PhD Studentship: Probing the Function of RNA Structural Elements in the FMDV Genome using Biophysical and Genetic Approaches

Project Ref: 2025/03
Anticipated Start Date: October 2025 **Duration:** 3.5 years full-time
Closing date to apply: 03.02.25

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 with 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. International applicants may apply, however funding for this studentship includes university tuition fees at the Home rate only - 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 Trevor Sweeney (The Pirbright institute); Dr Chris Hill (University of York)
Co-Supervisors: Dr Toby Tuthill (The Pirbright Institute); Dr Steven Quinn (University of York)

Project Details:

Foot-and-mouth disease is a highly contagious disease of cattle, sheep and pigs that causes huge economic loss in some of the poorest countries in the world and threatening food security. Outbreaks in the UK have previously led to mass culling and damaged national and international trade. The disease is caused by the foot-and-mouth disease virus (FMDV), a small single stranded RNA virus. The FMDV RNA genome is highly structured with different structural elements being important for different stages of the viral lifecycle.

We have previously shown that RNA structures, called pseudoknots, in the non-coding region at the 5' end of the genome are important for packaging viral RNA into new virus particles, a key stage in generating new viruses. A separate RNA structure termed the cis-replicative element (cre) acts as a template for VPg uridylation, essential for viral genome synthesis. As both these processes are restricted to viral replication they present novel targets for the development of novel, specific anti-viral approaches. However, we currently lack a detailed mechanistic understanding of how these processes work.

You will study the structural and mechanistic basis of dynamic pseudoknot formation and cre-directed VPg uridylation. This will involve the reconstitution of RNA-protein complexes in vitro, purification of complexes, biochemical assays to study VPg uridylation, sample optimization, X-ray crystallography and cryo-EM data collection and processing. You will also study protein-protein and protein-RNA-interactions using a variety of single-molecule imaging techniques (e.g. TIRF, FRET) to probe RNA conformational dynamics and the kinetics of complex assembly. Key findings will be further explored using FMDV reverse genetic approaches in virus-infected cells. No previous experience in these techniques is necessary and you will receive a thorough experimental training. Candidates from under-represented groups are particularly encouraged to apply.

You will join a vibrant, diverse and highly supportive training environment with the combined expertise of different supervisors with already well-established collaborative projects. You will benefit from rapid and frequent access to state-of the art X-ray crystallography and cryo-EM infrastructure at the York Structural Biology Laboratory

(https://www.york.ac.uk/chemistry/research/ysbl/facilities/eleanor-and-guy-dodson-building), and unique high containment facilities at The Pirbright Institute.

References for Background Reading:

Ward JC et al. 2022. The RNA pseudoknots in foot-and-mouth disease virus are dispensable for genome replication, but essential for the production of infectious virus. PLoS Pathogens. 18(6):e1010589. doi: 10.1371/journal.ppat.1010589.

Hill CH et al. 2021. Structural and molecular basis for Cardiovirus 2A protein as a viral gene expression switch. Nature Communications. 12(1):7166. doi: 10.1038/s41467-021-27400-7.

Roy R et al. 2008. A practical guide to single-molecule FRET. Nature Methods. 5:507. doi: 10.1038/nmeth.1208.

Registration, Training and Funding:

This is a Pirbright Institute/University of York fully funded studentship. The studentship covers stipend and Home rated university tuition fees. International students will attract tuition fees at the Overseas rate and must show evidence of their ability to cover the difference between Home fees and Overseas fees, which will be in excess of £23,000 per year.

The successful student will be registered with the University of York and spend a period of their PhD training at the University of York and The Pirbright Institute. The student will visit both locations to meet with their supervisors and undertake training or complete specific project tasks as required. Eligible students will receive a UKRI-aligned stipend (£19,237 for 2024/25) plus a cost of living 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: 03.02.25**

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.