OXFORD INTERDISCIPLINARY BIOSCIENCE
Doctoral Training Partnership

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Industrial CASE Studentship Advertisement – 2019-20

Academic Supervisors: Prof. Ilan Davis (*Drosophila* neurobiology expert), Dr. Alfredo Castello (RNA virus expert) and Prof. Martin Booth (Optical engineering expert)

Non-academic Supervisor: Dr. Phillipa Timmins, Aurox (in consultation with the CEO)

Department(s)/Organisations: Biochemistry, Biochemistry and Engineering (respectively), The University of Oxford, South Parks Road.

e-mail: Darragh.Ennis@bioch.ox.ac.uk

Tel (for enquiries from prospective students) Davis lab: +44 (0)1865 613271 (ask for Darragh Ennis)

Project Title: Elucidating how the brain develops from stem cells using revolutionary imaging technologies at single molecule and cell resolutions

Brief description of project (no more than 500 words): Your description should include
(i) The background and aims for the project, including information on potential opportunities for skills training provided by the proposed project. Do not include any information of a sensitive or confidential nature.

The overarching question and technological gap: Understanding how the brain and its full neuronal complexity develops from a limited number of stem cells is one of the most important questions in modern biology. A number of animal RNA viruses are known to infect the brain and affect neural stem cell behaviour, but their mechanism of infection is still poorly understood. The Davis lab has been using the highly accessible fruit fly model to address these questions by applying novel imaging technologies for direct visualisation of all the individual molecule transcripts in every cell in a whole brain (single molecule FISH), and live cell imaging of a developing explanted brain. The huge number of regulatory genes involved in regulating the stem cells, presents us with a major challenge for understanding normal development and the effects of RNA virus infections: visualising the expression of such a large number of genes and their mutations is not possible with current technologies.
The Project: We propose to fill this technology gap by leveraging existing hardware and software technologies and know-how in a highly interdisciplinary collaboration between the Davis lab and Martin Booth, one of the few world leaders in adaptive optics and rapid confocal scanning technologies. We will build an affordable very fast confocal microscope with a small footprint, dedicated to prolonged live cell imaging of explanted brains in 3D, as well as to rapid 3D imaging of multiple single molecule FISH samples simultaneously. Once built the microscope will have many applications, but will initially be used primarily for this highly interdisciplinary project. Depending on the background of the student, the work will involve a balance of optical engineering / biological experiments / data analysis. The student will have access to world leading training and collaborations through Micron Oxford to all the relevant expertise required for these three disciplines.

Specific Aims of the Project:

1) Build a bespoke, laser-free, confocal microscope based on the Clarity spinning disc with unprecedented speed and high throughput capacity.

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2) To undertake a systematic live analysis of the phenotypes and expression of numerous key factors already identified as required for correct stem cell behaviour.
3) To use this system to track at the single molecule and cell level the early stages of infection of a model insect RNA virus (Sinvis) in the insect brain.

(ii) The location(s) of the organisation(s) in which research will be carried out, noting that all iCASE students are required to undertake a placement with the non-academic partner organisation of no less than twelve-weeks duration.

Location of the Project:

The project is highly interdisciplinary. It will be based in Biochemistry, but will involve collaborations with optics and software engineers in the Department of Engineering Science (5 minute walk from Biochemistry). The student will also spend some time every year at the collaborating Oxford spinout company, Aurox Ltd., (the non-academic partner) for a total of twelve weeks.

Bibliography:

M. Garcia-Moreno, et al. and. **I. Davis**, B. Fischer, S. Mohammed, **A. Castello** (**2019**) System-wide Profiling of RNA-Binding Proteins Uncovers Key Regulators of Virus Infection. **Molecular Cell**, in press, https://www.biorxiv.org/content/10.1101/350686v1

2) Mantas Zurauskas, et al., **Ilan Davis**, and **Martin J. Booth** (**2019**) IsoSense: frequency enhanced sensorless adaptive optics through structured illumination**. Optica, Vol. 6, Issue 3, pp.370-379**

3) Yang L., et al. and **Davis I.** (**2017**) Single molecule fluorescence in situ hybridisation for quantitating post-transcriptional regulation in *Drosophila* brains. **Methods**. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5595163/

Attributes of suitable applicants: Please note any skills or qualifications you are seeking in a prospective applicant, e.g. academic background, driving licence, specific research skills or interests.
Funding notes: This project is funded for four years by the Biotechnology and Biological Sciences Research Council BBSRC. 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 £15,009 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 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.