

PhD Studentship: Investigation of the role of the s2m motif in IBV replication and pathogenicity



Project Ref: 2023/01

Anticipated Start Date: October 2023 **Duration:** 3.5 years full-time

Closing date to apply: 03.02.23



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 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 – 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 Sarah Keep](#) (The Pirbright Institute), [Dr Valeria Lulla](#) (University of Cambridge)

Co-Supervisors: [Dr Erica Bickerton](#), [Dr Trevor Sweeney](#) (The Pirbright Institute), [Prof Ian Brierley](#) (University of Cambridge)

Research Group: [Coronaviruses](#)

Project Details:

Coronaviruses are a large family of viruses that infect a diverse number of species, including humans, birds and livestock. Consequently, coronavirus infections have significant impact not only on human health but also animal health and welfare. The avian coronavirus Infectious Bronchitis Virus (IBV) is the aetiological agent of an acute highly contagious economically relevant respiratory disease of poultry. Vaccination and biosecurity protocols are used in an effort to control IBV infections however there is a constant emergence of new serotypes and genotypes. There is therefore a drive to understand IBV replication in order to establish novel control mechanisms, including the development of a new generation of vaccines.

The IBV genome consists of a large positive-sense, single-stranded molecule of RNA containing many RNA structures. One RNA structure, denoted s2m, is located within the 3' untranslated region (UTR) and is composed of a 41-nucleotide stem-loop structure. The s2m RNA structure is shared between some coronavirus species including SARS-CoV and SARS-CoV 2. The s2m structure has also been identified in astroviruses and in members of the *Caliciviridae* and *Picornaviridae*. Despite the presence of the s2m in several diverse families of viruses, the function and significance of the s2m in viral replication is poorly understood.

This project aims to investigate the role of the s2m motif in viral replication and pathogenicity of IBV and will indicate whether the s2m is an efficient target for vaccine or antiviral drug development. The project will include the following objectives:

- 1) Investigate whether changes to s2m impact on global RNA structure and stability within the IBV genome, particularly in the 3'UTR.
- 2) Identify host and viral factors interacting with the IBV s2m.
- 3) Use reverse genetics to make specific changes to the s2m primary nucleotide sequence and resulting RNA secondary structure to determine the effects on *in vitro*, *ex vivo* and *in vivo* replication.

The project will involve molecular virology, biochemical and cell culture techniques as well as more specialised techniques such as SHAPE RNA structure mapping, coronavirus reverse genetics and the use and preparation of *ex vivo* organ cultures. The student 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:

Jonassen et al (1998). A common RNA motif in the 3' end of the genomes of astroviruses, avian infectious bronchitis virus and an equine rhinovirus. *Journal of General Virology*. 79(Pt 4):715-8.

Tengs and Jonassen (2016). Distribution and evolutionary history of the mobile genetic element s2m in coronaviruses. *Diseases*. 2016;4(3):27.

Lulla, V. et al (2021). Targeting the conserved stem loop 2 motif in the SARS-CoV-2 genome. *Journal of Virology*. 95 (14) e00663-21.

Janowski et al (2022). The highly conserved stem-loop II motif is important for the lifecycle of astroviruses but dispensable for SARS-CoV-2. *bioRxiv*. 2022:2022.04.30.486882.

Keep, S. et al (2022). A temperature sensitive recombinant of avian coronavirus infectious bronchitis virus provides complete protection against homologous challenge. *Journal of Virology* 10.1128/jvi.01100-22.

Registration, Training and Funding:

This is a Pirbright Institute/University of Cambridge fully funded studentship. All students are eligible for the full award (stipend and **home rated** university tuition fees). **EU and International students will attract 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 registered with the University of Cambridge and based mainly at The Pirbright Institute, but will spend three terms at the University of Cambridge during the course of the studentship. Eligible students will receive a UKRI-aligned stipend (minimum of £17,668 per annum) 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 03.02.23.

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.