

BBSRC PhD Studentship in Synthetic biology engineering of Spy-protein pairs towards targeting of viral vectors for gene therapy and vaccination [Project 2022/05]

Department of Biochemistry, University of Oxford, in collaboration with Oxford Biomedica

Application Deadline: Fri 21st Jan 202 (12:00 midday GMT)

Project Start Date: October 2022

Supervisors

Primary Supervisor: Prof. Mark Howarth

Secondary Supervisors: Prof. Philipp Kukura, Department of Chemistry

About the Project

A major challenge for viral vectors is that their beneficial effects often depend on the transduction of one cell-type, whereas transduction of other cell-types may lead to harmful side-effects. New approaches are needed to address this challenge, to help fulfil the enormous potential of viral vectors for different areas of gene therapy and vaccine generation. SpyTag is a peptide that forms a spontaneous covalent bond to its protein partner SpyCatcher, previously developed by the Howarth group. Both SpyTag and SpyCatcher are genetically encodable and form an amide bond simply upon mixing together. SpyTag and SpyCatcher allow viral vectors to be irreversibly decorated with a specific targeting group (e.g. an antibody or a nanobody), towards enhanced infection of a specific cell-type of interest. In this project we will use innovative methods in rational protein engineering and directed evolution, to generate new SpyTag/SpyCatcher pairs to advance the potential of this approach. This includes new switchable versions of the pair for controlled capture and release, to facilitate clinical production and development of viral vectors. We will also apply innovative methods for nanoparticle analysis, harnessing mass photometry pioneered in the Kukura group, to give unique insight from single molecule investigation of re-decorated viral particles. Working with Oxford Biomedica, we will enhance the re-targeting of the viral vectors for specific transduction of different cell-types, with the overall goal of establishing a powerful approach for increasing the activity and safety of viral vectors.

Skills training will be provided in molecular biology, protein design, directed evolution, mass photometry, cell biology, fluorescence microscopy, and bioinformatics. According to the development of the project, there may also be the chance to learn structure determination by X-ray crystallography.

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

Our department is made up of around 850 talented researchers, students and support staff who share a common passion and purpose – to explore, explain and advance human life.

Our scientists are loosely grouped into five broad research areas: Cell Biology, Development and Genetics; Chromosomal and RNA Biology; Infection and Disease Processes; Microbiology and Systems Biology; and, Structural Biology and Molecular Biophysics. Research groups are organised across these Research Themes and many groups span more than one theme.

We are part of the Medical Sciences division at the University of Oxford, and are dedicated to teaching and biomedical research of the highest quality. Many of our researchers have achieved international recognition and our department has been home to four Nobel or Breakthrough Prize winners.

This depth of curiosity and commitment to excellence doesn't just drive our current research – it benefits the next generation of thinkers through our teaching. We have approximately 450 students on a variety of undergraduate and postgraduate courses, and many of our group leaders and postdoctoral researchers are involved in teaching. This allows our students to learn from world-class minds and engage directly with cutting-edge knowledge.

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 should be addressed to Mark Howarth (E-mail: mark.howarth@bioch.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>