MRC iCASE ‘Enterprise’ Studentships

Four industrial CASE studentships are available for doctoral study at Oxford, to start in October 2018. Each studentship is fully-funded for four years with a stipend of £20,000 p.a., all tuition fees paid, plus a research training support grant. The studentships will be based in the University as part of the Oxford-MRC Doctoral Training Partnership, and will also involve close collaboration with a commercial partner, including at least 3 months working at the company during the course of the D.Phil. project. All applications must be received by 12 noon (UK time) Monday 8 January 2018.

The four projects are:

1. **Probing presynaptic regulators of dopamine to identify new opportunities for therapy in Parkinson’s disease** *(Lead supervisor Prof Stephanie Cragg, commercial partner Cerevance Ltd)*

   Parkinson’s disease is a progressive degenerative disorder, with debilitating movement problems that arise from the demise of nigrostriatal dopamine neurons and striatal dopamine transmission. Current strategies to restore dopamine are limited, and the mainstay of therapy, L-DOPA, has disabling side effects such as dyskinesias that prevent its long-term use. Therefore, there is a need to identify new treatments. Strategies are needed that can either slow disease progression, treat symptoms or treat side effects. This project will apply new and emerging technologies to explore dopamine axons as targets for new therapies. More details [here](#).

2. **Computational methods for rapid structural modelling of antigen–antibody interactions to improve identification of antigen-specific antibodies from Ig-seq repertoire data** *(Lead supervisor Prof Charlotte Deane, commercial partner Kymab Ltd)*

   The exquisite antigen recognition specificity of antibodies has made them useful as diagnostics, research agents and the most successful class of biopharmaceuticals. The ability to discover better antibody-based therapeutics needs knowledge of the sequence and the 3D shape of individual antibodies within the context of the entire antibody repertoire. Next-generation sequencing methodologies (Ig-seq) can rapidly yield millions of antibody gene sequences and have been used to identify antigen-specific sequences. However, so far the inability to routinely overlay antibody structure on large Ig-seq datasets has limited their potential for antibody drug discovery. Computational methodologies offer a bridge between the two fields by allowing structural annotation of Ig-seq experiments. Here we aim to use this approach to advance our knowledge of
the antibodies in health and disease and hence, pave the way for more advanced antibody-based therapeutics. More details here.

3. Development of enhanced soluble gamma delta T cell receptors (Lead supervisor Prof Paul Klenerman, commercial partner Immunocore Ltd)

Gamma Delta T cells (γδ T cells) are an abundant human subset which “bridge” between innate and adaptive immunity. These cells show enrichment in mucosal tissues and infiltrate diverse types of tumours. Their activation occurs following T cell receptor (TCR) engagement or in response to pro-inflammatory cytokines. Stimulated γδ T cells are able to secrete a range of pro-inflammatory and anti-microbial cytokines, and also kill targets. Thus they are of potential interest in host defence and the therapy of cancer. Here we aim to generate soluble TCRs from γδ T cells for use in detection of their ligands bound to microbial and tumour antigens. These TCRs will be modified through mutational approaches to enhance binding and sensitivity and assessed for therapeutic development. More details here.

4. Discovery and investigation of the genetic and mechanistic basis of β-cell fragility (Lead supervisor Prof John Todd, commercial partner Novo Nordisk)

The prevalences of type 1 (T1D) and type 2 diabetes (T2D) are still increasing, but their aetiologies were until recently thought to be entirely distinct: islet β-cell failure to produce sufficient insulin to compensate for insulin resistance in T2D versus autoimmune destruction of pancreatic islet β cells in T1D. However, the discovery that a polymorphism of the GLIS3 gene predisposes to both T1D and T2D, through altering β-cell sensitivity to stress, has highlighted β-cell health as a common denominator. Here we will investigate how genes in several newly identified T1D regions (some of which overlap with T2D risk loci) cause diabetes through β-cell fragility and aim to discover new genes/pathways required for β-cell health by investigating the effects of stress and diabetes status on chromatin states and gene regulation in human donor islets. More details here.

Structure and Organisation of the Programme

Designed to nurture the academic entrepreneurs of the future, the Enterprise studentship programme offers a stimulating educational experience as part of the Oxford-MRC DTP cohort, with the additional benefit of working closely with a non-academic partner. This will provide industrial training opportunities and an insight into how commercial science is conducted alongside a superb academic base within the University.

Eligibility and Entry Requirements

To be eligible for a full award, applicants must have no restrictions on how long they can stay in the UK and must have been ordinarily resident in the UK for at least 3 years prior to the start of the studentship. Further details about residence requirements may be obtained here.

Details on Entry Requirements can be found here.

How to Apply

Before applying for these positions we recommend you contact the lead supervisors for informal discussions. To make a formal application, please complete the University’s online application form for the DPhil in Clinical Medicine (course code RD_CM1). In your application, you must indicate that
you are applying for an advertised studentship competition, using the reference code iCASE. Please indicate clearly which project(s) you are applying for, in order of preference. It is possible to apply for up to 3 MRC iCASE projects on your application. **You will need to provide a CV outlining your academic achievements and relevant experience, and a personal statement (500 words max) detailing your interest and fit for the studentship.** Note that no project proposal is required for the iCASE studentship applications.

If you wish to apply for a combination of iCASE and other projects within the administering department (the Nuffield Department of Clinical Medicine, NDM), this can be done on the same application form (3 projects max). If you wish to apply for both the iCASE projects and other projects in the Department of Physiology, Anatomy and Genetics (DPAG) and/or the Department of Statistics, you will have to make (an) separate application(s) directly through those departments in addition to your iCASE one.

If you have any specific queries about the iCASE application process, please email mrc@medsci.ox.ac.uk.

**All applications must be received by the deadline of 12 noon (UK time) Monday 8 January 2018.**

We expect to interview shortlisted applicants at the end of January and to make offers in February. Successful applicants will be rerouted onto the appropriate DPhil course for their chosen project.