

Project: Exploiting receptor trade-offs in *Pseudomonas aeruginosa* to optimise phage therapy strategies

Supervisors: Vicki Gold (LSI, Biosciences Streatham) & Stineke van Houte (Biosciences Penryn)

Antimicrobial resistance (AMR) is a critical global health challenge, with *Pseudomonas aeruginosa* classified by the World Health Organization as a priority pathogen. Phages are viruses that specifically infect bacteria and offer a promising alternative to conventional antibiotics. Phage infection is initiated through binding to receptors on the bacterial cell surface, making this interface a key point at which bacterial resistance often emerges.

This PhD project will focus on two phages, *Tor* and *Vale*. Previous work has shown that *P. aeruginosa* can develop resistance to *Tor* by modifying its surface receptor. However, this modification simultaneously exposes a different receptor, rendering the bacterium susceptible to infection by *Vale*. This evolutionary trade-off highlights the therapeutic potential of phage combinations, which have been shown to delay the emergence of resistance.

Building on existing high-resolution cryo-electron microscopy (cryo-EM) expertise in the [Gold lab](#) (see figure), this project will integrate structural biology with phage binding assays using *P. aeruginosa* clinical isolate collections in the [van Houte lab](#). High-throughput phage adsorption assays will be combined with genetic analyses of receptor loci to enable a comprehensive investigation of phage-host interactions. Key objectives include resolving the structures of receptor-binding proteins in complex with their target bacterial receptors, characterising the infection strategies of *Tor* and *Vale in situ*, and identifying the bacterial genetic determinants that govern phage receptor binding.

This work will generate fundamental insights into phage–host interactions and inform the rational design of phage cocktails based on receptor specificity. Such strategies are essential for minimising the emergence of phage resistance and improving the efficacy of phage therapy against AMR pathogens.

