Targeted Project / AY 2024 -2025

Aptamers as a tool for targeting bacterial outer membrane proteins

Project Code: TRG-PHAR-IM

Supervisor: Dr Ioana Mela (im337@cam.ac.uk)

Department/Institute: Pharmacology

Website: https://www.phar.cam.ac.uk/dna-nanostructure-development-and-aptamer-selection

Research area: DNA nanotechnology, targeted delivery, aptamer selection, microbiology, microscopy

BBSRC DTP main strategic theme: Transformative technologies

BBSRC DTP secondary strategic theme: Bioscience for an integrated understanding of health

Project outline:

In the Mela laboratory, we have combined DNA nanostructures and aptamer nanotechnology to create bacteria-specific delivery vehicles, with the potential to deliver a multitude of active compounds to bacterial targets. We will now build on this work, to develop novel, highly sophisticated DNA-based systems for targeted and controlled antimicrobial delivery and simultaneous blocking of bacterial receptors. The aim of this PhD project is the selection of aptamers (oligonucleotides that bind to specific target molecules with high affinity) that can bind specific surface proteins on particular bacterial strains, to maximise the specificity and efficiency of drug delivery. The focus will be on targeting aptamer-derivatised DNA nanostructures to two specific surface proteins that are crucial to the survival of MRSA and P. aeruginosa. On MRSA, the target proteins will be fibronectin-binding proteins A (FnBPA) and B (FnBPB). These proteins mediate adhesion of MRSA to the extracellular matrix and are involved in MRSA invasion of host organisms and in the formation of biofilms. The target proteins on P. aeruginosa will be pseudomonas haem uptake (Phu) and haem assimilation (Has) receptors. The Phu and Has receptors are crucial for P. aeruginosa, as they facilitate the sourcing of iron — an essential micronutrient for the survival and virulence of Gram negative pathogens — from haem. Once the best performing aptamers are selected, we will explore their potential as a tool against antibiotic resistance. We will assess the aptamers for their potential to drive the binding of nanostructures on the bacterial surface and as pharmacologically-relevant molecules, with the ability to disrupt crucial bacterial functions.