Rational design of phage-antibiotic therapies as the new frontier for tackling antibiotic resistance

Supervisory team:

Main supervisor: Dr Stefano Pagliara (University of Exeter)
Second supervisor: Dr Ben Ashby (University of Bath)
Dr Stineke van Houte (University of Exeter)

Collaborators: Dr Mark Blaskovich (University of Queensland), Dr Max Ryadnov (National Physical Laboratory), Dr Isobel Norville (Defence science and technology laboratory)

Host institution: University of Exeter (Streatham)

Project description:

We cannot see bacteria and viruses but there are around ten trillion of them in us or on us, thus ten times more the number of our own cells. Many bacteria are beneficial for us, some however, can cause infectious diseases such as meningitis or pneumonia. Indeed, bacterial infections are one of the leading causes of death worldwide and are estimated to lead to 300 million deaths by 2050. Antibiotics save millions of lives combatting infectious diseases. However, several bacteria, particularly those having a double membrane that makes them more impermeable, are resistant to antibiotic treatment. Therefore, we urgently need to develop strategies to overcome the current impasse by enhancing the uptake of antibiotics in bacteria or by using complementary tools for eradicating bacteria such as phage that are viruses targeting bacterial but not human cells (Lancet Infect Dis 19, 2, 2018).

In order to understand the biological mechanisms underlying antibiotic and phage uptake in gram-negative bacteria, you will use a novel microfluidic technology that has recently been developed in Dr Pagliara’s team at the Living Systems Institute, University of Exeter (BMC Biol. 15, 121 2017; Lab on a Chip DOI: 10.1039/d0lc00242a 2020; http://www.dailymail.co.uk/wires/pa/article-5201805). You will work in collaboration with the team of Dr Blaskovich at the University of Queensland, and Dr Van Houte at the Environment and Sustainability Institute, University of Exeter, to synthesise fluorescent derivatives of commonly used antibiotics and phage, respectively. Combined with a fluorescence microscope these microfluidic devices and fluorescent probes will allow you to measure antibiotics or phage entering or exiting individual bacteria as well as measuring the efficacy of these compounds in killing infecting bacteria. You will then apply mathematical models for analysing these data to understand how population heterogeneity detected in the single-cell data affects population and evolutionary dynamics. This work will be carried out under the supervision of Dr Ashby at the University of Bath and will allow to select potent phage and antibiotic combinations for the eradication of bacterial pathogens. This project also offers the possibility for collaboration visits to the National Physical Laboratory and the Defence Science and Technology Laboratory.

Over the past ten years, single-microbe research has taken off around the globe engaging teams of scientists from different disciplines. As part of our battle against antibiotic resistance, by studying phage and antibiotic uptake in single bacteria your project will provide crucial novel knowledge for the development of new antibacterial therapies and a better use of existing ones.