PCL/25/21 - Identification and prioritisation of macrophage microbicidal mechanisms required for clearance of intracellular Staphylococcus aureus.

The bacteria Staphylococcus aureus (S. aureus) is a common cause of serious infections, acquired both in the community and in hospital, often affecting people living with other long-term medical problems. These bacteria can enter the bloodstream then spread around the body, causing disease at multiple locations (e.g. bones, joints, heart, spine). S. aureus is the most common cause of death due to bacterial infection worldwide. Despite prolonged and appropriate antibiotic treatment, infection can recur. Antibiotic resistance makes treatment even more difficult.

Macrophages are a type of white blood (immune) cell, found throughout the body, which provide a first line of defence against invading bacteria. They can eat and kill most types of bacteria to prevent their spread around the body. However, S. aureus has a special ability to survive inside macrophages despite being eaten, disrupting the mechanisms macrophages usually use to kill bacteria, and sheltering from commonly used antibiotics.

Evidence suggests these bacteria surviving inside macrophages are important in the development of serious infection. A new approach to treatment would be to boost macrophage killing mechanisms to eradicate the bacteria inside them. This could reduce recurrences and death due to infection, and reduce our reliance on antibiotics. However, it is not known which macrophage responses are the best targets for this type of treatment approach.

My proposed research will study macrophage gene activation patterns and changes in metabolism that contribute to successful bacterial killing. I aim to identify which macrophage responses are most effective in killing S. aureus and could therefore be good targets for treatments. This will inform future studies to search for medicines to boost these important immune responses as part of a new approach to treating S. aureus disease.