

## **PhD Studentship: Host factors determining latency and reactivation of MDV-1 virus**



**Closing date:** 17.05.19  
**Project Ref:** 2019-18 YY/FG  
**Anticipated Start Date:** October 2019  
**Duration:** 3.5 years full-time

### **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 open to UK and EU students**.
- Students without English as a first language must 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: Dr Yongxiu Yao (The Pirbright Institute), Dr Finn Grey (The Roslin Institute, University of Edinburgh)  
Co-Supervisors: Prof Venu Nair (The Pirbright Institute)

### **Project Details:**

Herpesviruses are large dsDNA viruses that cause widespread, lifelong latent infections in different hosts, through multiple virus-host interactions to create a delicate balance between the virus and the host. CRISPR/Cas9-based gene editing is emerging as a powerful tool to investigate the precise determinants of latency in a number of herpesvirus infections. Marek's disease virus (MDV-1) is a lymphotropic  $\alpha$ -herpesvirus associated with latent infections and malignant CD4+ T-cell lymphomas in chicken. The rapid onset of tumours in Marek's disease (MD) makes it an ideal virus-induced lymphoma model in its natural host. MDV-1 has a two-phase life cycle, consisting of a lytic and a latent phase, the latter closely associated with the oncogenesis of the virus, yet the underlying molecular mechanisms of cell transformation remain unclear. Several viral genes such as Meq, vTR, vIL-8 and MDV1-miR-M4-5p, have been directly implicated in the oncogenic process.

Two major questions in this field are to understand (1) the factors that maintain the latency of the virus and (2) how the virus is reactivated from the latent state. Our hypothesis is that MDV latency and transformed phenotype in lymphoblastoid cell lines such as MSB-1 and HP8 is maintained by altered expression of a number of critical host genes, and that knockout of these gene(s) using a genome-wide screen approach can induce latency to lytic switch. Better understanding of these processes will provide insights into novel intervention strategies to interfere with the neoplastic process. We will use a high throughput genome-wide CRISPR/Cas9 gene knockout strategy, combined with next generation sequencing to identify the genes critical for both latent to lytic switch and maintenance of the transformed phenotype.

### **References for Background Reading:**

1. Nair V, Kung HJ. 2004. Marek's disease virus oncogenicity: Molecular Mechanisms, p 32-48. *In* Davison F, Nair V (ed), Marek's Disease: An Evolving Problem, 1st ed. Elsevier Academic Press, London.
2. Nair V. 2013. Latency and tumorigenesis in Marek's disease. *Avian Dis.* 57(2 Suppl):360-5.
3. Zhang Y, Tang N, Sadigh Y, Baigent S, Shen Z, Nair V, Yao Y. 2018. Application of CRISPR/Cas9 Gene Editing System on MDV-1 Genome for the Study of Gene Function. *Viruses* 10.

### **Registration, Training and Funding:**

This is a fully funded collaborative project between The Pirbright Institute and The Roslin Institute (University of Edinburgh). The student will be based at The Pirbright Institute and registered with the University of Edinburgh, with visits to The Roslin Institute and the University of Edinburgh to meet with their supervisor and undertake training as required. Eligible students will receive a minimum annual stipend of £15,009 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.

**Applications:**

Details of how to apply can be found here: [How to apply](#)

Essential documents:

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

Please email your application to [studentship@pirbright.ac.uk](mailto:studentship@pirbright.ac.uk) by the closing date noted above.