To apply:

Your application will only be considered if we have received the following documents:

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

Project Ref: 2017 05 HM/NL - Surrey **Closing Date:** 31 March 2017
Anticipated Start Date: October 2017 **Duration:** 3.5 years full-time

Title: Control of Host Cell Translation by Infectious Bronchitis Virus

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 fully-funded studentship only open to UK students and eligible EU students who qualify for home-rated fees, in line with BBSRC criteria: http://www.bbsrc.ac.uk/web/FILES/Guidelines/studentship_eligibility.pdf.
- Students without English as a first language must also provide evidence that they meet the English language requirement, e.g. with an IELTS score of 7.0 and no less than 6.5 in any of the subsections.

Supervision:

Principal Supervisors: Helena Maier, The Pirbright Institute; Nicolas Locker, University of Surrey
Co-Supervisor: Toby Tuthill, The Pirbright Institute

Project Details:

During infection, viruses often alter the cellular gene expression profile to favour viral replication, suppressing anti-viral genes and up-regulating pro-viral genes. This can be achieved by controlling several cellular processes including the translation of proteins. Although host translation shut-off has been characterised for several viruses, little is known about the mechanisms of post-transcriptional regulation of gene expression or "translational reprogramming" and how this affects the antiviral response.

During replication of economically important avian *gammacoronavirus* infectious bronchitis virus (IBV), we recently demonstrated that transcription and translation are decoupled; while interferon mRNA levels increase, protein levels do not. Viral protein 5b was found to contribute to this process. Therefore, IBV reprograms translation to limit the antiviral response. Furthermore, we demonstrated that IBV regulates translation via cellular Akt, potentially to maintain viral translation.

This project aims to characterise the role and mechanism of translational reprogramming during IBV replication. This will increase knowledge of this little studied point of virus-cell interaction. It will be also be possible to identify routes to interrupt virus-host interaction thereby altering virus replication, providing potential routes for development of novel vaccines and anti-virals, which may be transferrable to related human and livestock coronaviruses.

This project will test the hypothesis **"IBV interacts with cellular translation machinery to regulate host cell translation and create an environment favourable for virus replication"**. The student will investigate which cellular pathways IBV regulates during replication, how this is achieved and what the effect is on the subset of cellular mRNAs that are actively translated; the translatome. This will be achieved via the following objectives:

Objective 1: Identification of signalling pathways modulated by IBV to control translation.
IBV has been demonstrated to reduce global cellular translation via accessory protein 5b, through an undetermined mechanism. IBV also regulates translation via Akt signalling. A complete study of IBV interaction

with the cellular translation machinery will be performed.

Objective 2: Characterisation of the role of viral proteins in controlling translation.
The student will investigate the mechanism by which IBV 5b regulates translation, and identify any further IBV proteins that function to control translation.

Objective 3: Identification of the translatome in IBV infected cells.
IBV decouples transcription and translation during replication. Therefore, it is important to identify the subset of cellular mRNAs that are actively translated during infection to fully understand the purpose of that regulation and how it benefits virus replication.

References for Background Reading:

1. Kint, J *et al*. (2016) Infectious Bronchitis Coronavirus Limits Interferon Production by Inducing a Host Shutoff That Requires Accessory Protein 5b. Journal of Virology, 90: 7519-28.
2. Walsh, D *et al.* (2013) Tinkering with translation: protein synthesis in virus-infected cells. Cold Spring Harbor Perspectives in Biology, 5(1):a012351.
3. Royall, E *et al*. (2015) Murine norovirus 1 (MNV1) replication induces translational control of the host by regulating eIF4E activity during infection. Journal of Biological Chemistry, 290: 4748-58.

Registration, Training and Funding:

This is a Pirbright Institute/University of Surrey fully funded project. The student will be based at The Pirbright Institute and registered with the University of Surrey, with visits to the university to meet with their supervisor and undertake training as required. Eligible students will receive a minimum annual stipend of £14,553 and university registration fees will be paid. A full range of research and transferrable skills training will be made available to the student as appropriate.

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Further information regarding the partner institutions can be found at:

http://www.pirbright.ac.uk http://www.surrey.ac.uk/