**University of Leicester**

**BBSRC MIBTP Studentship Project 2024-5 entry.**

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| **Project Reference** |  |

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**Section 2 – *Project Information***

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| **Project Title** | **Bacterial communication and the switch between host species** |
| **Project Summary** | |
| *Background:* Many bacteria have the ability to adapt to and transition between different host species. *Staphylococcus aureus*, a Gram-positive bacterium primarily known as a human pathogen, also demonstrates increased capacity for causing diseases in various livestock species, including mastitis in cows, goats, sheep, and rabbits, skin infections in pigs and rabbits, as well as invasive infections in chickens (1). Moreover, infections linked to antibiotic-resistant strains of *S. aureus* in livestock are increasingly prevalent and cows represent a potential reservoir of new pandemic clones in humans. It is now understood that bacteria rarely exist in isolation. Instead, they live in complex polymicrobial communities where they can engage in interspecies signalling. Bacterial cell-to-cell signalling is known to play a pivotal role in influencing phenomena such as biofilm formation, virulence, and antibiotic resistance. Gram-positive bacteria engage in such communication by producing small peptides that are sensed by neighbouring cells. Several bacterial peptides have been elucidated and homologues are found in different bacterial species (2). Previously, it has been demonstrated that there is cross-talk between bacterial species, and that some bacteria can also block the signalling systems of others (3).  The increasing global burden of antimicrobial resistance and cross-species transmission poses a considerable risk for the agriculture sector as well as the broader public health landscape. Therefore, it is crucial to understand the fundamental role of interspecies communication in host adaption and cross-species transmission.  The *hypothesis* of this project posits that the ability of bacteria, such as *S. aureus*, to adapt to and switch between several hosts is significantly influenced by interspecies signalling events.  *Objectives:* The main objectives of this project are:  1) Determine the chemical, genetic, and environmental cues that facilitate communication between different organisms.  2) Examine the impact of bacterial signalling on bacterial fitness and survival under physiological conditions.  3) Analyse how these findings influence the ecological dynamics and transmission risks of human and livestock-associated bacteria.  *Methods:* We will study the transcriptional changes in response to communication signals, as well as assessing fitness and survival advantages over time in mono- and co-cultures mimicking relevant environmental and host conditions. The project employs a multidisciplinary approach, integrating bioinformatic analysis with experimental techniques such as next-generation sequencing, transcriptomics, proteomics, and mass spectrometry. This comprehensive strategy aims to provide profound insights into the communication network and enables the identification and characterisation of bacterial signalling molecules that play a pivotal role in shaping bacterial adaption and transmission between hosts.  *Impact:*  By investigating the influence of interspecies communication on host adaption and transmission events we will be able to *i)* reveal unique host specific patterns of bacterial signalling and *ii)* guide the design of strategies that prevent the emergence of new pandemic clones and cross-species transmission.  Techniques that will be undertaken during the project  The student will undergo comprehensive training in biosafety practices for bacteriological work which includes proficiency in bacterial genetics. Furthermore, the student will be instructed in cell culture techniques, RNA-sequencing, as well as proteomics and mass spectrometry methodologies. The training in confocal and scanning microscopy provided by the imaging facility at the University of Leicester will equip the student with proficiency in advanced microscope techniques. Additionally, the student will gain computational skills for analysing gene expression data and the training in mass spectrometry will cover all aspects from bacterial molecule extraction and processing to data analysis and molecular networking techniques. | |
| **References** | |
| (1) *Howden et al. Staphylococcus aureus host interactions and adaption. Nature Reviews Microbiology. 21:380-395 (2023).*  (2) *Schilcher et al. Processing, Export, and Identification of Novel Linear Peptides from Staphylococcus aureus. mBio. 11:e00112-20 (2020).*  (3) *Piewngam, et al. Pathogen elimination by probiotic Bacillus via signalling interference. Nature 562:532-537 (2018).* | |

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