

Synthesis and Analysis of Copper-Loaded Micelles to Address Antimicrobial Resistance

In this project, we will produce micelles containing copper complexes, which are known to switch off the resistance of bacteria 'super bugs' to drugs of last resort.

Names of Supervisors:

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Themes: polymer synthesis; micelle synthesis; antimicrobial copper complex synthesis; polymer characterization; micelle characterization; antimicrobial assays.

Background

Carbapenems are broad-spectrum β -lactams used as last-resort antibiotics. Worryingly, carbapenem-resistance is emerging, leading to increased deaths from bacterial infection. Metallo- β -lactamase (MBL) enzymes are linked to carbapenem-resistance. Inhibition of MBLs switches off antibiotic resistance and we have been studying copper pyrithione complexes as inhibitors of the MBL enzymes. These complexes are active, but uptake into the bacterial cell is a limiting factor. We have varied the pyrithione ligand in an attempt to increase uptake with some success. In this project, we will use polymeric micelles to improve uptake of the copper.

Project Details

The first aim of this project is to produce micelles loaded with the MBL-inhibitor copper-pyrithione complexes. This will involve chemical synthesis of pyrithione ligands, their copper complexes and polymer micelle precursors. Micelles will be characterized using dynamic light scattering and copper complex loading and release will be quantified. Next, biological assays will be carried out to assess the copper uptake (ICP-MS) and the extent of MBL inhibition within the bacteria. Beyond this initial aim, we hope to develop micelles that target the bacteria selectivity and to produce micelles that combine the copper complex with the carbapenem antibiotic – an all-in-one micelle that simultaneously delivers carbapenem antibiotic and inhibits the resistance mechanism.

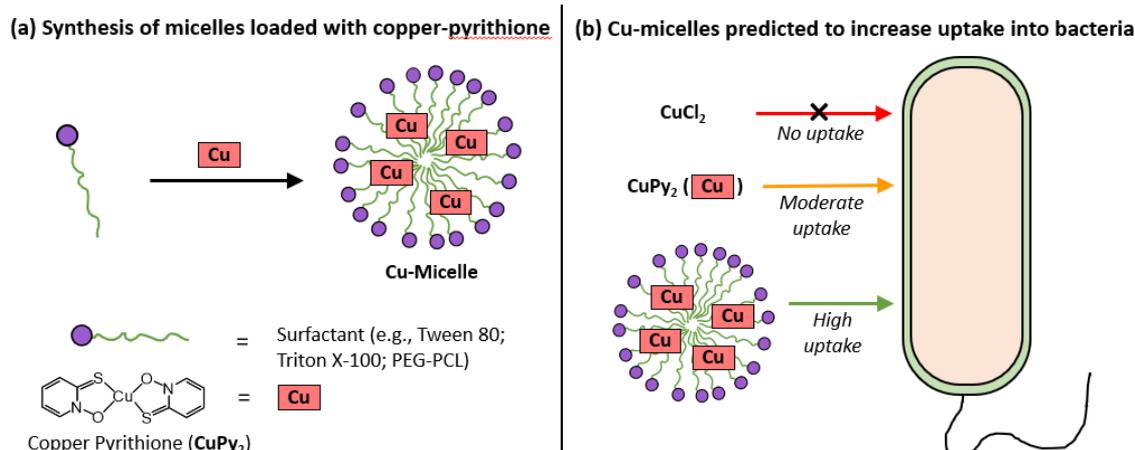


Figure 1

Beyond the practical training, the student on this project will join a dynamic research team and develop skills in collaboration, teamwork and communication. For more details, contact james.walton@durham.ac.uk