Medical Xpress

How our immune system backfires and allows bacteria like Salmonella to grow

February 6 2014

Our immune system wages an internal battle every day to protect us against a broad range of infections. However, researchers have found that our immune response can sometimes make us vulnerable to the very bacteria it is supposed to protect us from. A study published by Cell Press on February 6th in the journal *Immunity* reveals that the immune protein interleukin-22 (IL-22) actually enhances the growth of dangerous bacteria, like *Salmonella*, which causes food poisoning, and curbs the growth of healthy bacteria commonly found in the gut. The findings suggest that a supposedly protective immune response actually aids the growth of a gut pathogen by suppressing the growth of its closest competitors.

"Surprisingly, we found that interleukin-22 not only fell short in protecting the host against the spread of *Salmonella*, but it was also actually beneficial to these harmful bacteria," says senior study author Manuela Raffatellu of the University of California, Irvine. "Our findings have important implications for the development of treatment strategies against pathogens that can resist interleukin-22-induced responses."

To protect against disease-causing pathogens, IL-22 triggers the production of antimicrobial proteins that sequester metal ions such as iron, zinc, and manganese from microbes, starving them of these essential nutrients. But until now, it has been unclear how pathogens such as *Salmonella* escape IL-22's defenses.

To address this question, Raffatellu and her team first infected normal

mice, and mice genetically engineered to lack IL-22, with *Salmonella*. Whereas *Salmonella* outcompeted the common gut bacterium *Escherichia coli* (*E. coli*) in normal mice, the reverse was true for mice lacking IL-22. These findings suggest that IL-22 activity reduced the *E. coli* population, tipping the balance of gut microbes in favor of *Salmonella*.

The researchers then simultaneously infected the mice with normal *Salmonella* as well as mutant *Salmonella* strains lacking cell membrane proteins for absorbing iron and zinc from the environment. Normal *Salmonella* strongly outcompeted these mutant strains in normal mice, but this competitive advantage was reduced in mice lacking IL-22. These findings suggest that *Salmonella* relies on alternative pathways to overcome IL-22's defenses and acquire essential metal ion nutrients.

Even though IL-22 does not protect against all pathogens, the protein still plays a crucial role in controlling the spread of some harmful microbes. "Blocking interleukin-22 during infection would be too detrimental to the host, so a more promising therapeutic strategy would be to specifically target the alternative pathways used by *Salmonella* and potentially other pathogens to evade interleukin-22's defenses," Raffatellu says.

More information: *Immunity*, Behnsen et al.: "The Cytokine IL-22 Promotes Pathogen Colonization by Suppressing Related Commensal Bacteria." dx.doi.org/10.1016/j.immuni.2013.12.013

Provided by Cell Press

backfires-bacteria-salmonella.html