Specially designed protein fights several species of bacteria

December 13 2017

As resistance to existing antibiotics increases, new approaches to serious bacterial infections are needed. Now researchers at Lund University in Sweden, together with colleagues at the University of Massachusetts Medical School (UMMS) in the US, have investigated one such alternative.

"We were able to show that a tailor-made protein which previously worked against various kinds of Gram-negative bacteria also had promising results in mouse models against a Gram-positive pathogen", says David Ermert, one of the researchers behind the study published in *The Journal of Immunology*.

An important part of our innate immune system is known as the complement system. It protects us from pathogenic microorganisms such as bacteria which can enter the body but, because it is powerful, it must be carefully controlled so as not to attack our own cells. One way this happens is through a complement control protein known as Factor H, which circulates in the bloodstream and protects the body's own cells from complement attack. Some bacteria have succeeded in "kidnapping" this process: by covering their surface with the Factor H protein, they are able to deceive the immune system.

"Most, if not all, pathogenic bacteria have developed strategies to counteract complement attack, allowing them to establish infection", says Anna Blom, professor at Lund University who participated in the study.

Previous research has shown that a specially designed protein, developed and patented by the team of Sanjay Ram, professor at UMMS, and known as a fusion protein, can be used effectively as treatment in mice suffering from Gram-negative bacteria which can cause gonorrhoea, meningitis and respiratory infections. These bacteria specifically use Factor H to evade detection and removal from the immune system.

"With this fusion protein we are targeting an important virulence mechanism shared by several medically important microbes, which may be a novel way to combat the global threat of antimicrobial resistance. The promising data in rodent models against several pathogens provides us optimism to proceed further with product development", says Sanjay Ram, professor at UMMS.

Antibacterial effect

Now the Lund University researchers, together with the research team in Massachusetts, have shown that the fusion protein also functions against Gram-positive bacteria, specifically group A streptococci. The researchers added group A streptococci—that can cause everything from common tonsillitis to life-threatening sepsis—to human blood samples. They then analysed what happened when they added the fusion protein to the infected blood.

"We were then able to observe that the fusion protein drastically reduced the amount of bacteria in the blood. The protein removes Factor H from the surface of the bacteria and activates the immune system so that it kills the bacteria. We also investigated how the protein functioned in acute sepsis infection in mice, and were able to show a reduction in mortality", says David Ermert.

The next step will be to see whether the fusion protein functions against those multidrug-resistant resistant bacteria, which according to the

World Health Organisation (WHO) constitute the greatest threat to humanity.

"Currently, bacteria are cultivated to identify the pathogen that has infected the patient, which determines the appropriate treatment. But sometimes, it is not possible to wait for the results of the analysis, which can take up to 24 hours. Since this fusion protein functions against several species of bacteria, one could envision using it in the future to treat a broader spectrum of bacteria", says David Ermert.

More information: Anna M. Blom et al. Factor H–IgG Chimeric Proteins as a Therapeutic Approach against the Gram-Positive Bacterial PathogenStreptococcus pyogenes, *The Journal of Immunology* (2017). DOI: 10.4049/jimmunol.1700426

Provided by Lund University