Oxford Interdisciplinary Bioscience
Doctoral Training Partnership

Project Title: **Transcriptional Analysis of chIFITM knockout technology for increased vaccine yields.**

Supervisor(s) names: Dr Mark Fife, Dr Angela Steyn (co-supervisor) The Pirbright Institute
Prof. Adrian Smith, Department of Zoology, University of Oxford
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Deadline: 31st July 2017

Brief description of project:

Avian viruses create major challenges to poultry health through loss of productivity and mortality, and have concomitant effects on the global poultry industry through a reduction in the output of poultry meat and eggs. Developing effective and affordable vaccines against these viral diseases will help to increase **food security worldwide**, and **alleviate poverty** in developing countries.

Type I interferons protect cells from virus infection through the induction of interferon-stimulated genes (ISGs). Among these are the anti-viral genes, the *IFITMs* (interferon-inducible transmembrane). This Studentship will focus on the **Transcriptional Analysis** of CRISPR/Cas9 chIFITM **gene** knock-outs in commercially relevant and lab-adapted avian cell lines. These will undergo gene knockout targeting each *chIFITM* 1, 2, 3 and 5, individually, and to delete the entire locus. To assess the consequence of the chIFITM knock-out on possible perturbations to downstream pathways, we will perform global transcriptome analysis in wildtype and the respective K/O cell lines, with and without infection. This will allow us to detect significant changes in global gene expression in each chIFITM knock-out. Genes displaying statistically significant differential expression between the different biological groups analysed, will be subjected to gene ontology analysis to identify biological functions of each gene. This analysis will also provide insights into pathways that may be affected as a direct result of the gene edits. This project will allow us to ultimately investigate the changes in the gene expression in cells lacking *IFITM* genes when infected with avian viruses. Exploiting **Transcriptional Analysis** of CRISPR/Cas9 chIFITM knock-outs, we aim to prove the hypothesis that reduced/ablation of chIFITM gene expression, will result in a significant increase in viral replication and augment vaccine viral titre.
The PhD student will be a member of the Genetics and Genomics Group and be supervised by Dr Mark Fife and Dr Angel Steyn at **The Pirbright Institute.**

(This project is supported through the Oxford Interdisciplinary Bioscience Doctoral Training Partnership (DTP) BBSRC Industrial CASE (iCASE) studentship programme. The student recruited to this project will join a cohort of students enrolled in the DTP's interdisciplinary training programme, and will be able

to take full advantage of the training and networking opportunities available through the DTP. For further details please visit www.biodtp.ox.ac.uk.)

- **Attributes of suitable applicants:** 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.
- Students 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.

Funding notes:

This project is funded for four years by the Biotechnology and Biological Sciences Research Council BBSRC. BBSRC eligibility criteria apply (http://www.bbsrc.ac.uk/documents/studentship-eligibility-pdf/). EU nationals who do not meet BBSRC residence criteria are encouraged to contact the programme administrator to check their eligibility for BBSRC funding before submitting a formal application. Successful students will receive a stipend of no less than the standard RCUK stipend rate, currently set at £14,553 per year, which will usually be supplemented by the industrial partner.