OXFORD INTERDISCIPLINARY BIOSCIENCE
Doctoral Training Partnership

Industrial CASE Studentship Advertisement – 2021-22

Supervisor(s) names:	Dr Holly Shelton[1] Professor Adrian Smith[2] Dr Khalid Zakaria[1] Dr Mark Fife[3]
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Project Title: Assessing the functionality of avian BST2 as a viral restriction factor.

Brief description of project:

Cellular restriction factors act as a first line of defense for hosts against invading viruses. Restriction factors target critical steps of the viral replication cycle to prevent infection and/ or dissemination. A well characterised human restriction factor is the cellular protein bone marrow stromal antigen 2 (BST2) (also known as Tetherin or cluster of differentiation 317 (CD317)), which is known to restrict a panel of enveloped viruses by literally tethering budding virions at the plasma membrane to the cell surface preventing virion release. The non-specific interaction of BST2 with the virion membrane enables this restriction factor to inhibit a diverse set of enveloped viral families. Recently avian orthologs of BST2 have been identified in turkeys and chickens, these have a low sequence identity to the mammalian BST2 proteins but do retain the type 2 integral membrane topology thought to be important for the mechanism of viral restriction. In other bird species deletions in the genetic loci where BST2 should be located suggests a complete loss of this restriction factor from the genome. The BST2 ortholog in the chicken genome (cBST2) has been shown to restrict the avian retrovirus, Avian sarcoma leukosis virus (ASLV) in avian cells at the late phase of the replication cycle suggestive of inhibition at the release stage. In addition, over expression of the cBST2 in human cells restricted the replication of HIV virus like particles suggesting that the cBST functions in a similar manner to human BST2 with regards to restriction of retroviruses.

This project would focus on understanding which avian viruses' chicken and turkey BST2 was able to restrict and this would be achieved using classical virology *in vitro* in chicken and turkey cells that are either engineered to have no expression by CRISPR or over-expression of the cBST2 or tBST2 protein. Viruses to be examined would have viral envelopes and include Avian Influenza Viruses, Infectious Bronchitis virus and Newcastle Disease Virus (NDV), all of which cause significant problems for the poultry industry. The mechanisms of restriction or viral mechanisms of antagonism of BST2 will also be investigated.

The project will be primarily based at The Pirbright Institute in the Influenza viruses group led by Dr Holly Shelton and supervision will be supported by the avian immunological expertise of Professor Adrian Smith at The University of Oxford. In addition, this studentship is supported by Aviagen who are a world renown commercial broiler chicken producer. A 12-week placement at

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Aviagen's research and development facilities in Edinburgh where the student can understand the scientific, legislative, animal welfare and QA disciplines in a commercial environment will also form part of the studentship.

Attributes of suitable applicants:

Essential:

- Applicants should have an honours degree or clinical degree in a relevant subject area with a minimum predicted/achieved grade of 2.1 or equivalent, a Master's degree or substantive relevant work experience.
- Applicants should be able to evidence research skills.
- A condition of being accepted to work at The Pirbright Institute is that the student must have passed the Institute's security clearance. This is conducted on-line by Agenda Security Services and can take between 2 and 4 weeks; the Institute will administer this process and cover the associated costs.

Desirable:

- Good communication skills, written and oral are of benefit although training will be given.

Funding notes:

This project is funded for four years by the Biotechnology and Biological Sciences Research Council UKRI-BBSRC. UKRI-BBSRC eligibility criteria apply (https://www.ukri.org/files/funding/ukri-training-grant-terms-and-conditions-guidance-pdf/). Successful students will receive a stipend of no less than the standard UKRI stipend rate, currently set at £15,285 per year, which will usually be supplemented by the industrial partner

This project is supported through the Oxford Interdisciplinary Bioscience Doctoral Training Partnership (DTP) studentship programme. The student recruited to this project will join a cohort of students enrolled in the DTP's interdisciplinary training programme, and will participate in the training and networking opportunities available through the DTP. For further details, please visit www.biodtp.ox.ac.uk. The DTP and its associated partner organisations aim to create a community that is innovative, inclusive and collaborative, in which everyone feels valued, respected, and supported, and we encourage applications from a diverse range of qualified applicants.