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| **\*Title of studentship** | Microneedle delivery of non-ribosomal antimicrobial peptides to treat multidrug-resistant Gram-negative infections |
| **Value / what is covered?** |  |
| **Awarding body** |  |
| **Number of studentships** |  |
| **\*Summary descriptive text / Example of research project** | The increasing prevalence of infections caused by multidrug-resistant (MDR) bacteria is a major global concern, with global deaths due to antimicrobrial resistance expected to hit ten million per year by 2050. Gram-negative bacteria are particularly problematic as their outer-membrane renders them immune to many antibiotics, and the World Health Organization has designated the Gram-negative pathogens carbapenem-resistant Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* as critical targets. We need novel antibiotics and treatments.  Non-ribosomal antibacterial peptides (NRAPs) are a class of compounds that have found special use in the treatment of MDR bacteria. For example, colistin is a last resort antibiotic for the treatment of MDR *P. aeruginosa*, *Klebsiella pneumoniae* and *Acinetobacter* infections, and daptomycin is a key antibiotic for treating MDR enterococci. They typically kill bacteria through interactions with non-protein membrane targets, and are therefore less susceptible to many common resistance mechanisms. However, NRAPs like colistin can cause neurotoxicity and nephrotoxicity when administered intravenously. An alternative, slow release method may circumvent this problem, providing a novel treatment against critical priority pathogens. Microneedle arrays allow delivery of injectable medicines through the skin without causing pain or bleeding. They are self-applied by the patient and can be designed to sustain release over several days  This interdisciplinary project will involve peptide synthesis, polymer synthesis, antimicrobial efficacy assays and pharmacokinetic/pharmacodynamic studies. A series of novel NRAPs will be chemically synthesized and tested in advanced *in vitro* biological models to ascertain their efficacy against MDR Gram-negative bacteria and safety with respect to normal human cells. *In vivo* animal pharmacokinetic and infection studies will demonstare the clinical potential of these novel NRAP-microneedle combinations. |
| **\*Supervisor(s)** | Dr Stephen Cochrane, School of Chemistry  Professor Ryan Donnelly, School of Pharmacy |
| **\*Eligibility / residence Status** | International Scholarship, International self-funding |
| **Country** |  |
| **\*Start date and duration** | September 2022 |
| **\*Faculty** | Medicine Health and Life Sciences / Engineering and Physical Sciences |
| **\*Research centre / School** | School of Pharmacy / School of Chemistry |
| **Subject area** |  |
| **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** |  |
| **\*How to apply / contacts** | All postgraduate research applicants who are interested in the project must submit an application all required supporting documents via the Direct Applications Portal (link below)**.** Any interested applicants can informally contact Dr Cochrane by email at [s.cochrane@qub.ac.uk](mailto:s.cochrane@qub.ac.uk) and Prof. Donnelly by email at [r.donnelly@qub.ac.uk](mailto:r.donnelly@qub.ac.uk).  <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/>  <https://www.qub.ac.uk/schools/SchoolofPharmacy/Research/ResearchThemes/>  NanomedicineandBiotherapeutics/  <https://www.qub.ac.uk/schools/SchoolofPharmacy/Research/find-a-phd-supervisor/professor-ryan-donnelly.html> |
| **Keywords for search filters** | Antibiotics; peptide synthesis; antimicrobial peptides; microneedles; organic synthesis |
| **Training provided through the research project** | Synthesis of peptides by manual and automated peptide synthesis, purification of synthetic compounds by HPLC, analysis of synthetic compounds by NMR and mass spec, antibacterial susceptibility assays, pharmaceutical formulation, analysis and engineering |
| **Expected impact activities** | Demonstration of promising antimicrbial activity may lead to interest from the pharmaceutical industry, where development of new antibiotic classes and appropriate administration methods for difficult-to-deliver antibiotics are both in need of new innovative approaches. The supervisors have extensive experience of industrial engagement and promising data emanating from this project will be made available to potential industrial partners once intellectual property is protected, thus providing further potential opportunities for the student. |