Novel single-cells omics and microfluidics approaches to tackle antimicrobial resistance

Supervisory team:
Main supervisor: Dr Stefano Pagliara (University of Exeter)
Second supervisor: Dr Michaela Serpi (Cardiff University)
Non-academic (CASE) supervisor: Dr Isobel Norville (Defense Science and Technology Laboratory)

Host institution: University of Exeter (Streatham/St Luke's)

CASE partner: Defense Science and Technology Laboratory

Project description:

We cannot see bacteria 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 accumulation of antibiotics near their bacterial targets, for example by using combination therapies with multiple antibiotics (Nature 559, 259, 2018).

In order to understand the biological mechanisms underlying antibiotic uptake and efflux 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 Chip 20, 2765 2020; RSC Chem. Biol. 1, 395, 2020). You will work in collaboration with the team of Dr Blaskovich at the University of Queensland, and Dr Serpi, University of Cardiff, to synthesise fluorescent derivatives of commonly used antibiotics and novel antibiotics, respectively.

Combined with a fluorescence microscope, these microfluidic devices and fluorescent probes will allow you to measure antibiotics entering or exiting individual bacteria as well as measuring the efficacy of these compounds in killing bacteria. You will then apply omics approaches to identify genes and proteins that allow individual bacteria to avoid antibiotic accumulation.

Using this knowledge and bioinformatics you will identify compounds that help antibiotics to enter and kill individual bacteria. The latter work will be carried out under the supervision of Prof Tsaneva-Atanasova. This project also offers the possibility for a placement at the Defence Science and Technology Laboratory where you will test newly identified combination therapies in simple infection models, such as the wax moth Galleria mellonella.

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 antibiotic uptake and efflux in single bacteria your project will provide crucial novel knowledge for the development of new antibacterial therapies and a better use of existing ones.