Mimic molecules to protect against plague

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Bacteria that cause pneumonic plague can evade our first-line defences, making it difficult for the body to fight infection. In fact, a signature of the plague is the lack of an inflammatory response. Now, scientists have discovered a way to protect against death following infection with plague bacteria, by using molecules that can mimic the pathogens. According to research published in the July issue of *Microbiology,* these molecules make antibiotics more effective and can even be used to protect against other diseases.

The plague, caused by Yersinia pestis, has killed an estimated 200 million people worldwide. Although treatments have improved, it remains a threat to public health. It can be transmitted from human to human in aerosols and is therefore listed as a Category A bioterrorism agent.

"Yersinia pestis is successful in causing disease in mammals because it can dampen the normal non-specific immune response to infection," said Dr Scott Minnich from the University of Idaho, USA. "We found an intranasal therapy that stimulates the innate immune response and protects against pneumonic plague."

Following infection, lipid A (which is part of the bacterial surface) binds to receptors on our immune cells, triggering an immune response. Yersinia pestis circumvents this, stopping our cells from taking action. Molecules have been developed that mimic lipid A, eliciting a strong immune response that can prevent death in infected animals. Dr Minnich and his colleagues studied the effect of a nasal spray containing two such molecules, CRX-524 and CRX-527, on mice infected with Yersinia pestis.

"Treatment with synthetic modified lipid A molecules can directly protect animals against pneumonic plague infections," said Dr Minnich. "We also found that stimulating innate immunity using this nasal spray enhanced conventional antibiotic therapy. When it is given along with antibiotics, fewer doses and less antibiotic protects against pneumonic plague."

The results of this study suggest that synthetic modified lipid A compounds may provide a new therapeutic tool against plague infection. In a control group that did not receive the treatment, only 23% of mice survived for 3 days. When given the mimic molecules, up to 93% of mice survived for 3 days, 70% for 4 days and 34% recovered completely. This highlights the importance of the non-specific, first-line immune defences during the critical early phase of infection. Stimulating this response can over-ride a microorganism's counter measures to evade or disable the immune response.

Other studies have shown related therapeutic compounds are also effective against influenza and Listeria monocytogenes. "This work is still at a very basic animal model testing stage with regards to plague," said Dr Minnich. "What is exciting is that these studies provide insight into bacterial/host interactions in the disease process and promise new strategies to combat a variety of infectious agents."

Source: Society for General Microbiology