



## School of Pharmacy PhD Projects 2014

<b>Project Title</b>	Targeting Trypsin-Like Proteases in Cystic Fibrosis Airways as a Mechanism to Restore Mucociliary Function
<b>Supervisors</b>	Dr Lorraine Martin, Prof. Brian Walker & Prof. S Elborn
<b>Description</b>	<p>As an understanding of the pathophysiology of cystic fibrosis lung disease has broadened, interest has focused on the dependency of an optimal volume of airways surface liquid (ASL) in the maintenance of effective clearance mechanisms. 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.</p> <p>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 hold potential for the development of a drug discovery programme to silence aberrant ENaC activity. Rehydration of the airways and effective mucociliary clearance 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.</p> <p>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 which is supported by the Cystic Fibrosis Trust, UK. The project will entail culture of primary airways epithelial cells and a combination of "activity profiling", protein biochemistry and proteomic techniques, as well as chemical biology and genomic approaches to assess the effect of CAP knockdown in electrophysiological and mucociliary clearance models of ENaC activity. It is expected that the student will take an active role in our collaborations with colleagues at the University of North Carolina, Chapel Hill, USA and Royal College of Surgeons, Ireland.</p>
<b>Start Date</b>	1 October 2014
<b>Keywords</b>	Cystic fibrosis, proteases, protease inhibitors, ion transport, ENaC, cell biology, protein biochemistry, peptide synthesis.

### Contact Details

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### How to Apply

Postgraduate applications should be made using Queen's Online:

<http://go.qub.ac.uk/pgapply>

Please note that there are two application processes: one for admission to the university and another for postgraduate awards.

### Further Information

Additional information for prospective postgraduate students can be found on the School of Pharmacy website:

<http://www.qub.ac.uk/pha>

and the Queen's Postgraduate website:

<http://www.qub.ac.uk/home/ProspectiveStudents/PostgraduateStudents/>