

Environmental bacteria as a reservoir of novel antibiotic resistance mechanisms

Supervisory team:

Main supervisor: Dr Susanne Gebhard (University of Bath)

Second supervisor: Prof Eshwar Mahenthiralingam (Cardiff University)

Dr Brian Jones (University of Bath), Prof Mark Buttner (John Innes Centre, Norwich)

Host institution: University of Bath

Project description:

The soil is a competitive bacterial environment, reflected in the high prevalence of antibiotic production and antibiotic resistance. Streptomycetes are undisputedly the most important producers of antibiotics in the soil. However, while we understand much of how they produce antibiotics, we know surprisingly little about how they themselves resist antimicrobials present in the soil. This is concerning, because some of the most problematic resistance mechanisms we now see in the clinic have originated in the natural environment. It is therefore important to gain a better understanding of the arsenal of resistance mechanisms in the soil that have yet to be discovered.

Antimicrobial peptides (AMPs) have recently received much attention as promising new drugs. They are produced by low-GC Gram-positive bacteria (firmicutes), which often share the soil habitat with Streptomycetes. It is well-understood how firmicute bacteria resist AMPs, but the corresponding genes appear to be conspicuously absent from streptomycetes. Considering both groups share the same environment, it is safe to assume that streptomycetes will also be exposed to AMPs, and must therefore harbour resistance. However, the mechanisms remain unknown. This PhD project entails a detailed investigation of the nature of this unexplored resistance.

We recently discovered that *Streptomyces venezuelae* possesses a striking degree of resistance against AMPs. We were able to isolate sensitive mutants of this bacterium, but none of the mutations were located in known resistance genes. In this project, you will carry out a thorough characterisation of these strains, to understand the full spectrum of resistance, and how this allows *S. venezuelae* to succeed in the natural environment. This will involve physiological and ecological analyses, under the guidance of the primary supervisor, Dr Gebhard (Bath), together with Dr Jones (Bath) and Prof. Mahenthiralingam (Cardiff). Using molecular genetics approaches, you will also identify the genes responsible for resistance, and how the cell responds to antibiotic attack. You will build on genome and transcriptome data available in the Gebhard lab, and receive training in molecular biology by Prof. Buttner (Norwich), who is the world-expert on *S. venezuelae* genetics. Bringing together the environmental and molecular studies, you will then investigate the prevalence of the newly discovered genes among soil bacteria via genomics analyses.

The unique approach of this project, from the natural environment through to molecular mechanisms, supported by an expert supervisory team, will provide you with interdisciplinary training in a comprehensive range of techniques, equipping you for a successful scientific career.

