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Important step toward preventing and treating some MRSA post-implant infections

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New research published in the *Journal of Leukocyte Biology*, helps explain why Staphylococcus aureus infections take hold after prosthetic surgery that are resistant to both the body's natural defenses as well as antibiotic treatments. In the report, researchers from the University of Nebraska Medical Center show that the bacteria use a naturally occurring molecule called interleukin-10 to shield themselves and survive. This molecule is made by white blood cells called "myeloid-derived suppressor cells," which are produced by bone marrow. Understanding the process by which these bacteria take advantage of the body's normal defenses may lead to the development of new treatments that would ultimately reduce complications from infection that can occur after prosthetic surgery.

"The identification of MDSCs and their functions will hopefully allow us to transform infected tissues from an environment that helps bacterial persistence to one that enables one's own immune system to clear the infection," said Tammy Kielian, Ph.D., the senior scientist responsible for the work from the Department of Pathology and Microbiology at University of Nebraska Medical Center, Omaha, Nebraska.

To make this discovery, Kielian and colleagues used a mouse model of methicillin-resistant S. aureus orthopedic biofilm infection, which mimics complications that can arise following knee/hip replacement surgery. To identify the cell type(s) responsible for making IL-10 during S. aureus biofilm infection, they used a mouse that was specially engineered so that any cell that makes IL-10 would give off green light.

When they did this, they saw that nearly 70 percent of the cells in the tissue of infected mice were green. To determine the impact of high IL-10 production on the course of biofilm infection, the researchers used a mouse that is unable to make any IL-10. Removing IL-10 resulted in fewer myeloid-derived suppressor cells in infected tissue. This caused a larger number of cells important for bacterial killing (monocytes and macrophages) to arrive at the infection site, ultimately reducing the amount of bacteria.

"The immune system must balance killing of germs with limiting damage to normal tissues. The latter set of pathways often suppresses immune responses once germs have been eliminated. However, there are an amazing number of ways germs such as bacteria and viruses have exploited immune pathways to facilitate persistence and spread," said John Wherry, Ph.D., Deputy Editor of the *Journal of Leukocyte Biology*. "This new work defines a new way that S. aureus may exploit one of these pathways opening the door for new therapeutics based on this IL-10 pathway."

More information: C. E. Heim et al. Interleukin-10 production by myeloid-derived suppressor cells contributes to bacterial persistence during Staphylococcus aureus orthopedic biofilm infection, *Journal of Leukocyte Biology* (2015). DOI: 10.1189/jlb.4VMA0315-125RR

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