



QUEEN'S UNIVERSITY BELFAST

*Title of studentship	Peptide hydrogels as a long-acting multipurpose drug delivery platform for combined contraception and HIV prevention
Value / what is covered?	Fully funded 100% of UK/EU tuition fees paid and an annual stipend for UK residents only (living expenses), currently at £14,777
Awarding body	DFE
Number of studentships	1
*Summary descriptive text / Example of research project	<p>HIV/AIDS is the leading cause of death in women of reproductive age worldwide. HIV and unintended pregnancies are prevalent in developing nations due to the lack of effective female contraceptive choice. HIV/AIDS remains one of the key challenges facing the UK (428 deaths from AIDS-related illnesses in 2017) and our rate of unintended pregnancies are the highest in Western Europe (one in six pregnancies). One of the key issues is that patients struggle to adhere to the complex regimens of HIV and contraceptive therapies, which often require multiple dosing at very specific times each day. Recent strategies have focused on solving patient adherence issues by using long-acting injectable technologies. However, such products have several significant issues that limit their wider use as combined HIV and contraceptive therapies, such as:</p> <ul style="list-style-type: none"> -the use of water-insoluble drugs that limit the type of drugs that can be incorporated into the product meaning a dual HIV-contraceptive technology is difficult to achieve -fast drug release after insertion leading to potential toxicity issues/concerns over dose received -a need for surgery for implant insertion and removal -a requirement for large needles -stability issues upon storage/transport to the developing world which can result in clogging of syringes and incomplete dosing of drugs. <p>Our project aims to overcome these issues by creating a soluble injection of enhanced stability, for improved ease of administration under the skin. This will form a hydrogel implant in response to enzymes present within the skin to release drugs long-term, removing the need for daily dosing. Our injectable implant is composed of peptide-like molecules which are capable of forming tissue-like hydrogels that can be tailored to gradually release drugs for at least 28 days. This will remove the need for patients to comply with complex drug dosing regimens on a daily basis and improve their adherence to medication. Natural peptides form the building blocks of proteins and tissues. Their use as a drug releasing hydrogel</p>

	<p>implant for administration under the skin is promising due to their high biocompatibility, but limited by their rapid degradation within hours by enzymes present in the human body. This project overcomes stability issues by studying peptide-mimetics, which retain the positive properties of peptides (e.g. biocompatibility, easy drug attachment) with the ability to form hydrogels that will be stable for the duration of therapy. Peptide-mimetics can be tailored to degrade within the body over months into non-toxic components that are eliminated from the patient, meaning surgical removal is not necessary.</p> <p>Our peptide-mimetics possess high chemical versatility (i.e. wide choice of chemical functional groups). Therefore multiple drugs can be attached directly to the peptide-mimetic hydrogel enabling large quantities of drug to be incorporated to meet in vivo therapeutic need for at least 28 days. Drug detachment proceeds in physiological conditions after the hydrogel forms reducing potential for rapid burst release of drug upon injection. Drug release studies will assess the potential for sustained drug administration in a bid to minimise pharmacokinetic peaks and troughs in drug concentrations. The peptide-mimetics studied in this project are purposefully small molecules that are cheap to manufacture, improving their potential to be clinically translated as a pharmaceutical product and effectively utilised within healthcare budgets for patient and societal benefit.</p> <p>The data obtained will allow the practical utility of this peptide-mimetic hydrogel approach to long-acting injectable administration of drugs to be assessed. This platform has high potential to be adopted as a novel implant for the sustained delivery of drugs for conditions where patients have difficulty adhering to their medicines (e.g. Alzheimer's, tuberculosis, depression, schizophrenia, malaria).</p>
*Supervisor(s)	Dr Garry Laverty; Prof Karl Malcolm
*Eligibility / residence Status	UK/EU only
Country	Northern Ireland
*Start date and duration	1 October 2019 Funding covers a three-year full-time PhD.
*Faculty	MHLS
*Research centre / School	Pharmacy
Subject area	Drug Delivery; Biofunctional nanomaterials
Candidate requirements / Key skills required for the post	Applicants should have a 1st or 2.1 honours degree (or equivalent) in a relevant subject. Relevant subjects include Pharmacy, Molecular Biology, Pharmaceutical Sciences, Biochemistry, Biological/Biomedical Sciences, Chemistry, Engineering, or a closely related discipline.
*Deadline for applications	7 th January 2019
*How to apply /	Postgraduate Research applicants for Pharmacy who are interested in applying for a fully funded DFE studentship must have applied to Queen's, via the Direct

