufacturing as well as IBV research and diagnostics. Using a variety of diverse molecular biology, cell culture and virology techniques including primary and continuous cell culture, reverse genetics for the generation of recombinant IBV, drug inhibition assays, pseudovirus entry assays and virus neutralization assays, the student will carry out research focusing on the following objectives:

1. Determine mutations that increase IBV replication in Vero cells.
2. Investigation of protease treatment to improve IBV replication in Vero cells.
3. Generation of a cell-viral system for enhanced replication of a wide range of IBV strains.
4. Investigation of the pathogenicity and *in vivo* tropism of recombinant IBVs containing mutations in the Spike gene.

The student will join a supportive environment and will be encouraged to present their work at seminars, journal clubs and conferences in order to develop skills in communication, networking and scientific collaboration.

REFERENCES FOR BACKGROUND READING:

- Peacock et al (2021). The furin cleavage site in the SARS-CoV-2 spike protein is required for transmission in ferrets. Nature Microbiology 6, 899-909.
- Keep 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.
- Stevenson-Leggett et al (2020). Treatment with Exogenous Trypsin Expands *In Vitro* Cellular Tropism of the Avian Coronavirus Infectious Bronchitis Virus. doi: 10.3390/v12101102.
- Ellis, S. et al (2018). Recombinant Infectious Bronchitis Viruses expressing chimaeric spike glycoproteins induce partial protective immunity against homologous challenge despite limited replication *in vivo*. DOI: 10.1128/JVI.01473-18.
- Bickerton et al (2018). The S2 Subunit of Infectious Bronchitis Virus Beaudette Is a Determinant of Cellular Tropism. doi.org/10.1128/jvi.01044-18

REGISTRATION, TRAINING AND FUNDING:

This is a Pirbright Institute/University of Bristol/British Egg Marketing Board fully funded studentship, which includes stipend and home rated university tuition fees. The successful student will be based primarily at The Pirbright Institute and registered with the University of Bristol. The student will visit the university to meet with their supervisors and undertake training or complete specific project tasks as required. Students will receive a UKRI-aligned stipend (currently £18,622 for 2023/24) plus a cost of living top-up allowance of £2,200 per annum. Home rated university registration 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: 19.02.24

Essential documents:

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

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