

Diamond-Pirbright Studentship Advertisement – 2020-21

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Project Title: Understanding coronavirus replication using soft x-ray and electron tomography

Brief description of project:

Coronaviruses (CoV) are positive strand RNA (+RNA) viruses that cause important diseases in humans and livestock. As highlighted by the current SARS-CoV-2 (COVID-19) outbreak, CoVs can also cross the species barrier and therefore pose a significant threat to human health. A critical step of the CoV life cycle is the replication of viral RNA and, like all +RNA viruses, this process is closely associated with cellular membranes.

CoVs rearrange host cell membranes to form the replication organelle (RO), providing an enclosed site to protect viral RNA. Our recent work has shown that the appearance CoV ROs is conserved, comprising double membrane vesicles (DMVs) and double membrane spherules (DMSs) tethered to modified endoplasmic reticulum (Fig. 1). However, current analyses have been unable to address several important questions, including how ROs form, how many exist within an infected cell, how ROs are connected to one another and the rest of the cell and whether DMVs and DMSs have different functions from one another. A better understanding of this critical conserved stage of the CoV life cycle will underpin the development of unique One Health approaches to control CoV replication in several hosts. We hypothesise that **CoV ROs form a complex, 3-dimensional membrane network within the cell, supported by a framework of proteins**. Using our extensive experience working with avian CoV, infectious bronchitis virus (IBV), and expert knowledge of the IBV RO, the student will (i) generate recombinant viruses expressing tagged replicase proteins to allow direct visualisation of ROs (Pirbright), (ii) characterise the entire RO network in whole infected cells using soft x-ray tomography (B24, Diamond) and (iii) characterise ROs at high resolution using cryo-electron tomography (eBIC, Diamond).

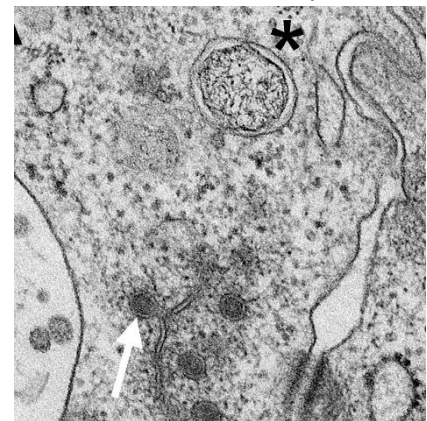


Fig. 1 Replication organelles induced by infectious bronchitis virus. Double membrane vesicle indicated by asterisk, double membrane spherule indicated by arrow.



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The student will be part of the 2020 entry cohort and undertake training in the University of Oxford's Interdisciplinary Bioscience Doctoral Training Programme. The student will then be based at The Pirbright Institute for years 1 to 1.5 and Diamond for years 1.5 to 4. The student may return to Pirbright towards the end of the project. Timeframes are an indication and are dependent upon development of the project.

Attributes of suitable applicants: Candidates should have a background in virology or microscopy with an interest in virus-host cell interactions and advanced imaging techniques. It is desirable, but not essential, to have experience of electron microscopy. It will be an advantage to have a driving license.

Funding notes: This project is funded for four years by The Pirbright Institute, Diamond Light Source, and the University of Oxford's Interdisciplinary Bioscience Doctoral Training Programme. BBSRC eligibility criteria apply (<https://www.ukri.org/files/legacy/publications/rcuk-training-grant-guide-pdf/> Annexe 1). 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 £15,285 per year.

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 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.