PhD studentship (PhD_BIOT2_NIBSC)

A 3-year full-time PhD studentship is available in the Biotherapeutics and Advanced Therapies Team within the Science, Research and Innovation operational group (SR&I) of the Medicines and Healthcare Products Regulatory Agency (MHRA), in collaboration with the department of Biochemical Engineering at University College London.

The project will be supervised by Dr Clive Metcalfe at MHRA and Professor Paul Dalby at UCL. The studentship is anticipated to commence in 2023.

About the Project

Understanding the consequences of redox modification of monoclonal antibody therapies: Improving current treatments and developing next generation therapies.

Monoclonal antibody (mAb) therapies have enjoyed great success in treating many inflammatory diseases and cancers, however, they are not 100% efficacious. Two patients with seemingly the same disease can be treated with the same mAb therapy and have differential outcomes. Recently we have shown that redox enzymes in the inflammatory micro-environment can alter the therapeutic potential of mAbs, namely increasing antigen binding potency but diminishing Fc effector function. *In vivo* this can lead to loss of efficacy and safety of the therapy. Conversely this characteristic of mAbs could be utilized in potential new therapies for diseases where Fc function can lead to unwanted effects. mAbs for virus neutralization, like those developed for SARS-CoV-2, is one such application where unwanted Fc function can lead antibody directed disease enhancement (ADE).

The project will focus on three main areas, 1) Further understanding the mechanisms and consequences of mAb modification *in vivo*; 2) Engineering mAbs to be resistant to modifications, thus improving their efficacy and safety and 3) Exploring the potential for redox modified mAbs as Fc “silent” next generation therapies.
This is a multi-disciplinary project with elements of mAb synthesis and characterization, mAb engineering based on *in silico* structural analysis, and structural and function studies utilizing biochemical, biophysical, and cellular bioassays.

About MHRA

The Medicines and Healthcare products Regulatory Agency enhances and improves the health of millions of people every day through the effective regulation of medicines and medical devices, underpinned by science and research.

About SR&I

Based at a state-of-the-art scientific facility in South Mimms Hertfordshire, SR&I is an operational group of the MHRA. We are a global leader in the characterisation, standardisation and control of biological medicines with the objective to deliver public health impact via world-leading science, research and innovation. The successful candidate will have the unique experience of undertaking the PhD research at a government facility.

About the Team

The Antibodies team, within the Biotherapeutics and Advanced Therapies Team of SR&I, is a leader in developing new mAb and nanobody technologies and studying their structure and function. This underpins the development of WHO international standards, novel diagnostics, potential new therapies and improvement of existing mAb therapies.

Awarding Institution

The successful candidate will be registered with the Department of Biochemical Engineering at University College London, one of the UK's top research Universities, and a global leader in bioprocessing research for the manufacturing and formulation of biological therapies, including monoclonal antibodies.

About You

As a candidate you will be a motivated individual with a passion for wanting to improve patient outcomes. You will have a keen interest in undertaking research in the field of molecular immunology with a focus on antibody engineering and protein structure and function analysis.

Your key responsibilities will be:

- 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 your supervisors and interact appropriately and effectively with other staff.
- To meet the expectations of the study for a PhD by the awarding body (University).

The studentship is only available for students eligible for home UK fees. You will have or expect to achieve a 1st or 2:1 (or international equivalents) in a relevant degree subject (Immunology, Biochemistry, Molecular Biology, Biochemical Engineering, or Chemistry); or a 2:2 (or international equivalent) and a masters' degree (or substantial experience), both in a relevant degree subject. UCL actively supports equality, diversity and inclusion and encourages applications from all sections of society. We strongly encourage applications from those who are currently under-represented within our research student community: BAME British applicants, applicants with disabilities and older applicants.

Funding

Tuition fees for home students as set out by the university are covered; there is provision for laboratory consumables and travel to conferences and the University; there is a student stipend of £ 18,500 p.a.

How to Apply

You should submit a covering letter and a CV, detailing what you can bring to the project and what you would anticipate achieving from the studentship to studentship@nibsc.org by 31 January 2023. Please quote the relevant reference number in your letter. Informal enquiries can be directed to clive.metcalfe@nibsc.org

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.

Medicines & Healthcare products Regulatory Agency

UCL