contacts	Applications Portal, and submitted all required supporting documents by the closing date, which will be announced later in the Academic year. https://dap.qub.ac.uk/portal/user/u_login.php
Relevant links / more information	http://www.qub.ac.uk/schools/SchoolofPharmacy/Research/PostgraduatePositions/ http://www.qub.ac.uk/schools/SchoolofPharmacy/Research/ Research group website: https://www.lavertylab.com
Keywords for search filters	Drug Delivery; Peptides; HIV
Training provided through the research project	This research will be conducted at the School of Pharmacy Queen's University Belfast which in 2018 was ranked 2nd in the UK for Pharmacy and Pharmacology according to the Guardian University Guide 2018, underpinning the school's investment in and commitment to world-class facilities and staff, with internationally leading research programmes. The School of Pharmacy Queen's University Belfast was particularly outstanding ranking as first amongst Pharmacy submissions in REF 2014. The School of Pharmacy is a leading UK centre for pharmaceutical research and has been supported by philanthropic donations of more than £7 million for strategic research developments. The School's research strategy has focused on developing high profile projects, including in cancer and dermatological therapies that ultimately have the potential to meet identified clinical needs and, consequently, also have high priority status with the pharmaceutical industry. As a member of the Russell Group, Queen's University Belfast which is consistently recognised as one of the leading universities for knowledge exchange in the UK, thus ensuring research is creating jobs, wealth, skills and innovation. The projects lead investigator Dr Laverty is a PhD graduate from the School of Pharmacy and has first-hand knowledge experience of the successful pathway a PhD from Queens University Belfast can provide. The Postgraduate Research Committee (PGRC) advises and supports all PGR students, ensures appropriate training is provided, considers all matters relating to recruitment, admission, progress and examination for postgraduate degrees, monitors and reviews supervision, appoints external examiners, reviews complaints, refers student appeals to the University Postgraduate Appeals Committee and also submits an annual report to the University Postgraduate Office. The School of Pharmacy expects monthly meetings with students where electronic records must be kept. Students must also complete a three-month initial review and annual progress review to proceed to years two and three. The annual progress review involves written work, presentation and/or mini viva. These are the standard management and monitoring arrangements that must be adhered to by the academic partners. As such the School of Pharmacy has the best PhD completion rates within Queen's University Belfast. Each PhD student must also complete the centrally organised Queen's University Belfast researcher development framework program consisting of 30 days of training. These have been created by vitae, and endorsed by the QAA and Research Councils UK. The training areas include four

	<p>domains that encompass: (A) knowledge and intellectual abilities, (B) personal effectiveness, (C) research governance and organisation and (D) engagement influence and impact. For this studentship the student will be trained in the following generic skills; developing writing skills, developing presentation skills, power point for academic presentations and posters, communication skills, introduction to research design, academic plagiarism, basic and advanced statistics, networking and negotiating, lab demonstrating and introduction to ref works. Students are also encouraged to use the Personal Development Planning (PDP) process to build a portfolio on learning, performance and achievement. PDP encourages the students to adopt a good work practice and supports the timely submission of thesis. The student will receive formal training in the following specialist skills necessary for this project; peptide synthesis, drug release protocols, confocal microscopy, scanning and transmission electron microscopy, tissue culture, HPLC, Fourier Transform infra-red spectrometry, circular dichroism, Mass Spectroscopy, NMR, and <i>in vivo</i> facilities. The combination of these skills is highly transferable and should give the student a distinct advantage in the employment sector.</p>
<p>Expected impact activities</p>	<p>Healthcare Professionals– This project will result in a novel drug delivery system that will serve as a superior alternative to existing formulations for healthcare professionals involved in supplying HIV antimicrobials and contraceptives. The student will engage with the Belfast Health Trust’s HIV Service and individual consultants/physicians, providing knowledge input relating to clinical experimental design and result interpretation. We recognise it is important to instill healthcare practitioner confidence in the technology and obtain their feedback early in development.</p> <p>Patients– The student will also engage with HIV charities to provide stakeholder engagement activities (patient questionnaires, focus groups). We will explore: patient related factors in HIV; in-depth views on experiences and gauge their opinion on current treatments and our peptide-based platform.</p> <ul style="list-style-type: none"> -Involved in development of intellectual property -Attendance at relevant conferences -Engagement with industry -Generation of publications