Project Details	
Project Code	IIAR27Ex Westra
Title	Bacterial pathogen evolution during antibiotic-phage combination treatment
Research Theme	Infection, Immunity & Antimicrobial Resistance
Project Type	Wet lab
Summary	Antimicrobial resistance is a major threat to modern medicine, and bacteriophage therapy is a promising route to treat drug-resistant infections. Yet phage therapy can fail when bacteria evolve resistance or deploy defence systems that block infection. This project will ask how antibiotics reshape phage-bacteria interactions, resistance evolution, and cell-to-cell variation in bacterial responses. The student will combine experimental evolution, microbiology, single-cell imaging and biochemistry, working across Exeter, Bath and Bristol. Patient and public involvement will help keep the project focused on clinically relevant questions and the future use of phage therapy.
Description	Access to effective antimicrobial drugs underpins modern healthcare, agriculture and food production. The rapid rise of antimicrobial resistance (AMR) threatens this foundation, making infections harder to treat and increasing the risk associated with routine medical procedures. Phage therapy, the use of lytic bacteriophages to kill bacterial pathogens, is a promising alternative or complement to antibiotics. However, its outcome remains difficult to predict. Bacteria carry diverse and often co-occurring defence mechanisms that protect them from phage infection, including CRISPR-Cas, restriction-modification, CBASS and phenotypic, non-genetic resistance strategies. We still do not understand which of these mechanisms matter most during phage therapy, how they interact with antibiotics, or why genetically similar bacteria show different responses to the same treatment. The key research question is: how do antibiotics alter the evolutionary routes by which bacterial pathogens survive phage therapy? This project will identify general principles that explain how bacterial genotype and cell-to-cell heterogeneity shape the outcome of antibiotic-phage combination treatment. It will focus on clinically relevant bacterial pathogen-phage systems in which treatment responses can be followed using high-throughput population-level and single-cell assays. Patient and public involvement and engagement (PPIE) will ensure that the clinical contexts, outcomes and communication of the work remain relevant to people affected by antimicrobial-resistant infections. The student will work towards three linked objectives. First, they will identify general rules that predict bacterial pathogen susceptibility to antibiotic-phage combination treatment. Using high-throughput assays, the student will test how different antibiotic types and concentrations interact with different phage types and doses across a diverse panel of clinical bacterial isolates. Treatment outcomes will then be linked to bacterial genotype, focusing on features predicted to influence response, including AMR genes, efflux systems and anti-phage defence mechanisms. This will reveal whether particular genetic backgrounds or defence repertoires predict responsiveness to antibiotic–phage combinations.

	Second, the student will use representative isolate-phage-antibiotic combinations from this screen to investigate how treatment shapes bacterial evolutionary trajectories. They will test when bacteria evolve phage resistance, whether antibiotics constrain or redirect this evolution, and which genetic or phenotypic mechanisms dominate under different treatment regimes. Mechanistic interpretation will be supported by biochemical insight from Professor Mark Szczelkun's group, helping connect treatment outcomes to the underlying mechanisms of defence against phage. Third, the student will determine how cell-to-cell heterogeneity influences the outcome of antibiotic-phage treatment. Using microfluidics and single-cell imaging, they will ask whether subpopulations such as persister cells, cells with phenotypic phage resistance, or cells with altered antibiotic uptake survive treatments that appear effective at the population level. Labelled antibiotic analogues will be used to relate antibiotic accumulation to phage susceptibility and bacterial survival. Together, these experiments will connect high-throughput population-level patterns with the behaviour of individual cells. Patient and public involvement and engagement will be integrated across the studentship. In discussion with patient and public contributors with lived experience of antimicrobial-resistant infection, the student will consider which infection contexts, treatment outcomes and communication routes should be prioritised. The final stage of the project will integrate the high-throughput population-level and single-cell findings to identify principles for designing more effective antibiotic–phage combinations. This studentship will be led by Professor Edze Westra at the University of Exeter, whose lab specialises in the ecology and evolution of bacteria-phage interactions. The student will be co-supervised by Professor Stefano Pagliara at the University of Exeter, whose group develops microfluidics-based single-cell microscopy approaches to study heterogeneity in bacterial populations; Professor Tiffany Taylor at the University of Bath will contribute key expertise in experimental evolution, molecular biology and bioinformatics to understand the evolutionary drivers and trade-offs underlying bacterial defence systems; Professor Mark Szczelkun at the University of Bristol, will contribute mechanistic and biochemistry expertise of bacterial defence systems such as restriction-modification and CRISPR-Cas. Together, this supervisory team gives the student access to expertise across the full spectrum from bacterial genomics and high-throughput screening to molecular mechanism, single-cell behaviour and evolutionary dynamics, while providing the cross-institutional and interdisciplinary training central to the GW4 BioMed3 MRC DLA. The project will be shaped substantially by the student in discussion with the supervisory team. There will be flexibility in which bacterial phages will be selected and which antibiotic–phage combinations are prioritised for detailed study, which defence or resistance mechanisms receive the most mechanistic attention, how the balance is struck between population-level evolution experiments and single-cell imaging, and how the PPIE strand is designed. During the initial Prep period, the student

	will work with the supervisory team to refine the final research questions, prioritise objectives, identify training needs and develop an experimental plan that reflects their interests and emerging expertise. The project will remain open to revision as findings emerge, giving the student genuine ownership while retaining a coherent focus on the evolution of bacterial pathogens during antibiotic–phage combination treatment.
Can be completed part time?	Yes
Supervisory Team	
Lead Supervisor	
Name	Professor Edze Westra
Affiliation	Exeter
College/Faculty	ESE
Department/School	CEC
Email Address	E.R.Westra@exeter.ac.uk
Co-Supervisor 1	
Name	Professor Stefano Pagliara
Affiliation	Exeter
College/Faculty	HLS
Department/School	LSI
Co-Supervisor 2	
Name	Professor Tiffany Taylor
Affiliation	Bath
College/Faculty	Milner Centre for Evolution
Department/School	Department of Life Sciences
Co-Supervisor 3	
Name	Professor Mark Szczelkun
Affiliation	Bristol
College/Faculty	Faculty of Life Sciences
Department/School	School of Biochemistry