Understanding virulence of group A streptococcus, the flesh eating bacterium

Streptococcus pyogenes (group A streptococcus, or GAS) is a common, normally harmless, bacterium. But as University of Auckland molecular biologist Dr Thomas Proft explains, they have a deadly side.

“Many people carry them around with them. They can cause mild diseases like pharyngitis and tonsillitis, but they can also cause quite serious, invasive diseases like the flesh eating disease necrotising fasciitis, and toxic shock syndrome.”

Dr Proft, a Senior Research Fellow in the University of Auckland’s Department of Molecular Medicine and Pathology is carrying out vital research into the reasons for these more virulent conditions using funding provided through an HRC Sir Charles Hercus Research Fellowship.

“If you go back to the 19th century for example GAS caused huge epidemics of rheumatic fever and scarlet fever. In the 20th century, antibiotics brought a decline, but for some reason since the late 80s there is a re-emergence of GAS and, in particular, more aggressive diseases like toxic shock.”

Dr Proft says it appears that these more aggressive strains have acquired novel virulence factors. Many of them sit on mobile DNA elements which get shuffled around between strains and, sometimes, between organisms.

With more of the S. pyogenes genome being uncovered Dr Proft has been working to identify ‘superantigens’ (SAgs), proteins that send our immune system haywire, putting the body into shock and eventual organ failure.

In the process he identified some structurally similar proteins in S. aureus which, while not superantigens, are nonetheless toxins. A vital collaboration with Prof Ted Baker at the University’s Structural Biology Lab, has enabled them to crystallise three of them and publish their structures.

Understanding these proteins opens the way for the development of a vaccine. For example, Dr Proft and his team were the first to discover the presence of active circulating superantigens in blood serum from toxic shock patients and these could be used as targets for vaccinations.

“We’ve produced a number of mutants in which we knocked out certain residues so the SAgs can’t bind to the T-cell receptors anymore and therefore are no longer toxic. These mutants could be used as the basis for a toxoid vaccine. It would help the body produce neutralising antibodies against these toxins.”

These mutants are currently used in colleague Prof. John Fraser’s lab as peptide delivery vehicles to enhance peptide immunogenicity for the development of a novel strategy for vaccination and tumour immune therapy.

Dr Proft says that there are now three whole GAS genomes completed and that opens up a whole new area with researchers looking for new genes.

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