



PhD studentship (SCI05P)

A 3-year full-time PhD studentship is available at the Division of Biotherapeutics, National Institute for Biological Standards and Control (NIBSC), in collaboration with the Division of Medicine, University College London (UCL). The studentship is anticipated to commence on 1 October 2019.

Title

Studies on targeting VEGF-induced changes in the function and metabolism of intraocular cells to gain insights into the molecular mechanisms of resistance to antiangiogenic therapy for eye neovascular diseases.

Project description

Neovascular age-related macular degeneration (AMD) and diabetic macular edema (DME) are leading causes of blindness in elderly and working-age populations worldwide, representing significant challenges for global public health. Excessive new blood vessels, which arise from pre-existing ones in the process of angiogenesis, produce fluid leakage in the macula underlying the progression of these eye diseases. In both AMD and DME, the abnormal angiogenesis is predominantly driven by overexpressed vascular endothelial growth factor (VEGF), a pivotal regulator of angiogenesis and vascular permeability. Consequently, anti-VEGF drugs including monoclonal antibodies, ranibizumab and bevacizumab (off-label use), have revolutionized the treatment of AMD and DME. Despite favourable clinical results, a proportion of patients develop resistance towards anti-VEGF agents, and the mechanisms for this have not been defined.

The hypothesis of this PhD project is that anti-VEGF treatment can cause the switch to VEGF-independent signalling and metabolic reprogramming in intraocular cells, which in turn potentially bypasses VEGF blockade and promotes resistance to VEGF antagonism responsible for recurrence of intraocular neovascular diseases. The aim of the project will be to investigate (1) whether anti-VEGF drugs influence the biological activities and metabolic profiles of cultured human intraocular cells in the key interest areas including the expression and function of neuropilin-1, a co-receptor for VEGF and other ligands, glycolytic metabolism and insulin signalling, and (2) how the drug-induced alterations of molecules of interest regulate angiogenesis and blood-retinal barrier function *in-vitro* and affect anti-VEGF efficacy to gain an in-depth understanding of their mechanisms of action.

The successful candidate will benefit from training in a variety of techniques in cell biology (including primary human microvascular endothelial cell-based bioassays), protein biochemistry (including meso scale discovery-based multiplex assays and surface plasmon resonance-biosensor assays) and molecular biology. In addition, the student will have access to the latest developments in *in-vitro* models of angiogenesis and permeability including the use of human induced pluripotent stem cell-derived endothelial cells.

Key responsibilities

- To undertake the research projects in line with the project aims
- To communicate effectively, orally and through written media, undertake presentations at scientific meetings and maintain excellent records
- To interact regularly and effectively with the supervisors and interact appropriately and effectively with other staff
- To fulfil the requirements of the University PhD programme and to undertake specific training as required by the host institutions

In addition to meeting all the academic, security and residency requirements, you will have:

- an academic background in molecular and cellular biology or relevant life sciences
- a demonstrated aptitude in a laboratory setting and motivation to undertake research
- a demonstrated interest in the field of study and ability to work accurately and precisely
- a demonstrated excellent oral and written communication, and IT skills
- a previous experience in one or more of the key interest areas that would be an advantage
- some theoretical knowledge of growth factors, cytokines and vascular endothelial cell biology

NIBSC, the Centre of the Medicines and Healthcare products Regulatory Agency (MHRA), is a global leader in the characterisation, standardisation and control of biological medicines and has a major role in protecting and improving public health worldwide. NIBSC is the leading WHO International Laboratory for Biological Standardisation and is responsible for producing and distributing over 90% of all WHO International Standards introduced for the quality assurance of biological medicines. NIBSC scientists also test products, carry out valuable research and provide advice on a routine basis and in response to emergencies. The importance of the Institute's work is well recognised nationally and internationally.

The Division of Biotherapeutics is a central element of NIBSC, covering a wide range of biological medicines used in treatment or diagnosis of diseases, and is internationally recognised. It establishes and provides primary standards and undertakes monitoring of therapeutic biologics. This is underpinned by cutting-edge research, carried out by highly skilled and motivated expert scientists and staff, supported by the Institute's modern equipment.

UCL is one of the world's leading multi-disciplinary universities and operates in a global context. UCL is committed to excellence, innovation and the promotion of global understanding in its activities: research, teaching, learning, enterprise and community engagement. UCL's distinctive approach to research, education and innovation inspires the staff, students and partners to transform how the world is understood, how knowledge is created and shared and the way that global problems are solved.

The Division of Medicine, part of Medical Sciences Faculty UCL, brings together clinical and basic scientists undertaking world-leading interdisciplinary research, teaching and patient-care. Its aims are to understand the basis of disease, and to develop better diagnostics and treatments for diseases with an emphasis on Experimental Medicine. This is achieved through world-leading research in Medicine and Biological Sciences and PhD courses which attract the best students from all over the world.

The student will be supervised by Drs Haiyan Jia, Chris Burns and Meenu Wadhwa (NIBSC) and Prof Ian Zachary (UCL). The student will be based primarily at NIBSC with the opportunity for attendance at the University for additional training and work when required.

Qualification requirements for UCL Division of Medicine

A first or upper second-class UK Bachelor's degree in an appropriate subject from a UK university, or an overseas qualification of an equivalent standard in a relevant discipline from a recognised higher education institution.

Funding

Tuition fees and consumables are covered and there is a student stipend of £18,500 p.a.

English language requirements

Applicants whose first language is not English are normally expected to meet the minimum University requirements (e.g. 6.5 IELTS). For further information see:

<https://www.ucl.ac.uk/prospective-students/graduate/learning-and-living-ucl/international-students/english-language-requirements>

Visas and immigration

Applications are open to UK and EU students only, with demonstration of a right to reside in the UK.

To apply

Send (i) your CV including the name and contact details of two academic referees and (ii) a personal statement of no more than 1000 words explaining your interest in this project and aspirations for undertaking a PhD to studentship@nibsc.org by 5 pm (UK time) on Monday 11 February 2019.

Please ensure the studentship reference number is included in the subject line of the email and your personal statement.

If you have a disability defined by the Equality Act 2010 (<https://www.gov.uk/definition-of-disability-under-equality-act-2010>) you may apply under the UK Civil Service Guaranteed Interview Scheme provided that you meet all of the qualifications, skills, requirements and experience defined as essential for the studentship. You must submit the Guaranteed Interview Scheme Declaration form with your application: this can be found at <https://www.gov.uk/government/publications/guaranteed-interview-scheme>. At interview all applicants will be assessed solely on merit.

Any offer of a studentship is conditional upon successful background screening which includes, but is not limited to, checks on identity, qualifications and right to study in the UK.