Investigating the efficacy of natural compounds on bacterial biofilm formation in the mouse replacement model, Galleria mellonella

Supervisory team:
Lead supervisors: Prof James Wakefield (University of Exeter) and Dr Emmanuel Adukwu (University of the West of England; UWE)
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Host institution: University of Exeter (Streatham) / University of the West of England; UWE
Submit applications for this project to University of Exeter

Project description:
Acinetobacter baumannii is a common nosocomial pathogen causing pneumonia, bacteraemia, wound and urinary tract infections. Due to improper and frequent antibiotic use A. baumannii has become multi-drug resistant, the World Health Organization has classified it as a priority pathogen of which novel antibiotics are desperately needed. Research into natural antimicrobial compounds is essential in developing novel strategies to treat multidrug resistant infections but high throughput antimicrobial compound screening technologies are currently limited to in vitro or in silico approaches.

The use of the larvae of the waxmoth, Galleria larvae, as an in vivo partial mammalian replacement model is growing, primarily in the field of infection biology due to their broad susceptibility to microbial pathogens, low cost and ease of use. Crucially, in contrast with other non-mammalian model systems, Galleria can be reared healthily at 37°C, and mimic both human host-pathogen interactions and pharmacodynamics of drug clearance.

Currently, Galleria are used for low and medium throughput studies of microbial infection, injecting pathogens into the larvae. In this PhD you will seek to transform Galleria into a high throughput system, investigating ways to compromise the cuticle of the larvae, sensitising it to infection. You will take three complementary approaches: physical disruption – exploring methods that take a “batch” approach to wounding; chemical disruption – incubating larvae with chemicals and enzymes; genetic disruption – generating CRISPR/Cas knockouts of key cuticle genes. You will then test the ability of A. baumannii to colonise the compromised cuticle as a biolfilm, analysing the effect at a variety of spatial and temporal scales, before investigating the antimicrobial efficacy of a series of natural compounds, including essential oils.

This PhD project is an opportunity for an ambitious scientist with an interest in applied infection biology. Through this study, you will not only hope to identify new antimicrobial compounds but also pave the way for the application of Galleria to applied and industrial drug discovery settings.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.