Project Details	
Project Code	MRCIIAR25Ba Preston
Title	Airborne transmission of pathogens: defining microbial and environmental factors affecting survival in aerosols.
Research Theme	Infection, Immunity, Antimicrobial Resistance & Repair
Summary	Numerous bacteria transmit between hosts via the air, representing a key step in the pathogen lifecycle. However, we know little about the microbial and environmental factors that impact pathogen survival during airborne transmission. This is largely because it is difficult to study them in tiny droplets (aerosols), which are an environment unlike any other. This project combines molecular microbiology, genomics and a unique aerosol survival model to study how bacteria adapt under the unique conditions found in aerosols. Elucidating these processes and how the environment affects them will aid the development of novel interventions to interrupt airborne transmission.
Description	During human-to-human aerosol transmission bacteria are present in droplets of high surface-to-volume ratio and must survive in droplets with compositions uniquely accessed in the aerosol phase. For example, typical salts in respiratory fluids can reach supersaturated concentrations many times their solubility limits at ambient relative humidities (RHs) with the aerosol remaining in solution form rather than crystallising. This places a significant osmotic stress on bacteria that cannot be replicated in a bulk solution. Most studies of bacteria use growth conditions that are very different to those experienced in aerosol droplets, typically growth on the surface of solid media (e.g. agar) or submerged in nutrient rich, osmotically balanced broths. Unsurprisingly, these studies have largely failed to identify the processes important to the airborne spread phase of infection. Combining molecular microbiology and functional genomics and using a state-of-the-art aerosol droplet generation and control system developed in Bristol (CELEBS) we aim to study how airborne bacteria including Bordetella pertussis, Haemophilus influenzae, and Moraxella catarrhalis adapt, or are selected for phenotypically, during airborne transmission. The CELEBS system generates individual aerosol droplets in which single, or a few, microbes are trapped. The aerosols can be generated using carefully formulated fluids, designed to match the composition of respiratory fluids. The environmental conditions (e.g temperature, humidity) can be controlled and in this system the aerosol droplets undergo dehydration creating the large changes in internal conditions experienced by microbes during natural aerosol transmission. Understanding the phenotypic differences displayed by airborne organisms could better inform vaccine design, infection control procedures, and epidemiological modelling, and facilitate the rational design of drugs or even engineering strategies (e.g. heating and air conditioning usage in public spaces) to reduce the longevity of airborne organisms, thereby reducing their transmission rate. In this project, we will explore the following aims: Aim 1. To determine the survival of bacteria in aerosols, and the impact of temperature and humidity. We will subject strains of B. pertussis, H. influenzae and M. catarrhalis to a range of temperature and humidity conditions reflecting those found indoors and outdoors during peak

	disease months in the UK. Using the CELEBS platform, the survival of bacteria in aerosols will be compared. The aerosols will be generated using mimics of respiratory fluids. Aim 2. Transcriptional profiling of adaptation to the aerosol environment. Using the latest RNA sequencing approaches for use on low biomass samples, the processes involved in adaptation of the bacteria to aerosol survival will be defined. Aim 3. Determine the microbial factors and processes required for bacterial survival. Information from the transcriptional profiling in Aim 2 will be used to identify microbial factors and processes involved in adaptation to the aerosol environment. Their involvement will be validated by constructing defined mutations in these factors or regulators and comparing aerosol survival of mutants to the WT. The project offers excellent opportunities for the student to develop ownership and to direct the project. They will have scope to focus on one or two bacterial species or to identify other bacterial respiratory pathogens to include. They will be able to identify through their own research specific microbial factors and test their involvement in aerosol survival. They will have scope to focus on the conditions experienced by the bacteria within aerosols and focus on defining the role of specific ions or molecules and/or developing novel formulations of artificial respiratory fluids. The project can pivot to focus on the functional genomics aspect, for example using high throughput mutation screening.
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