***Title of studentship**	Tackling the Bad Bugs: Chemical Tools to Study Bacterial Pathogenicity and Antimicrobial Resistance (2 studentships)
Value / what is covered?	4-years (fully funded)
Awarding body	DfE / Public Health England
Number of studentships	2
***Summary descriptive text / Example of research project**	Two exciting, fully funded PhD projects in chemical biology are available in the group of Professor Gerd Wagner (Queen's University Belfast). Both projects are concerned with the development of chemical tools to understand fundamental aspects of bacterial pathogenicity and antimicrobial resistance (AMR). Both projects are ideally suited for students with a strong background in organic synthesis, who want to significantly expand their experimental skill set, and apply their chemistry knowledge to one of the most urgent healthcare challenges today. In collaboration with Public Health England (PHE), both projects will provide extensive multidisciplinary training at the chemistry/microbiology interface, as well as placement opportunities at PHE. PROJECT 1: TRACKING BACTERIAL PORIN SWITCHING: A CHEMICAL BIOLOGY APPROACH. The goal of this project is to understand how porin switching drives the development of AMR in the nosocomial pathogen *Klebsiella pneumoniae*, the causative agent of pneumonia and a WHO "priority pathogen". Porins are water-filled open channels in the outer membrane (OM) of Gram-negative bacteria that allow the passive transport of small, hydrophilic molecules across the OM. Individual bacteria possess up to 8-10 different porin-encoding genes, whose expression is finely regulated in response to environmental factors, including antibiotics. Switching between different porins allows pathogens to modulate the permeability of their cell envelope. Porin switching has been linked to the stepwise increase in AMR and the phenomenon of "MIC creep", which plays a decisive role in the gradual increase in global resistance. Although porins have been directly implicated in a new form of carbapenem resistance in *Klebsiella pneumoniae*, a detailed understanding of the factors that drive porin switching, and how this is linked to resistance development and bacterial pathogenicity, is currently lacking. We have recently discovered a chemical probe for the labelling of bacterial porins. From this starting point, the student will develop a novel bioanalytical tool for bacterial porin tracking and use this tool to identify critical environmental factors that drive porin switching in *Klebsiella pneumoniae*. This novel tool will also form the

	basis for the development of a novel, point-of-care diagnostic for resistant bacterial infections. PROJECT 2: LIGHTING UP THE BAD BUGS: A CHEMICAL TOOLBOX TO STUDY BACTERIAL PATHOGENS The goal of this project is the development of a chemical toolbox for the identification of molecular markers of bacterial pathogenicity, virulence, and antimicrobial resistance as targets for novel antibiotics and diagnostics. Sugars and small carbohydrates play an important role in the life cycle of bacterial pathogens, as nutrients, intermediates of energy metabolism, and building blocks for the bacterial cell wall. A large and important section of the bacterial proteome therefore includes proteins that recognize carbohydrates as ligands or substrates. Synthetic chemical probes based on carbohydrates are therefore ideal for the interrogation of the bacterial proteome and the identification of disease-relevant molecular markers. We have recently demonstrated proof-of-concept for the successful labelling of protein targets in the bacterial pathogens *Haemophilus influenzae* and *Klebsiella pneumoniae* with such a carbohydrate-based probe. Building on these exciting results, we will in this project develop a toolbox of chemical probes for the efficient mapping of the bacterial proteome and the labelling of living cells. We will use this chemical toolbox to identify novel molecular markers of bacterial pathogenicity, virulence, and antimicrobial resistance. We will also use our probes to establish a highly sensitive and operationally simple system for the detection, profiling, identification and differentiation of bacterial pathogens.
***Supervisor(s)**	Professor Gerd Wagner
***Eligibility / residence Status**	UK/EU
Country	Northern Ireland
***Start date and duration**	1 January 2020
***Faculty**	MHLS
***Research centre / School**	Pharmacy
Subject area	Chemistry, Medicinal Chemistry, Organic Chemistry, Chemical Biology, Pharmacy, Pharmaceutical Sciences
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 Chemistry, Pharmacy, Pharmaceutical Sciences, Biochemistry, Biological/Biomedical Sciences, 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**	15 November 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. 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	organic synthesis, medicinal chemistry, chemical biology, antimicrobial resistance, multidisciplinary, carbohydrates
Training provided through the research project	Students will receive in-depth training in a broad range of scientific techniques, including advanced organic synthesis (carbohydrate chemistry, heterocyclic chemistry), chemical tool development, bacterial cell culture, protein mass spectrometry, bacterial proteomics, containment microbiology, and analysis of multi-drug resistant clinical pathogens. Both projects are highly collaborative and will give students exposure to different research environments, both at Queen's and at partner organisations (e.g., Public Health England). They will also provide an ideal opportunity for students to acquire transferable and generic skills such as time/project management and organisational skills, and experience in commercialization and science outreach.
Expected impact activities	(1) Public engagement. We will contribute to the global public awareness campaign called for by the recent O'Neill review on antimicrobial resistance (AMR), "to educate all of us about the problem of drug resistance, and in particular children and teenagers". We will develop an interactive experiment around AMR for school children and other lay audiences, which will be presented at outreach events at Queen's and beyond (e.g. with "Native Scientist", a network of international scientists, which aims to tackle educational disadvantage through science outreach: www.nativescientist.com). (2) Research translation. We will seek to exploit the opportunities created by these projects for the development of novel point-of-care (PoC) diagnostics for resistant bacterial infections. Such PoC diagnostics will allow clinicians to make immediate, evidence-based decisions about the correct choice of antibiotic. This is not easily possible at present, and the development of such diagnostics has been identified by the O'Neill review as a priority in the fight against AMR. Reference: https://amr-review.org/