PhD Studentship: Characterising coronavirus replication organelle dynamics and maturation

Project Ref: 2024/04
Anticipated Start Date: September 2024 **Duration:** 3.5 years full-time
Closing date to apply: 15.04.24

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 an undergraduate degree, or a 2:2 or equivalent in a relevant biological subject in an undergraduate degree and a Masters with Merit - 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. International applicants are welcome to apply, however overseas university tuition fees are **not included** in the studentship 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: Helena Maier (The Pirbright Institute), Nicole Robb (University of Warwick)
Co-Supervisors: Trevor Sweeney, Sarah Keep (The Pirbright Institute)

Research Groups: Coronavirus Cellular Biology

Project Details:

Coronaviruses (CoV) are an important family of positive strand RNA viruses causing significant impacts on human and animal health and impacting food security. Infectious bronchitis virus (IBV) is a highly economically significant *Gammacoronavirus* that infects chickens causing respiratory disease and reductions in poultry production. In addition, IBV is an ideal model CoV to decipher aspects of virus replication and virus-host interactions. A critical stage of the CoV lifecycle is the rearrangement of host cell membranes to form replication organelles (RO), the site of viral RNA synthesis. The appearance of ROs has been well documented by us and others, demonstrating that ROs are highly conserved across the CoV family. However, many questions remain including the location of very early RO formation and RO dynamics and maturation over time. It is not understood whether there is organisation of viral genomic and sub-genomic RNAs or positive and negative sense RNAs within the RO. Furthermore, although CoVs are known to use genomic recombination to facilitate evolution, the processes involved in allowing the genomes of coinfecting viruses to come together for recombination are not understood.

The student will use recently developed recombinant IBVs expressing tagged viral proteins to directly visualise ROs in infected cells. Combining these unique tools with advanced microscopy techniques such as single molecule imaging and super-resolution microscopy, the student will study the earliest stages of RO formation, RO movement and maturation, arrangement of viral RNA within ROs and mixing of RNAs during coinfection. Exploiting facilities at both Pirbright and Warwick, the student will gain experience of a range of cell biology, virology, molecular biology and microscopy techniques including confocal and live cell confocal microscopy, single molecule fluorescent *in situ* hybridisation, CoV reverse genetics and RNAi.

References for Background Reading:

V'kovski P, Kratzel A, Steiner S, Stalder H, Thiel V. Coronavirus biology and replication: implications for SARS-CoV-2. Nat Rev Microbiol. 2021 Mar;19(3):155-170.

Maier HJ, Hawes PC, Cottam EM, Mantell J, Verkade P, Monaghan P, Wileman T, Britton P. Infectious bronchitis virus generates spherules from zippered endoplasmic reticulum membranes. mBio. 2013 Oct 22;4(5):e00801-13.

Wolff G, Melia CE, Snijder EJ, Bárcena M. Double-Membrane Vesicles as Platforms for Viral Replication. Trends Microbiol. 2020 Dec;28(12):1022-1033.

Hepp C, Shiaelis N, Robb NC, Vaughan A, Matthews PC, Stoesser N, Crook D & Kapanidis AN. Viral detection and identification in 20 minutes by rapid single-particle fluorescence in-situ hybridization of viral RNA. Scientific Reports. 11(1):19579.

McMahon A, Andrews R, Groves D, Ghani SV, Cordes T, Kapanidis AN & Robb NC. High-throughput super-resolution analysis of influenza virus pleomorphism reveals insights into viral spatial organisation. PLOS Pathogens. 19(6): e1011484.

Boersma S, Rabouw HH, Bruurs LJM, Pavlovič T, van Vliet ALW, Beumer J, Clevers H, van Kuppeveld FJM, Tanenbaum ME. Translation and Replication Dynamics of Single RNA Viruses. Cell. 2020 Dec 23;183(7):1930-1945.e23.

Registration, Training and Funding:

This is a Pirbright Institute/University of Warwick fully funded studentship. All students are eligible for the full award (stipend and **home rated** university tuition fees). **International students will attract tuition fees at the overseas rate and must therefore 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 B)**.

The student will be registered with the University of Warwick. The student will be based initially at The Pirbright Institute and will be expected to spend 1.5 years at the University of Warwick during the course of studentship. Eligible students will receive a UKRI-aligned stipend (minimum £18,622 for 2023/24) plus a cost of living top-up allowance of £2,200 per annum. Home rated university tuition 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 15.04.24

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.