# Determining the regulatory control of prokaryotic antiviral defence systems

**Supervisory team:**
**Main supervisor:** Prof Tiffany Taylor (University of Bath)
**Second supervisor:** Prof Edze Westra (University of Exeter)
Dr Catherine Tooke (University of Bath)

**Collaborators:** Prof Mario Recker (University of Exeter)

**Host institution:** University of Bath

**Project description:**
The spread of antimicrobial resistance is a slow-moving pandemic that has been identified by the WHO as one of the top 10 threats facing humanity. It has been estimated that in 2050 approximately 10 million people will die each year as a result of antimicrobial resistance.

Bacterial immune systems are key determinants of the spread of antimicrobial resistance. Moreover, they can severely hamper the efficacy of therapeutic application of phages in clinical settings, which is considered a viable alternative to conventional antibiotics to treat infections with resistant pathogens. For these reasons it is critical to identify bacterial defence systems and to understand how they operate. Recent work has revealed that bacteria carry many more defences than previously thought, and we are only just beginning to understand how they work. In this project, the student will study the interplay between a novel innate defence system that was identified in our lab (MADS) and the CRISPR-Cas adaptive immune system of the important opportunistic pathogen Pseudomonas aeruginosa. This WHO priority pathogen is one of the leading causes of hospital acquired infections and a major cause of lung infections in cystic fibrosis patients. Because of its high levels of antimicrobial resistance, phage therapy is in some cases already being used to treat patients.

The project will benefit from expertise in evolution of novel regulatory and genetic innovations (Taylor, Bath), P. aeruginosa CRISPR-Cas evolution and discovery of the novel MADS immune system (Westra, Exeter), and modelling the co-evolution of host and pathogen interactions (Recker, Exeter). Throughout this interdisciplinary project, the student will receive extensive training in experimental evolution, molecular microbiology, genetics and modelling. The student will be based in the Taylor lab as part of the Milner Centre for Evolution at the University of Bath with opportunities to work in the Westra lab at the Environment and Sustainability Institute at the Cornwall campus of the University of Exeter, and with the Recker lab at the University of Exeter (Falmouth).

**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.**