***Title of studentship**	IGNITE: **IG**nifying Tumours: **N**anotechnology for **I**mmune Oncology **T**arg**E**ts
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 £16,777
Awarding body	DfE CAST Studentship with pHion Therapeutics
Number of studentships	1
***Summary descriptive text / Example of research project**	It is thought that the ultimate cure for cancer will arise from harnessing the host immune system that could eradicate cancer cells even as they evolve. One such stragegy is the use of Immune Checkpoint Inhibitors, which need 'immune-hot' tumours. However, only 1 in 8 tumours are "immune-hot" with the remainder termed "immune-cold". Cancers such as triple negative breast cancer, ovarian and pancreatic cancer are all generally "immune cold" which may underpin the associated poor clinical outcome. There has been significant research into turning these "cold" tumours "hot" resulting in tumour kill. One such approach has been to use cyclic dinucleotides (cDNs) to activate the innate immune pathway through the cGAS/STING pathway. While promising results have been shown using direct intratumoural injection, systemic delivery has not been possible due to enzymatic destruction. This limits clinical application to accessible tumours and means application to the metastatic setting, where there is a significant unmet clinical need, is almost impossible. The focus of this PhD is to use a novel patented drug delivery system to overcome these limitations. The industrial partner, Phion Therapeutics, has developed a patented technology, RALA, that can be used to deliver nucleoside and nucleotide analogue drugs specifically to solid tumours following intravenous administration in a nano-formulation. This composite peptide-based nanoparticle has been designed to prevent cell entry except in the tumour microenvironment, thus enhancing the efficacy of the drug (30x) at its intended site. This is a key advantage in the metastatic setting where disease can be dispersed in small tumours throughout the body and requires sufficient drug accumulation in each site to achieve response. <u>Aim1: Novel Targeted Delivery of cyclic Dinucleotides</u> RALA will be used to deliver cDNs facilitating escape from enzymatic destruction and limiting adverse immune responses often observed using systemically-delivered immune agonists. Nanoparticle formulation will be optimised and assessed *in vitro* and *in vivo* for immune activation and tumour kill using "immune cold" syngeneic models (e.g. 4T1 (breast), ID8 (ovarian) and Panc02 (pancreatic)).

	Aim2: Targeting the metastatic setting Our data indicates that STING, the obligate effector of this cDN-based therapy, is lost during drug resistance meaning use of cDNs may not be effective in the metastatic/resistant setting. Therefore, targeting other key immune effectors (e.g. TLR9, RIG-1, NLRP3) will be explored. Commercially available nucleotide-based agonists (CpG DNA and RLR ligand) will be formulated with RALA to develop tumour targeting particles and assessed *in vitro* and *in vivo* as described in Aim1. Agonists may also be combined in a single nanoparticle formulation to maximise therapeutic efficacy in both the primary and resistant setting which may prevent the development of resistance through upregulation of a parallel signalling pathway. This multidisciplary project is in direct alignment with the strategic goals of the CCRCB and School of Pharmacy to develop novel personalised medicine strategies to improve cancer care. The partnership brings together the molecular and translational oncology expertise of Drs Buckley and Parkes with the extensive experience of pHion Therapeutics developing the next generation of cancer medicines.
***Supervisor(s)**	Dr Niamh Buckley, Dr Eileen Parkes and Prof Helen McCarthy
***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	Cancer, immune oncology and Nanomedicine
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. Students who have a 2.2 honours degree and a Master's degree may also be considered, but the School reserves the right to shortlist for interview only those applicants who have demonstrated high academic attainment to date
***Deadline for applications**	March 15th 2019
***How to apply / contacts**	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 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/ http://www.qub.ac.uk/schools/SchoolofPharmacy/Research/ResearchThemes/NanomedicineandBiotherapeutics/ProfessorHelenMcCarthy/ http://www.qub.ac.uk/schools/SchoolofPharmacy/Research/ResearchThemes/NanomedicineandBiotherapeutics/DrNiamhBuckley/ https://pure.qub.ac.uk/portal/en/persons/eileen-parkes(ce4faa0b-d93b-4c16-805c-4cdfd5e400e4).html
Keywords for search filters	Nanomedicine, cancer, immune oncology, STING agonists,
Training provided through the research project	Research Skills: the supervisors will ensure excellent training in physiochemical, in vitro and in vivo techniques providing the student with a broad spectrum of knowledge and expertise. The supervisors will ensure the student is aware of the translational relevance of the project and its potential impact on patient care, Record keeping & monitoring: Monthly meetings with the student will take place with electronic records. Students must also complete a 3-month initial review and annual progress review to proceed to years 2 & 3. The annual progress review involves written work, presentation and/or mini *viva*.
Expected impact activities	The technologies developed in this project have significant potential to overcome the substantial limitations currently associated with the use of innate immune agonists to active an anti-cancer immune response. This therapeutic strategy will allow systemic delivery of the targeted therapy with therapeutic efficacy in both the primary and metastatic setting and provides a novel treatment option for hard to treat cancers such as triple negative breast, ovarian and pancreatic cancers.