BBSRC PhD Studentship in Improved viral vector design for homology-independent targeted integration (HITI)  [Project 2022/08]

Radcliffe Department of Medicine (NDCLS), University of Oxford, in collaboration with Oxford Biomedica

Application Deadline: Fri 21st Jan 2022 (12:00 midday GMT)
Project Start Date: October 2022

Supervisors
Primary Supervisor: Professor Deborah Gill
Secondary Supervisors: Dr Tom Roberts

About the Project
Gene therapies for recessive disorders are becoming commonplace, but treatments for dominant gain-of-function disorders are under-researched due to the need to achieve both knock down of the dominant mutant allele and replacement of normal function. This project aims to design high-efficiency AAV vectors with the additional complexity required to tackle dominant disorders. Cas9-mediated Homology-Independent Targeted Integration (HITI) facilitates insertion of an arbitrary sequence at any selected gene editing nuclease cleaved PAM site (Suzuki 2016 PMID:27851729). HITI utilises the NHEJ-pathway, which is substantially more efficient than conventional HDR pathways, and therefore offers more realistic in vivo gene editing strategies. We have a ‘HITI reporter’ mouse model to allow in vivo HITI to be assessed in any organ. We have preliminary data with AAV Cas9 HITI vectors showing controlled, error-free, PAM-targeted, DNA insertion into mouse liver cells in vivo. As a disease exemplar, we plan to use HITI for the dominant liver disorder, alpha-1 antitrypsin (AAT) deficiency. Specifically, we will target the common, dominant AAT genetic variant (PiZ) that leads to AAT protein precipitation in hepatocytes causing deficient disease-causing levels in the lung. Depending on project progression there is also the opportunity to develop the HITI vector platform for other organs.

About the BBSRC Collaborative Training Partnership in Advanced Bioscience of Viral Products (ABViP)

This PhD studentship is part of the Biotechnology and Biological Sciences Research Council (BBSRC) Collaborative Training Partnership (CTP) in Advanced Bioscience of Viral Products (ABViP). The ABViP CTP is a comprehensive, multidisciplinary training programme designed to deliver the next generation of bioscience leaders who will advance research on the underpinning bioscience of viral products for future gene therapies and vaccines. Led by Oxford Biomedica and involving both UCL and University of Oxford, CTP students will have access to a wide ranging portfolio of training opportunities at the Partner sites including taught courses and case studies designed to complement the doctoral research. Students trained through the ABViP CTP will gain a holistic insight into the research and development activities required to develop the medicines of the future, with the ability to see the world of medicines development through both an academic and industrial lens. For more information about the ABViP CTP, please click on the following link.

A webinar will be held on Thu 13th January 2022 17.00 – 18.30 (GMT) which will introduce the ABViP Programme, introduce each of the projects and provide an opportunity to have your questions answered. The final 30 minutes of the webinar will be an opportunity for potential applicants to meet with current doctoral students at UCL and University of Oxford. To register for this webinar, please click here.
About the Department

The Radcliffe Department of Medicine (RDM) is a large multi-disciplinary department that aims to tackle some of the world’s biggest health challenges by integrating innovative basic biology with cutting edge clinical research.

We are made up of 5 smaller Divisions with internationally renowned programmes in areas such as cardiovascular medicine, diabetes and endocrinology, immunology, haematology and pathology. The Nuffield Division of Clinical Laboratory Sciences (NDCLS) is based at the John Radcliffe Hospital and studies the pathology of human disease from the molecular to the systems level; and aims to translate these findings into treatments for human disorders.

We also provide training to medical students, trainees and fellows in the area of clinical laboratory science through internationally acclaimed training programmes, bringing together all the clinical laboratory-based disciplines within the Oxford Medical School, including: microbiology, genetics, cellular pathology, haematology and clinical biochemistry.

About Oxford Biomedica

Oxford Biomedica (OXB) is a pioneer of gene and cell therapy with a leading position in viral vector research and bioprocessing. Our mission is to deliver life-changing gene therapies to patients. OXB is an innovation and science focussed company which has developed a leading platform of novel technologies and capabilities. The OXB team provide design, development, bioprocessing and analytical development for gene-based medicines based on viral vectors, both for in-house products and for those developed with partner organisations. OXB has contract development and manufacturing organisation (CDMO) capabilities that support development of novel gene based medicines through all phases of clinical development to commercial manufacture. At Oxford Biomedica, we drive credible science to realise incredible results.

Entry requirements

A UK Master’s degree, or a minimum of an upper second-class UK Bachelor’s degree, in a relevant discipline, or an overseas qualification of an equivalent standard. We particularly welcome applicants from disadvantaged backgrounds, or via an unconventional career path. If you’re unclear as to whether you are eligible we would encourage you to submit an application regardless. You can also contact the project supervisor (see details below).

To learn more about the policies in relation to diversity and inclusion at Oxford, please click here for further information.

Informal enquiries about the project should be addressed to: Deborah.gill@ndcls.ox.ac.uk

Funding

This BBSRC CTP ABViP Studentship is available to UK and Overseas (including EU) students. Full maintenance (stipend & fees) is available to UK and Overseas students for the duration of the four-year PhD. Note that up to a maximum of one fully-funded studentship allocations is available for Overseas students across the programme. The annual tax-free stipend for the PhD studentship is £16,077 (estimated).

English language requirements

If your education has not been conducted in the English language, you will be expected to demonstrate evidence of an adequate level of English proficiency. The English language level for this programme is: Standard

Deadline and Application Process

The deadline for submission is 12:00 midday on Fri 21st Jan 2022

To apply for this PhD studentship, you must submit a formal application to the DPhil in Advanced Bioscience of Viral Products course (Course code RD_NG1) through UOXFs application portal by the above deadline. More information about the course and application process is available here: https://www.ox.ac.uk/admissions/graduate/courses/dphil-advanced-bioscience-of-viral-products