

BBSRC DPhil Studentship: Hitching a ride with a humanized retroelement

Nuffield Division of Clinical Laboratory Sciences (NDCLS), Radcliffe Department of Medicine, *University of Oxford*
in collaboration with *Oxford Biomedica*

Application Deadline: Friday 5th July 2024 (12:00 midday GMT)

Project Start Date: 13th October 2024

Supervisors

Primary Supervisor: Professor Stephen Hyde

Secondary Supervisor: Dr Jakob Haldrup

About the Project

We have recently demonstrated that lentivirus-derived nanoparticles (LVNPs) generated from HIV-1 can provide transient ribonucleoprotein (RNP) delivery of genome editors to mammalian cells (Haldrup *et al* 2023; PMID: 37678882). LVNP delivery addresses multiple long-standing disadvantages associated with lentiviral and AAV vector delivery of genome editing tools which both suffer from: (i) limited packaging capacity, (ii) unwanted genomic integration, and (iii) unnecessarily prolonged expression. Importantly, as with conventional lentiviral vectors, LVNP cell tropism can be controlled via judicious selection of appropriate envelope proteins.

One potentially limiting factor that we have not addressed in our current LVNP designs is the potential for HIV-1 driven host immune responses to the LVNP platform. In this project, we hypothesise that host immunological responses to LVNPs can be modulated by replacing both the HIV-1 derived components and the pseudotyping envelope proteins with biologically active homologues rescued from the human genome. Our source of these homologues will be endogenous retroviruses (ERVs), remnants of viral elements that have become passengers in the human genome. Amongst the ~5% of the human genome derived from ERV sequences are homologues of HIV-1 Gag/GagPol, a subset of which can self-assemble to form capsids that can deliver nucleic acid cargos to specific cell types. Since ERVs are already present in the human genome, and have been inherited for millennia, they are anticipated to be immunologically inert and thus less likely to trigger host immune responses than HIV-1 derived viral vectors or LVNPs.

This project focuses on engineering a radical enhancement of our LVNP approach to generate an advanced genome editing platform suitable for the treatment of a wide array of both inherited and acquired human diseases using CRISPR technology.

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

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 (OXB) and involving both UCL and the 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 activities required to develop the medicines of the future, with the ability to see the maturation of new medicines through both an academic and industrial lens. For more information about the ABViP CTP, please click on the following [link](#).

About the Department

The Gene Medicine Group directed by Professors Stephen Hyde and Deborah Gill is developing genetic therapy solutions for a range of lung diseases. We have expertise in the generation of both viral and non-viral vectors, evaluation in pre-clinical models, large-scale manufacturing, and transfer to clinical trials. The Gene Medicine Group is also part of The UK Respiratory Gene Therapy Consortium which has progressed results from laboratory studies to the first demonstration that gene therapy can produce improvements in the lungs of patients with Cystic Fibrosis (CF). Our Lentiviral gene therapy platform has been licensed by Boehringer Ingelheim for the treatment of CF and we have formed a university spin-out company to exploit this technology for other diseases. We have well-equipped laboratory facilities to aid the design of novel gene therapy formulations based on lentivirus and lentivirus-derived nanoparticles and evaluate these reagents in both *in vitro* and *in vivo* test systems.

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 the 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

Applicants should hold or be predicted to achieve the following UK qualifications or their equivalent: a first-class or strong upper second-class undergraduate degree with honours in a relevant discipline such as biology, biochemistry, or medicine, although those who have not achieved this level of qualification will be considered if they show strong performance in a master's course. A previous master's degree is not required.

We are looking for strong academic credentials, but we also recognise that some applicants may not have followed the traditional academic route. Substantial professional experience may be a substitute for a lower grade at undergraduate level. We would encourage you to speak to the project supervisor who will be able to discuss this with you.

Informal enquiries should be addressed to: Professor Stephen Hyde (E-mail: steve.hyde@ndcls.ox.ac.uk) with Subject Header: ABVIP Studentship

Funding

This BBSRC CTP ABVIP Studentship is available to UK and Overseas (including EU) students will full maintenance (stipend & fees) for the duration of the 4-year PhD. The annual tax-free stipend for the PhD studentship is £21,237 (estimated), which includes a top-up from Oxford Biomedica.

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 Friday 5th July 2024.

Interviews will take place on: Thursday July 25th.

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 the 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>