

Bacteria responsible for common infections may protect themselves by stealing immune molecules

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Bacteria responsible for middle ear infections, pink eye and sinusitis protect themselves from further immune attack by transporting molecules meant to destroy them away from their inner membrane target, according to a study from Nationwide Children's Hospital. The study, published in the November issue of *PLoS Pathogens*, is the first to describe a transporter system that bacteria use to ensure their survival.

When the body senses an infection, one of the first lines of defense is to send immune molecules called host-derived antimicrobial peptides (AMPs) to target and kill bacteria. However, bacteria have learned to resist AMPs through a series of countermeasures such as remodeling their outer membrane surface to be less permeable. Nontypeable Haemophilus influenzae (NTHI) is such a bacterium.

NTHI resides in the human upper airway, typically without causing any harm. However, NTHI has the ability to change from a non-harmful bacterium to a disease causing pathogen, responsible for pink eye, sinusitis, middle ear infection and complications of cystic fibrosis. "When transitioning to a harmful pathogen, NTHI defends against increased production of AMPs by using the Sap, which stands for sensitivity to antimicrobial peptides, proteins to arm against attack, "said Kevin M. Mason, PhD, principal investigator in the Center for Microbial Pathogenesis at The Research Institute at Nationwide Children's Hospital and lead study author. "Yet, it's unclear just how the



Sap transporter complex provides protection against AMPs."

To help explain the mechanisms that NTHI uses to protect itself from AMPs, Dr. Mason's team examined an animal model of middle ear infection. They had previously shown that NTHI bacteria lacking the protein SapA were susceptible to AMP attack. In the study, they describe the Sap transporter system that recognizes and transports host immune defense molecules into the bacterial cell. This system is necessary for the bacteria to survive in the host.

"It seems that NTHI senses the presence of these immune molecules, steals them from the host and arms itself to protect against future attacks," said Dr. Mason. "NTHI imports AMPs into the bacterial cell and then degrades them in the interior of the cell. By remodeling its membranes, the bacterium appears as already attacked, which protects it from being bothered by additional AMPs. Basically, transporting AMPs acts as a counter strategy to evade innate immune defense and ultimately benefits the bacterium nutritionally." This study provides the first direct evidence that the protein SapA contributes to bacterial survival by providing protection from AMPs in the host.

Dr. Mason says that targeting the Sap transport system may provide a way to use AMP derivatives as alternatives to antibiotics to treat NTHI infections. "Our long-range goal is to block this uptake system and starve the bacterium of essential nutrients. If we could develop a small molecule inhibitor that could block binding and transport, we could render NTHI susceptible to <u>immune attack</u>, while preserving the body's normal bacteria that are often disrupted by conventional antibiotic use."

Provided by Nationwide Children's Hospital

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