



Industrial CASE Studentship Advertisement – 2021-22

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Project Title: SOMAmer technology to diagnose coronavirus infection: veterinary and zoonotic implications.

Brief description of project:

Coronaviruses have an ability to cross species barriers, causing pandemics of devastating proportions. Genetic evidence suggests that the newly emergent *Betacoronavirus*, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), originated in bats. Other members of the *Betacoronavirus* genus include SARS-CoV and Middle East respiratory syndrome (MERS)-CoV, which also emerged from bats via intermediate hosts to cause major outbreaks in the human population in recent years. Human coronavirus (HCoV)-OC43, a cause of the common cold in humans, is closely related to bovine CoV, and is also thought to have emerged as a result of cross-species transmission. Swine acute diarrhoea syndrome coronavirus (SADS-CoV) emerged in 2017 and re-emerged in 2019, causing the deaths of many thousands of piglets in China. Alphacoronaviruses SADS-CoV and porcine epidemic diarrhoea virus (PEDV) have close phylogenetic relations with viruses found in bats and other mammals, and are related to the endemic human coronaviruses 229E and NL63. The avian *Gammacoronavirus* infectious bronchitis virus (IBV) causes a severe and recurrent problem of infectious bronchitis in domestic fowl. It is increasingly realized that protecting animal and human health in the face of these agents requires a joined-up approach (the “One Health Agenda”) and new technologies.

This project, conducted at The Pirbright Institute and University of Oxford, will feed into the disease diagnostic and surveillance platform being developed by Hutano Diagnostics, and will facilitate the development of a pan-coronavirus diagnostic solution with the potential to detect emerging coronaviruses in humans or animals. Our approach will seek to identify a Slow Off-Rate Modified Aptamer (SOMAmer®; an aptamer with aromatic/hydrophobic 5-U substitutions) with broad spectrum cross-reactivity, which will be developed with the capability to act as a first-line diagnostic in the event of zoonotic transfer by other emerging coronaviruses.



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We will build on our earlier work, demonstrating the effectiveness of neutralizing aptamers to lentiviruses and herpesviruses, which confirmed our hypothesis that aptamers could bind to sites on viral envelope glycoproteins that were sterically shielded from antibodies, and so remained evolutionarily conserved. The student will study the cross-reactivity of these aptamers to divergent coronavirus S glycoproteins, including those of veterinary significance studied at The Pirbright Institute, through virus neutralisation and binding assays in cell culture. They will go on to use structural information on the SOMAmer® binding sites, obtained by our collaborators at STRUBI, to design and test bivalent SOMAMers® with the potential to bind with greater affinity, to both the “closed” conformation of the spike, found in free virions, and the “open” form transiently available during the cellular infection process. The potential of such agents as wide-spectrum anti-coronavirus diagnostic agents is evident, and this project aims to develop SOMAmer® based lateral flow devices as low-cost, easy to use, robust, low-tech, point of need diagnostics for viruses of both veterinary and medical importance, with cross-reactivity across the coronavirus family. The student will develop practical virology and molecular biology skills as well as experience in translating research into real-world diagnostic solutions.

Attributes of suitable applicants:

The candidate will spend significant periods of time working at The Pirbright Institute, as well as placements at University of Oxford and Hutano Diagnostics Ltd. We are seeking a candidate with drive and enthusiasm, who is flexible and works well in a team. Experience of working in a CL2 or CL3 laboratory (particularly skills in virology, molecular biology and cell culture) would be beneficial, but there is also potential to expand your practical skills during the project. Candidates must have an interest in virology and in the translation of research into real-world solutions.

To be eligible for UKRI studentship funding a candidate should have an honours degree with a predicted or achieved grade of 2.1 or above, a Master’s degree or substantive relevant work experience.

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.