Phenotypic and Genotypic diversity in Moraxella catarrhalis: Using Population Biology to Understand Antimicrobial Resistance and Pathogenesis

Supervisory team:
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Submit applications for this project to the University of Bristol

Project description:

The global spread of antibiotic resistance is a significant and increasing threat to global human health. Challenging threats to our health include opportunistic bacteria such as Moraxella catarrhalis. These bacteria can colonise us without ever causing disease and sometimes they can lead to severe infections such as recurrent otitis media, exacerbation of pulmonary disorders and sepsis. Resistance to some antibiotics is now ubiquitous amongst strains of M. catarrhalis. There is an urgent need to understand the biology of this under-appreciated pathogen to prevent the spread of antibiotic resistance and to develops novel preventative strategies. The population and genomic dynamics of M. catarrhalis and their relationship with disease versus benign colonisation is poorly understood. complex and non-clonal due to the high level of genetic recombination that occurs between isolates. Studies focussing on limited gene numbers such as Multi-locus sequence typing (MLST) have offered some insights into the population structure of M. catarrhalis. However, genetic plasticity may allow these bacteria to generate a range of phenotypes though gene phasing and recombination, the fittest of which can be selected for in vivo, facilitating rapid adaptation within the different mucosal niches infected by these bacteria.

This PhD aims to profile the antibiotic resistance of M. catarrhalis isolates from distinct sites of isolation and disease states and study the genomic and virulence related phenotype of these isolates. Linkage of these traits to the dynamics of infection transmission will be examined through bioinformatic approaches. The successful candidate will determine the presence of key virulence factors by distinct immunoassays and proteomics, as well as infect cell lines mimicking in vivo conditions with a diverse range of clinical isolates. Minimal inhibitory concentrations (MICs) for clinically relevant antibiotics will be assayed. For each isolate selection the genome will be sequenced plus any associated plasmid identified. Finally, data for MIC, virulence factor presence genomic diversity and cell line infectivity will inform models to investigate potential evolutionary mechanisms of action.

The outcomes are of translational importance: we will improve understanding of in vivo selection in relation to antimicrobial susceptibility and virulence. In addition, we will identify if niche specificity is an important consideration for bacterial phenotypes that may then be utilised in using antimicrobials. Overall, this project will provide multi-discipline training and improve our understanding of Moraxella population biology.