# PhD Studentship: Investigation of canonical and non-canonical transcription during coronavirus replication

**Project Ref:** 2021/11/EB/IB
**Anticipated Start Date**: January 2022 **Duration:** 3.5 years full-time
**Closing date to apply:** 12.07.21

**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 overseas university tuition fees will apply and these are not included in the funding – please 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 Erica Bickerton (The Pirbright Institute), Prof Ian Brierley (University of Cambridge)
**Co-Supervisors**: Dr Sarah Keep, Dr Graham Freimanis (The Pirbright Institute), Dr Andrew Firth (University of Cambridge)

**Project Details:**

Coronavirus structural and accessory genes are transcribed via discontinuous transcription during negative strand synthesis; a process unique to the *Nidovirales*. Complementary transcription regulatory sequences (TRS) are in the leader (L) and body (B) of the genome, upstream of each gene. The TRS-B used by each coronavirus is thought to be conserved throughout the genome however our recent research on *Gammacoronavirus* infectious bronchitis virus (IBV) has identified several new sgmRNAs produced from non-canonical TRS-Bs [1,2], which result in the translation of three previously unrecognised accessory proteins, 4b, 4c and 7 [3].

We hypothesise that non-canonical transcription is a method to increase the coding capacity of the coronavirus genome and products of non-canonical transcription play important roles during coronavirus infection and disease progression. To test this hypothesis, we will study coronaviruses of several genera, that all cause respiratory disease in the natural host, to identify common mechanisms of transcription:

1: Determine the sequence of canonically and non-canonically transcribed sgmRNAs produced during coronavirus infection and identify the sites of the TRS-L and TRS-B recombination.

2: Determine the viral proteins produced during infection through ribosomal profiling. This will indicate whether any non-canonically transcribed sgmRNAs identified in objective 1 are translated, therefore potentially identifying additional previously unrecognised viral proteins.

3: Investigate the regulatory mechanisms within the coronavirus genome that impact the process of non-canonical transcription.

**References for Background Reading:**

1. Bentley K, Keep S, Armesto M and Britton P (2013). Identification of a Noncanonically Transcribed Subgenomic mRNA of Infectious Bronchitis Virus and Other Gammacoronaviruses.
J Virol. 87: 2128-2136; DOI: 10.1128/JVI.02967-12.

2. Keep S, Oade MS, Lidzbarski-Silvestre F, Bentley K, Stevenson-Leggett P, Freimanis GL, Tennakoon C, Sanderson N, Hammond JA, Jones RC, Britton P, Bickerton E (2020). Multiple novel non-canonically transcribed sub-genomic mRNAs produced by avian coronavirus infectious bronchitis virus. J Gen Virol. 101:1103-1118. DOI: 10.1099/jgv.0.001474.

3. Dinan AM, Keep S, Bickerton E, Britton P, Firth AE, Brierley I (2019). Comparative Analysis of Gene Expression in Virulent and Attenuated Strains of Infectious Bronchitis Virus at Subcodon Resolution. J Virol. 93:e00714-19. DOI: 10.1128/JVI.00714-19.

**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). **From 1st August 2021, EU and International students will be liable for 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. The student will be based mainly at The Pirbright Institute but will spend at least one year at the University of Cambridge during the course of the studentship. Eligible students will receive a minimum annual stipend of £15,609 plus a cost of living top-up allowance of £2,200 per annum. Home rated university registration fees will be paid. A full range of research and transferrable skills training will be made available to the student as appropriate.

**Applications:**

How to Apply: Closing date: 12.07.21

Essential documents:

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

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