

PhD studentship in medical microbiology

## Title: Stressing the superbug: Using bacterial stress sensors to understand how the antibiotic-resistant pathogen *Staphylococcus aureus* survives harsh environments

Applications are welcomed for one fully funded, four-year, full-time PhD position at University College Dublin, Ireland.

PhD Project area: Microbiology and antimicrobial resistance.

PhD supervisor: Dr Rebecca Corrigan

Proposed Start Date: Sept 2025.

Location: School of Medicine, University College Dublin, Ireland

**Positions**: 1x 4-year, Full-time PhD studentships (A University College Dublin Ad Astra PhD Studentship).

Stipend: €25,000 per annum tax-free plus tuition fees.

**Summary of Project(s)**: The "superbug", methicillin resistant *Staphylococcus aureus* (MRSA) is a major threat to global health. Bacteria, such as MRSA, can sense external stresses like nutrient deprivation or the presence of innate immune effectors, conditions that can drive antimicrobial tolerance or chronic infections. The transition from colonisation to infection is exceptionally stressful for bacteria, as is treatment with antibiotics. To cope, they activate complex regulatory circuits controlled by two "alarmone" phospho-nucleotides that signal this stress, regulating bacterial functions in ways that maximise survival. These nucleotides are produced specifically in response to stress and are responsible for coordinating cellular events that turn off growth and turn on genes for stress adaptation and survival. Whilst alarmone signalling has been linked to persistent and chronic infections, little is known about how they function to coordinate this adaptation on a molecular level in the host.

In *S. aureus,* these nucleotides are synthesised by three different enzymes, however relatively little is known about the production and regulation of these proteins. This project will use molecular genetics to construct biosensors that will be used to identify environmental signals, such as antibiotics or immune responses that trigger activation of these enzymes. Additionally, this project will make use of an *S. aureus* mutant library to identify regulator(s) that control the production of these enzymes on a molecular level. Altogether, this project will provide key insights into the synthesis of alarmone nucleotides by these enzymes and in doing so generate important mechanistic data on the pathogenesis of *S. aureus* and the importance of this system for antimicrobial resistance.

All the techniques and approaches are established in the Corrigan lab. We provide training in writing, presenting and science outreach, as well as bench science and you will work in an exciting and thriving community of like-minded scientists at the UCD AMR hub. You should possess a high 2.1 or 1<sup>st</sup> class degree or an MSc in microbiology, biochemistry or similar area. Relevant laboratory experience is not required, but passion and enthusiasm for making a difference in the field of antimicrobial resistance is a must!

**Research Team and Environment**: The successful candidates will join the newly established Corrigan lab in University College Dublin's School of Medicine. Our lab has recently relocated from the University of Sheffield. The group focuses primarily on understanding nucleotide signalling systems and their contribution to bacterial survival, infection and antimicrobial resistance. The studentship will also benefit from opportunities to contribute to other projects as well as from planned local and international collaborations that we have in the UK, Germany, USA and Peru to ensure the success of this project.

**Requirements Qualifications/Expertise**: Applications are sought from inquisitive and dedicated candidates with interest in scientific methodology and discovery. Candidates should have, or expect to soon be awarded, a BSc (grade 2.1 or above), or an MSc, in the area microbiology, infection studies or biochemistry.

**To apply for these positions**: Please send your CV, a cover letter, and the contact details of at least two referees to <u>rebecca.corrigan@ucd.ie</u> by 6th June 2025. Informal enquiries in relation to the position are welcome and encouraged.

## **Relevant publications:**

- Adedeji-Olulana AF, Wacnik K, Lafage L, Pasquina-Lemonche L, Tinajero-Trejo M, Bilyk B, Irving S, Portman-Ross C, Meacock O, Randerson S, Beattie E, Owen D, Florence J, Durham W, Hornby D, Corrigan RM, Green J, Hobbs JK, Foster SJ (2024) Two codependent routes lead to high-level MRSA. *Science* 386:573-580. doi <u>10.1126/science.adn1369</u>.
- Urwin L, Savva O, Corrigan RM (2024) Microbial Primer: what is the stringent response and how does it allow bacteria to survive stress? *Microbiology (Reading)* 170(7). doi <u>10.1099/mic.0.001483</u>
- 3. Irving SE, Choudhury NR, **Corrigan RM** (2021) The Stringent Response and Physiological roles of (pp)pGpp in bacteria. *Nature Reviews Microbiology*. 19(4):256-271. Invited Review. doi:<u>10.1038/s41579-020-00470-y</u>
- 4. Corrigan RM<sup>1</sup>, Bellows LE, \*Wood A, Gründling A<sup>1</sup> (2016) ppGpp negatively impacts ribosome assembly affecting growth and antimicrobial tolerance in Gram-positive bacteria. *PNAS* 113(12):E1710-1719. doi: 10.1073/pnas.1522179113