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Project Ref: 2016 07 - MM/YJ Surrey **Closing Date:** 18 March 2016
Anticipated Start Date: October 2016 **Duration:** 4 years full-time

PROJECT TITLE: DEVELOPMENT OF SEMI-SUPERVISED ENSEMBLE LEARNING MODELS FOR SEROTYPE O AND A FMDV VACCINE STRAIN SELECTION USING HETEROGENEOUS DATA

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 only open to UK students and eligible EU students who qualify for home-rated fees, in line with BBSRC criteria: http://www.bbsrc.ac.uk/web/FILES/Guidelines/studentship_eligibility.pdf.
- Students without English as a first language 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.

Supervision:

Principal Supervisors: Mana Mahapatra, The Pirbright Institute; Yaochu Jin, University of Surrey
Co-Supervisors: Paolo Ribeca, The Pirbright Institute; Daniel Horton, University of Surrey

Abstract:

The current method of Foot-and-Mouth Disease (FMD) vaccine strain selection is based on the serological tests that determine the antigenic relationships (r1 value) of circulating viruses with vaccine strains using antisera raised in bovines. This method is time consuming, expensive and the selected vaccines may not be able to provide broad-spectrum protection against emerging antigenically novel strains. In addition, the in-vivo cross-protection tests do not always agree with the in-vitro serological test results.

As the antigenic determinants of FMD viruses (FMDV) lie in the viral capsid proteins, viral capsid sequences provide an alternative dataset for vaccine strain selection. A powerful computational model that incorporates viral immunogenic protein or RNA level changes can effectively predict antigenically variant strains (1-Rahman et al., 2015; 2-Reeve et al., 2010), and minimise the amount of resources spent on serological testing of vaccines.

Using evolutionary algorithms, we have developed anon-linear (1) regression model for FMDV vaccine strains selection that revealed better performance than the -linear model (2). Although the non-linear model optimized by an evolutionary algorithm has shown to be very promising with 80% accuracy (1), the availability of limited serological data has seriously affected further improvement of the prediction accuracy so far.

This project aims at developing the ability to predict the antigenic sites of serotype O and A FMD viruses from in-vitro vaccine matching and capsid sequence data using computational and statistical models. This will involve improving the level of accuracy achieved by non-linear model by using a huge data set (already available in the laboratory), including antigenic distances (antigenic cartography) and more powerful learning techniques, in particular semi-supervised ensemble classification models. This would be a significant break-through as it would allow rapid selection of FMD vaccine strain in the event of an outbreak leading to better control of the disease. Furthermore, analysis of the data will result in identification of antigenically important motifs that can be tested using an existing cDNA clone.

References for Background Reading:

1. Rahman T., Mahapatra M., Laing E., and Jin Y. (2015). Evolutionary non-linear modelling for selecting vaccines against antigenically variable viruses, Bioinformatics, 31(6):834-840.
2. Reeve R, Blignaut B, Esterhuysen JJ, Opperman P, Matthews L, Fry EE, de Beer TA, Theron J, Rieder E, Vosloo W, O'Neill HG, Haydon DT, Maree FF. Sequence-based prediction for vaccine strain selection and identification of antigenic variability in foot-and-mouth disease virus. PLoS Comput Biol. 9; 6 (12):e1001027.
3. Bari FD, Parida S, Tekleghiorghis T, Dekker A, Sangula A, Reeve R, Haydon DT, Paton DJ, Mahapatra M (2014). Genetic and antigenic characterisation of serotype A FMD viruses from East Africa to select new vaccine strains. Vaccine**.** 2014 Oct 7; 32 (44):5794-800.
4. Asfor AS, Upadhyaya S, Knowles NJ, King DP, Paton DJ, Mahapatra M (2014). Novel antibody binding determinants on the capsid surface of serotype O foot-and-mouth disease virus. J Gen Virol., 95 (Pt 5):1104-16.
5. Bari FD, Parida S, Asfor AS, Haydon DT, Reeve R, Paton DJ, Mahapatra M (2015). Prediction and characterisation of novel epitopes of serotype A FMD viruses circulating in East Africa using site-directed mutagenesis. J Gen Virol., 96 (Pt 5):1033-41.

Registration, Training and Funding:

This is a BBSRC/University of Surrey/Merial fully funded project. The student will be based at The Pirbright Institute and registered with the University of Surrey, with visits to the university to meet with their supervisor and undertake training as required. Eligible students will receive a minimum annual stipend of £14,057 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.

Further information regarding the partner institutions can be found at:

http://www.pirbright.ac.uk http://www.surrey.ac.uk/

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