

Defining the role of membrane stability in the ability of *Staphylococcus aureus* to form part of the human microbiome

Supervisory team:

Main supervisor: Prof Ruth Massey (University of Bristol)

Second supervisor: Dr Maisem Laabei (University of Bath)

Dr Darryl Hill (University of Bristol)

Collaborators: Dr Jean van den Elsen (University of Bath)

Host institution: University of Bristol

Project description:

Background: The human microbiome consists of all of the microorganisms that exist in symbiosis with us on the non-sterile parts of our bodies, including our skin, respiratory tract, digestive tract and genitourinary system. The composition of the microbiome at these sites is key to our health, such that perturbations can increase our susceptibility to many inflammatory and infectious diseases. Despite its importance, our understanding of how bacteria within the microbiome maintain their presence despite the onslaught of our immune system, and in the face of competition from other microorganisms remains unclear. However, one feature that is likely to be key to this is their ability to rapidly sense and respond to environmental changes. As unicellular organisms, this ability of bacteria is entirely reliant on their membrane, and in particular the stability of this membrane as it acts as a platform for all the proteins and molecules that are embedded there that allow it to sense and respond.

Model organism: The bacterium *Staphylococcus aureus* is a member of the nasal and skin microbiome of approximately 30% of the human population. Several molecules have been identified as playing a key role in the membrane stability of *S. aureus* including its characteristic golden pigment, staphyloxanthin, and a recently identified a small (105 residue) protein that that is key to the stability of the bacterial membrane, MspA (membrane stabilising protein).

Aim: The overarching aim of this project is to determine the importance of membrane stability to the ability of *S. aureus* to withstand both immune attack and competition from other members of the nasal microbiome.

Competition: Competitive strategies that exist between bacteria can range from the rate at which the bacteria consume the nutrients available within the shared environment, through to the direct physical attack on one bacterium by another. This aspect of the project will examine the relative competitive abilities of a range of *S. aureus* mutants with varying levels of membrane stability when co-cultured with other members of the nasal microbiome.

Immune attack: Several aspects of our immune system that protects us from infection focus on attacking the membrane of bacteria to kill them. This presents a challenge for members of our microbiome who must withstand this attack. This aspect of the project will examine the ability of a range of *S. aureus* mutants with varying levels of membrane stability to withstand membrane attack by aspect of the human immune system.