



Staph Bacteria: Blood-Sucking Superbug Prefers Taste of Humans



"Staph" bacteria feed on blood. They need the iron that's hidden away inside red blood cells to grow and cause infections. It turns out that these microbial vampires prefer the taste of human blood,

The researchers report in the Dec. 16 issue of *Cell Host & Microbe* that *Staphylococcus aureus* (staph) favors human hemoglobin -- the oxygen-carrying protein that contains iron -- over hemoglobin from other animals. The findings help explain why staph preferentially infects people and suggest that genetic variations in hemoglobin may make some individuals more susceptible to staph infections. Staph lives in the noses of about 30 percent of all people -- usually without making them ill, said Eric Skaar, Ph.D., M.P.H., associate professor of Microbiology and Immunology.

"A big question in staph biology is: why do some people continuously get infected, or suffer very serious staph infections, while other people do not? Variations in hemoglobin could contribute," he said. If that is the case -- something Skaar and his team plan to explore -- it might be possible to identify patients who are more susceptible to a staph infection and provide them with prophylactic therapy in advance of a hospital stay or surgery.

Staph is a significant threat to global public health. It is the leading cause of pus-forming skin and soft tissue infections, the leading cause of infectious heart disease, the No. 1 hospital-acquired infection, and one of four leading causes of food-borne illness. Antibiotic-resistant strains of *S. aureus* -- such as MRSA -- are on the rise in hospitals and communities. "It seems as if complete and total antibiotic resistance of the organism is inevitable at this point," Skaar said.

This dire outlook motivates Skaar and his colleagues in their search for new antibiotic targets. The group has focused on staph's nutritional requirements, searching for ways to "starve" the bug of the metals (such as iron) that it needs. Staph obtains iron by popping open red blood cells, binding to the hemoglobin, and extracting iron from it. Skaar and colleagues previously identified the staph receptor for hemoglobin, a protein called IsdB.

In the current studies, they showed that *S. aureus* bacteria bind human hemoglobin preferentially over other animal hemoglobins, and that this binding occurs through the IsdB receptor. The preferential recognition of human hemoglobin by *S. aureus* is due to the increased affinity of IsdB for human hemoglobin compared to other animal hemoglobins. The team studied staph's ability to infect a mouse expressing human hemoglobin (a "humanized" mouse model) and found that these mice were more susceptible to a systemic staph infection than control mice.

The investigators also examined the hemoglobin-binding preferences of other microbes and found that bacterial pathogens that exclusively infect humans, such as the bacteria that cause diphtheria, prefer human hemoglobin compared to other animal hemoglobins. In contrast, pathogens such as *Pseudomonas* and *Bacillus anthracis*

(the cause of anthrax), which infect a number of different animals, "didn't exhibit a hemoglobin preference," Skaar said. The human hemoglobin-expressing mice will be a valuable research tool, Skaar said, because staph infects these mice in a way that more closely mimics the infectious process in humans. His team will also explore whether these mice provide a good model for studying the infectious biology of other pathogens.

Skaar hopes to utilize Vanderbilt's DNA Databank, BioVU, to examine whether genetic variations in hemoglobin contribute to individual susceptibility to staph infections. His team will continue to study the molecular interaction between hemoglobin and the IsdB receptor, with the aim of disrupting this interaction with new antibiotic therapeutics. Graduate student Gleb Pishchany is the first author of the Cell Host & Microbe paper. Other Vanderbilt authors include Amanda McCoy, Victor Torres, Ph.D., Jens Krause, M.D., and James Crowe Jr., M.D. The studies were supported by the National Institutes of Health, the American Heart Association and the Burroughs Wellcome Fund.

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