



Project Title: iCASE Studentship with the Pirbright Institute and Aerogen Ltd:
Active and Passive Immunity induced by aerosols

Supervisor(s) names: Prof Alain Townsend FRS, Dr Elma Tchilian, Dr Ronan MacLoughlin

Department(s)/Organisation(s):

Weatherall Institute of Molecular Medicine, University of Oxford, UK
Swine Influenza Immunology Group, Pirbright Institute, Pirbright, UK
Aerogen Ltd, Galway Business Park, Dangan, Galway, Ireland

e-mail: elma.tchilian@pirbright.ac.uk

Tel: 01483 232410

Deadline: Applications accepted all year round

Brief description of project:

Respiratory tract infections (RTIs) are a major health problem with significant economic impact on farming. Vaccines are cost-effective but improved immunisation strategies are needed. Local mucosal immunity is critical for protection against RTIs, leading to the successful deployment of an aerosol measles vaccines and live attenuated influenza virus (IV) vaccine, Flumist, delivered by nasal spray. However, Flumist, delivered to the upper respiratory tract (URT) of humans by large droplets, still has to be updated annually to match the evolving surface glycoproteins of IV, whereas when delivered to the lower respiratory tract (LRT) of ferrets and mice it is protective against diverse IVs. Nevertheless, it is not known what part of the RT should be targeted in large animal species for optimal protection, neither are practical devices for aerosol delivery available for field use in livestock.

Pigs are natural hosts of IV and have a critical role in the emergence and epidemiology of novel IV. Swine are physiologically closely related to humans, show similar clinical signs and pathology after IV infection and are therefore an excellent model for humans. To compare for the first time in a large animal species immunisation of the URT by nasal spray or the LRT by aerosol, the student will use a novel live attenuated vaccine, S-FLU, which induces cross-protective cell mediated immunity against IV strains in mice, ferrets and pigs.

The student will establish whether a universal influenza vaccine is effective in pigs, the nature of protective immune responses, whether broadly neutralizing antibodies can be used therapeutically against IV infection and how best to deliver them to pigs. The following questions will be addressed:

1) What are the properties of droplets and devices needed to target the LRT in pigs? The student will determine the properties and distribution of aerosols in the lung using breathing simulators, laser diffraction and cascade impaction at Aerogen Ltd.

2) Does aerosolisation affect the potency of vaccine and antibodies? Universal S-FLU vaccine and broadly neutralising influenza antibodies against NA and HA will be developed in Alain Townsend's



lab in Oxford. The student will establish the retention of S-FLU potency and neutralising activity of therapeutic antibodies following aerosolisation.

3) What is the protective efficacy of S-FLU vaccine and broadly neutralising antibodies against influenza challenge in pigs? We will test whether aerosol delivery of S-FLU or antibodies is protective against homologous and heterologous influenza challenge by assessing viral load in the respiratory tract, pathology and immune responses.

The student will acquire expertise in human and veterinary virology and immunology, and the technology of aerosol devices. He/she will learn to produce recombinant influenza viruses and pseudotyped influenza S-FLU vaccine virus. In addition the technology of isolation and production of human (or in principle swine) monoclonal antibodies will be available. With this powerful combination of technologies the student will establish how best to target the respiratory tract of pigs to develop protective immune responses against IV. This information will be valuable for design of vaccine delivery strategies for other livestock species and humans.

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.

Prospective applicants should contact the project supervisor Dr Elma Tchilian (elma.tchilian@pirbright.ac.uk) prior to submitting an application.

Applications for this project will be made via the Oxford Interdisciplinary Bioscience DTP. For further details please visit www.biodtp.ox.ac.uk.

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 £14,296 per year, which will usually be supplemented by the industrial partner.