

OXFORD INTERDISCIPLINARY BIOSCIENCE – Doctoral Training Partnership

Industrial CASE Studentship Advertisement – 2023-24

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Project Title:	Modelling brain development with microglia-containing three-dimensional cerebellar organoids

Brief description of project:

This project aims to generate three-dimensional (3D) cerebellar organoids from human induced pluripotent stem cells (iPSCs) as innovative models to better understand early processes underpinning human brain development. Specifically, the project will focus on the development of cerebellar organoids from human iPSCs. Although we have learned much from animal studies, it has become apparent that the human cerebellum is different from other species. As such, to better understand the mechanisms driving the development of the human cerebellum, we need improved and humanized models. Human iPSC-derived models also hold great promise for the development of new therapeutic compounds for brain diseases as animal models do not always recapitulate a suitable phenotype for studying efficacy of novel therapeutics.

The Becker lab is one of the pioneers of generating cerebellar models from human iPSCs. However, current models are limited in that they do not contain other important cell types of non-neuronal origin such as microglia. Cerebellar microglia have been shown to be distinct from other brain populations and play important roles in regulating the development and function of cerebellar neurons. The goal of this studentship will be the generation and characterization of human iPSC-derived cerebellar organoids that contain microglia to more accurately recapitulate processes in the developing cerebellum. The models will then be used to better understand the role of activated microglia in cerebellar neuron development and excitability.

This iCASE studentship provides an exciting opportunity to work on a collaborative project between leading academic labs and industry. The project brings together the expertise of the Becker group in cerebellar biology and the Cowley group in iPSC-derived microglia with the knowhow of the industrial partner Insmed. The student will be based at the University of Oxford but also benefit from an extended industrial placement with Insmed in Cambridge, where they will use the developed cerebellar models for target validation and drug discovery assay



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development. Importantly, the student will also have the opportunity to benefit from the training and networking opportunities available as part of the Interdisciplinary Bioscience DTP.

Attributes of suitable applicants:

We are looking for a highly motivated and intellectually curious student, who has an interest in using stem cell models for understanding neurodevelopment. The successful candidate is expected to be capable of working both independently and in teams and to possess good communication skills. Candidates should be on target for a first-class or strong upper second-class undergraduate degree in a relevant discipline. Previous experience in molecular biology and/or cell culture is strongly desirable. Training in all required techniques will be provided.

Funding notes:

This project is funded for four years by the Biotechnology and Biological Sciences Research Council UKRI-BBSRC. UKRI-BBSRC eligibility criteria apply (<u>https://www.ukri.org/files/funding/ukri-training-grant-terms-and-conditions-guidance-pdf/</u>). Successful students will receive a stipend of no less than the standard UKRI stipend rate, currently set at £18,622 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 <u>www.biodtp.ox.ac.uk</u>. 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.