Project title: Development of Carbon Monoxide Releasing Molecule (CO-RM) antimicrobials against *Pseudomonas aeruginosa* bacterial pathogen
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**Project Description:**
The rise of antibiotic-resistant bacteria represents a significant threat to human health and therefore novel therapeutic agents are required to treat infections. Carbon monoxide-releasing molecules (CO-RMs) are a potentially highly effective new class of antibiotics. These are small-molecule compounds which, on exposure to suitable stimuli, release controlled amounts of carbon monoxide. In a range of experiments, we have shown than CO-RMs are highly effective at inhibiting the growth of a range of bacterial strains but at the concentrations used have little effect on mammalian cells. The observed activity is thought to be due to the CO-released by the compounds.

This project seeks to capitalise on these findings by exploring the activity of CO-RMs again *P. aeruginosa*, a pathogen which may readily develop high-levels of resistance. Initial work will involve screening the activity of CO-RMs against bacteria *in vivo* followed by investigation into how CO-RMs affect *P. aeruginosa* in bacterial communities. Such communities are often found in polymicrobial Cystic Fibrosis lung infections; therefore, these latter studies are vital if we are to translate CO-RMs from the laboratory to the clinic.

A key focus of the project will be to link the results from the microbiology experiments to the design and synthesis of novel CO-RM structures. In order to optimise the activity of the small molecules a range of species with different structure classes and triggers for the CO-release process will be employed and evaluated. These data will then be employed to rationally design subsequent generations of CO-RMs whose activity will, in turn, be assessed.

The student undertaking this project will develop a broad range of chemical and biochemical skills. These will include the skills required to identify new CO-RM structures and prepare them, coupled evaluating their behaviour in a microbiology laboratory.

**Training:**
This prestigious BBSRC funded Doctoral Training Partnership (DTP) brings together the very best molecular, chemical and cellular bioscience research across the White Rose Consortium of Universities (Leeds, Sheffield and York), which maps on to the research themes of the BBSRC. Students will benefit from a regional PhD training programme that has interdisciplinary collaboration at its core. The aim is to enable students to develop a range of research skills in biological and biochemical areas as well as equip them with core mathematical, data analysis and generic professional skills that are necessary for bioscience research in the coming decades. At York, the White Rose Partnership brings together researchers from the Departments of Biology and Chemistry. Additionally, all Chemistry research students have access to our innovative Doctoral Training in Chemistry (iDTC): cohort-based training to support the development of scientific, transferable and employability skills.

**Equality and Diversity:**
The Department of Chemistry holds an Athena SWAN Gold Award and is committed to supporting equality and diversity for all staff and students. The Department strives to provide a working environment which allows all staff and students to contribute fully, to flourish, and to excel. Chemistry at York was the first academic department in the UK to receive the Athena SWAN Gold award, first attained in 2007 and then renewed in October 2010 and in April 2015. This PhD project is available to study full-time or part-time (50%).
Funding:

Value: Studentships are fully funded by BBSRC and cover: (i) a tax-free annual stipend at the standard Research Council rate (£14,296 for 2016-2017, to be confirmed for 2017-2018 but typically increases annually in line with inflation), (ii) research costs, and (iii) tuition fees at the UK/EU rate.

Eligibility: The studentships are available to UK and EU students who meet the UK residency requirements. Students from EU countries who do not meet the residency requirements may still be eligible for a fees-only award. Further information about eligibility for Research Council UK funding can be found at the following website: [http://www.bbsrc.ac.uk/documents/studentship-eligibility-pdf/](http://www.bbsrc.ac.uk/documents/studentship-eligibility-pdf/)

Candidate selection process:

- Applicants should submit an application for a PhD in Biological Chemistry by midnight on Sunday 7 January 2018
- Supervisors will contact their preferred candidates either by email, telephone, web-chat or in person
- Supervisors may nominate up to two candidates to the assessment panel
- The assessment panel will shortlist candidates for interview from all those nominated
- Shortlisted candidates will be invited to a panel interview at the University of York on Tuesday 6 February 2018
- The York BBSRC White Rose DTP awarding committee will award studentships following the panel interviews
- Candidates will be notified of the outcome of the panel’s decision by email

For more information contact chemgrad@york.ac.uk
or see our web page: [http://www.york.ac.uk/chemistry/postgraduate/](http://www.york.ac.uk/chemistry/postgraduate/)