PhD Studentship: Understanding the importance of the PI3K pathway in modulating influenza virus replication in chickens and ducks

Project Ref: 2020/06/HS/SD
Anticipated Start Date: October 2020  Duration: 3.5 years full-time
Closing date to apply: 09.03.20

Eligibility:

- This studentship is open to applicants who have (or who anticipate obtaining) a minimum of a 2:1 undergraduate degree, or a minimum of a 2:2 undergraduate degree and a Master’s degree, in biological or veterinary sciences or similar subjects. 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 Residential Guidelines for Research Council Studentships.
- Students without English as a first language must provide evidence that they meet the English language requirement, e.g. with an IELTS score of 6.5 and no less than 6.0 in any of the subsections.

Supervision:
Principal Supervisors: Dr Holly Shelton (The Pirbright Institute), Dr Stephen Dunham (University of Nottingham)  
Co-Supervisors: Prof Munir Iqbal (The Pirbright Institute), Dr Janet Daly, (University of Nottingham)

Project Details:
Avian influenza virus (AIV) is a pathogen that causes significant economic and welfare issues for the poultry industry. In addition, there is the additional concern that avian influenza strains may be able to cross the species barrier and infect humans. Increasing our knowledge about AIV is fundamental to devising practical and effective control strategies for AIV in avian species.

Ducks and chickens often have different clinical disease manifestations to the same influenza A virus (IAV) isolate. Previous work at Nottingham university has demonstrated that infected duck cells underwent rapid cell death and thus limited the spread of virus, whereas chicken cells survived for longer and replicated the virus to significantly higher titres. The phosphoinositide 3-kinase (PI3K) cell-signalling pathway is a key regulator of cell survival and is often activated by viruses to promote survival following infection. Our previous work has demonstrated that IAV activates the PI3K pathway in chicken cells but not in duck cells. We have also shown that the kinetics and pattern of induction of the PI3K pathway is IAV strain dependant in chicken cells. Some strains induce the phosphorylation of AKT at 6 hours whereas others have a delay to 24 hours post infection which may influence the cell survival and virus yield. It has been shown in human cells that activation of PI3K pathways was mediated by the IAV NS1 protein which binds directly to the p85beta regulatory subunit of PI3K and causes PI3K-dependent phosphorylation of Akt, preventing premature apoptosis. Our analysis of the chicken and duck p85beta regulatory subunit sequence shows several differences that may influence the ability of NS1 to bind to and activate this protein in a host dependant manner, which suggests a possible mechanism for the differences in clinical outcome observed.

The hypothesis of this project is that differential activation of the PI3K during influenza virus infection impacts the disease phenotype in avian species. The studentship will investigate the following research questions that relate to the hypothesis; 1. What viral characteristics result in the strain-related differences in PI3K pathway activation that have been observed and 2. What impact the differences in the chicken and duck PI3K-p85 subunits have on the activation of the PI3K pathway by influenza viruses.

A combination of classical virology techniques including reverse genetics for influenza viruses as well as cutting edge genetic editing of cells using CRISPR will be utilised in this project. Training in skills including bioinformatic analysis of viral sequences and PI3K-p85 sequences will be performed and the preparation of samples and analysis of mass spectroscopy data will also be offered in this project. This studentship has the advantage of spending time in two thriving and inspiring science organisations; The Pirbright Institute and The University of Nottingham which offers multiple opportunities to the student. We are looking for an enthusiastic, team player who wants to learn and be part of our research teams.
References for Background Reading:


Registration, Training and Funding:

This is a Pirbright Institute/University of Nottingham fully funded project. The student will be based initially at the University of Nottingham, and subsequently at The Pirbright Institute as the project dictates. The student will be registered with the University of Nottingham. Eligible students will receive a minimum annual stipend of £15,009 (subject to change for the 2020/21 academic year) plus a cost of living top-up allowance whilst based at The Pirbright Institute. University registration fees will be paid for Home and EU students. A full range of research and transferrable skills training will be made available to the student as appropriate.

Applications:

Closing date to apply: 09.03.20

Click here for details of how to apply

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.