04 Understanding and targeting antibiotic resistant bacteria

Joan Geoghegan

The prevention and treatment of infectious disease is a major challenge to healthcare worldwide. The threat of rising antibiotic resistance in bacteria means that new measures for controlling and treating infection are urgently needed.

My laboratory at the Department of Microbiology at Trinity studies antibiotic resistant bacteria, in particular, methicillin resistant *Staphylococcus aureus* (MRSA). MRSA is a leading cause of serious life-threatening infections in hospitals and serious skin infections in the community. We study proteins attached to the surface of the bacteria that interact with human cells and proteins. These interactions are important because the bacteria need to attach to sites in the body to begin to establish an infection. After they attach, the MRSA bacteria can begin to link to each other to build accumulations of bacteria called "biofilm". These biofilm communities grow on heart valves, artificial joints, human skin and other tissues and are able to avoid being killed by antibiotics and the human immune system.

Work in my laboratory has provided new insights into this process and has contributed to the identification of the parts of the bacterial proteins that are crucial for attaching to surfaces and building the biofilm. This information gives us the opportunity to precisely target the molecular interactions occurring between bacteria and the human body. In the laboratory setting, it has proved possible to prevent adhesion and biofilm formation by bacteria by blocking binding sites on bacterial proteins. This approach works even when conventional antibiotics are not effective due to resistance. The next steps will involve identifying new drugs with the same mechanism of action that are suitable for use in the treatment of human patients.

We are also interested in understanding how infectious bacteria avert the normal killing mechanisms of human immune cells. For example, we have recently found that the bacterial genes that allow MRSA to resist the antibacterial effects of copper also help the bacteria to withstand killing by human immune cells. Our ongoing research on this topic will hopefully inform the future development of new drugs to treat human infections caused by antibiotic resistant bacteria.

Preventing skin infection in atopic dermatitis – Atopic dermatitis (a form of eczema) is the most common skin disease in children. Skin infections are a frequent problem for children with atopic dermatitis and occur when bacteria begin to grow on the skin. This increases symptoms such as redness and inflammation. The most usual cause of infection is *Staphylococcus aureus*.

Our research team are currently interested in learning how *Staphylococcus aureus* attaches to cells on the outermost surface of human skin known as corneocytes. We have identified a number of bacterial proteins that recognise skin proteins exposed on corneocytes in the skin of atopic dermatitis patients. We hope that by understanding the interactions between *Staphylococcus* and the skin we can target these to develop new therapies to reduce skin infection in atopic dermatitis.

Joan Geoghegan received her BA and PhD from Trinity and was appointed Lecturer in Microbiology in 2012. She is Assistant Professor at the School of Genetics and Microbiology and leads the Pathogenesis research group. Her research is funded by the Irish Research Council, British Skin Foundation and European Union Horizon 2020. She has published more than 50 articles in peer-reviewed journals. Her research focuses on understanding how antibiotic resistant bacteria cause infection in humans.
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Fig 1 – Biofilm formation by Staphylococcus aureus (A). The bacteria (gold) attach to a surface inside the body (such as human cells, shown here) during the initial stages of infection. Once they attach, the bacteria begin to grow and link together. They build large accumulations of bacteria known as biofilms. Precisely targeting the binding sites on bacterial proteins can prevent attachment to the host surface (B) or prevent linkages from forming during biofilm formation (C).

Fig 2 – False colour scanning electron micrograph of *Staphylococcus aureus*.

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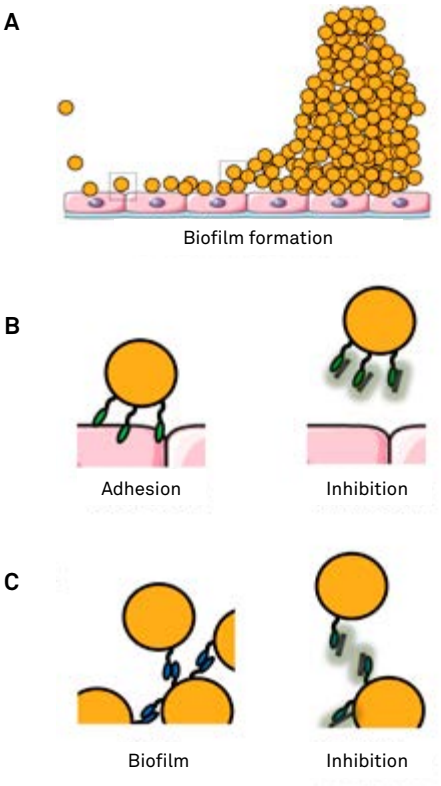

Fig 1

Fig 2

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