Project Details	
Project Code	IIAR27Ex Padfield
Title	How does temperature shape selection for resistance across different antibiotics, strains, and species
Research Theme	Infection, Immunity & Antimicrobial Resistance
Project Type	Wet lab
Summary	Climate warming is linked to rising antimicrobial resistance (AMR), but the biological mechanisms remain poorly understood. This project asks how temperature shapes selection for resistance across different antibiotics, strains, and species of Klebsiella, a clinically important pathogen. Combining eco-evolutionary theory, lab experiments, and genomic sequencing, you will help build and validate a model predicting how antibiotic selection shifts with temperature — advancing our ability to control AMR in a warmer world.
Description	Recent studies have found a positive association between environmental temperatures and levels of AMR in environmental and pathogenic bacteria. If causal, resistant bacteria might gain advantages in a warmer world, which risks us underestimating the future AMR burden. Resistance in the wider environment is commonly inferred and predicted using phenotypic and genome data that has been collected under clinical conditions (specialist media at 37ºC). This oversight ignores that the environmental variation - and temperature in particular - likely modulates selection for AMR through altering the efficacy and concentration of the antibiotic compounds, how they impact susceptible bacteria, and the metabolic costs of resistance. By integrating eco-evolutionary principles with predictive modelling and high-resolution phenotyping, this project will uncover mechanisms underlying these broad scale patterns. Selection for - and evolution of - antimicrobial resistance (AMR) occurs when resistant bacteria have higher fitness than susceptible bacteria. Multi-stressor ecology predicts that this selection is not fixed, but will instead change with other abiotic and biotic variables. Our preliminary work supports this; we found that the minimum inhibitory concentration (MIC) of kanamycin varies 5-fold across the thermal tolerance range of E. coli. This project's key research question is: how does temperature modulate the efficacy of antibiotics and the strength of selection for resistance across antibiotic classes, bacterial strains, and species? This will build a predictive understanding of how temperature alters the selection, spread, and evolution of antibiotic resistance, with direct implications for surveillance, antibiotic stewardship, and risk assessments. We suggest three different components of this project, but will encourage any PhD student to lead the design of their own project. The project can take advantage of available libraries of >3000 well-characterised isolates of Klebsiella spp. isolates collected from the environment and from humans. These isolates cover 15 species, including the human pathogen K. pneumoniae, have variation in resistance profiles, and have high-quality genomes from previous work. This gives us an unprecedented study system to understand how temperature alters the selection of AMR across a diverse set of closely-related isolates, including many opportunistic pathogens. Objectives

	1. Test how the degradation of antibiotics changes across temperatures. Higher temperatures generally result in faster antibiotic degradation, but this has rarely been tested under environmentally realistic conditions. 2. Measure how temperature changes antibiotic selection. We will quantify how the antibiotic dose response curve changes across temperatures and look for generalities between antibiotic classes, Klebsiella strains and species to understand genetic and environmental variation in selection for resistance. 3. Integrate temperature effects on AMR selection into a machine learning model to better predict antibiotic susceptibility of Klebsiella in a warming world. We will combine whole genome sequencing and phenotypic data from previous Objectives to build a machine learning model to predict antibiotic susceptibility across temperatures. This model can be validated on a subset of previously untested Klebsiella strains. The successful candidate will be primarily based in the lab of Dr Daniel Padfield at Exeter's Cornwall campus, who is a NERC Independent Research Fellow with an inclusive and expanding team working on microbial ecology and evolution, AMR, and climate change, as well as a passion for open and reproducible science. This interdisciplinary project will combine experiments, sequencing, and bioinformatics and predictive modelling to increase our mechanistic understanding of how temperature alters the selection and spread of antibiotic resistance in the Klebsiella group. The experimental work will be supervised by Padfield, Kasprzyk-Hordern and Buckling utilising approaches well developed from previous work, such as chromatographic techniques and mass spectrometry to measure antibiotic concentrations, phenotypic assays to measure dose responses across temperatures, and metagenomic sequencing. Statistics, bioinformatics, and modelling training will be provided by Padfield, Feil, and Iqbal. Depending on the student's interests, there are opportunities to do long-term experimental evolution to understand how warming impacts AMR resistance evolution, mine existing metagenomic datasets to test questions about temperature and AMR, and use results from experiments to inform risk models for human exposure to opportunistic pathogens and AMR.
Can be completed part time?	Yes
Supervisory Team	
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