***Title of studentship**	**Targeting Trypsin-Like Proteases in Cystic Fibrosis Airways as a Mechanism to Restore Mucociliary Function**
Value / what is covered?	Available as self-funded project
Awarding body	Self-funded
Number of studentships	1
***Summary descriptive text / Example of research project**	Cystic fibrosis (CF) is a chronic genetic disease which affects over 70,000 people worldwide. Mutations in an ion channel called the cystic fibrosis transmembrane regulator (CFTR) result in the build-up and inability to clear mucus in the airways and results in chronic cycles of infection and inflammation which cause lung injury and pulmonary decline, ultimately contributing to the premature mortality associated with the disease. As an understanding of the pathophysiology of CF lung disease has broadened, interest has focused on the dependency of an optimal volume of airways surface liquid (ASL) in the maintenance of effective mucociliary clearance mechanisms which are essential for the maintenance of lung health. The depletion of ASL in CF and the incontrovertible role of the epithelial sodium channel (ENaC) in airway dehydration has been the focus of ground-breaking research therefore the identification of specific protease activators/regulators of ENaC is of imminent clinical relevance. We have developed a library of specific molecular tools with which to dissect the trypsin-like, channel activating proteases (CAPs). In addition, our studies to date have shown that QUB compounds are unique in their ability to specifically investigate the effect of surface inhibition of CAPs on ENaC activation and regulation and were able to increase ASL height and normalise mucocoliary clearance using primary bronchial epithelial cells *in vitro* (Reihill et al, 2016), therefore hold potential for the development of a drug discovery programme to silence aberrant ENaC activity. Rehydration of the airways and the establishment of effective mucociliary clearance mechanisms could reduce inflammation, infection and lung injury, thus delaying the progression of CF lung disease. Significant benefits would therefore be apparent not only in an improvement in the quality of life and life expectancy of individuals with CF but in disease management. This project will undertake a mechanistic approach to investigate the effect of CAP inhibition on ENaC expression, regulation and physiology and will contribute to a multi-disciplinary, collaborative programme of work focussed on the role of ENaC in chronic airways diseases. In addition, clinical samples collected at the beginning, end and post-exacerbation will allow for a greater understanding of how trypsin-like, channel activating proteases correlate with disease progression.
***Supervisor(s)**	Professor Lorraine Martin and Dr Damian Downey
***Eligibility / residence Status**	UK/EU and International subject to Visa acceptance

Country	Northern Ireland
***Start date and duration**	1 October 2018 Three-year full-time PhD
***Faculty**	MHLS
***Research centre / School**	Pharmacy
Subject area	Cell biology, protein biochemistry and electrophysiology
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/Biotechnology, Biochemistry, Biological/Biomedical Sciences 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**	Open
***How to apply / contacts**	Potential applicants should contact Professor Lorraine Martin, l.martin@qub.ac.uk, to discuss their potential application. Postgraduate Research applicants for Pharmacy should apply through the direct application portal 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/
Keywords for search filters	Experimental medicine, clinical research, respiratory, cystic fibrosis, biomarkers, inflammation, infection, proteases, ion channels, epithelial sodium channel, ENaC, airways disease
Training provided through the research project	Professor Martin's research interests are focussed on protein-degrading enzymes (proteases) and their role in health and disease which includes the profiling, delineation and inhibition of proteases involved in infection and inflammation in chronic airways diseases, such as cystic fibrosis and chronic obstructive pulmonary disease (COPD). To date, she has supervised 13 PhD projects to completion. Dr Damian Downey is a Consultant Respiratory Physician and Senior Clinical Lecturer (QUB) specializing in cystic fibrosis and bronchiectasis. The student will receive specific training in cell culture to include the differentiation of primary bronchial epithelial cells at airways-liquid interface, functional assays to include electrophysiology and advanced imaging techniques as well as a range of protein biochemistry, chemical biology, proteomic and genomic techniques to measure and profile protease activities and their inhibition. The student will also gain experience in the handling and processing of clinical samples. In addition, opportunities will be provided for development of communication and inter-personal skills through attendance at weekly lab meetings and presentations at relevant conferences.

Expected impact activities	• Engagement with clinicians, allied health professionals, patients and key stakeholders • Generation of scientific publications • Attendance at relevant conferences • Collaboration with potential industry partners