Research reveals superbug's secret to success

Research involving scientists from New Zealand and Denmark has unlocked the mechanisms *Staphylococcus aureus* uses to counteract the body's immune responses.

Professor John Fraser, Deputy Director of the Maurice Wilkins Centre at The University of Auckland, says the HRC-funded work conducted in collaboration with the University of Aarhus in Denmark, focused on a small protein from the superbug that blocks the work of antibodies in our immune system.

S. aureus is a major pathogen worldwide and one of the hardest to treat. It causes many hospital-acquired infections and is also one of the more robust, virulent and pathogenic infections that occur in the community. "It grows anywhere in the body – from bone to blood to soft tissue – you name it, it can grow there," he says.

"It is quite an extraordinary organism because about 30 per cent of the population carries it around in their noses. It is essentially a commensal organism for most people. We still don't understand what triggers S. aureus, that sits quietly in the nose and doesn't cause any trouble, to suddenly erupt into a full-blown florid infection which becomes extremely difficult to treat and often is life-threatening."

But it is the ability to develop antibiotic resistance that has given S. aureus its superbug status. "Staph is the master, with many different mechanisms. It's capable of shuttling genetic cassettes around between strains that carry antibiotic resistance or virulence genes making it extremely difficult to treat by traditional antibiotics." He says there are strains of S. aureus that are now resistant to most common antibiotics and these cause a lot of morbidity.

It has a vast array of virulence and pathogenicity factors that are extremely potent against host immunity and Professor Fraser says the one they have recently published on, SSL7 (Staphylococcal Superantigen-Like protein 7), is extraordinarily potent. This binds to Immunoglobulin A (IgA), a defense antibody in the gut and lung, and also binds to complement C5, one of several proteins that "complement" the work of antibodies in destroying bacteria.

"So SSL7 binds two important immune molecules at the same time forming a large trimeric structure, taking out both IgA and complement C5, and it is an extremely potent inhibitor of complement activation. It essentially leaves the host with a disabled complement system, so we think SSL7 is a pretty important virulence factor for Staph."

The research team and Professor John Fraser (far right)

Key words:

- *Staphylococcus aureus*, superbug, pathogen, immune system, antibiotics, virulent

Aims of this research:

- To establish the mechanisms *Staphylococcus aureus* uses to counteract the body's immune responses

Their research also suggests that the organism has two clear states. "One is the 'invasive state' where it is producing all these pathogenicity factors that allow it to invade effectively. Once a niche is established, it switches to the 'evasive state' where it wants to sit happily and grow. That's where molecules like SSL7 are produced which are designed to keep the innate immune response at bay so the organism can grow in a relatively unhindered environment."

Understanding the importance of SSL7 not only provides them with a very good new vaccine target but it also raises the possibility that this protein it produces can be used therapeutically itself. "There are lots of situations where you have an inflammatory response caused by the activation of complement and C5 which induces all sorts of unwanted conditions. The market for inhibitors of complement activation is very large indeed, so another avenue for this work is the potential for using this molecule or modified versions of this molecule as an anti-inflammatory agent."

The findings were published in 2010 in the journal *Proceedings of the National Academy of Sciences USA*.

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