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# Why Salmonella wants its host to have a healthy appetite

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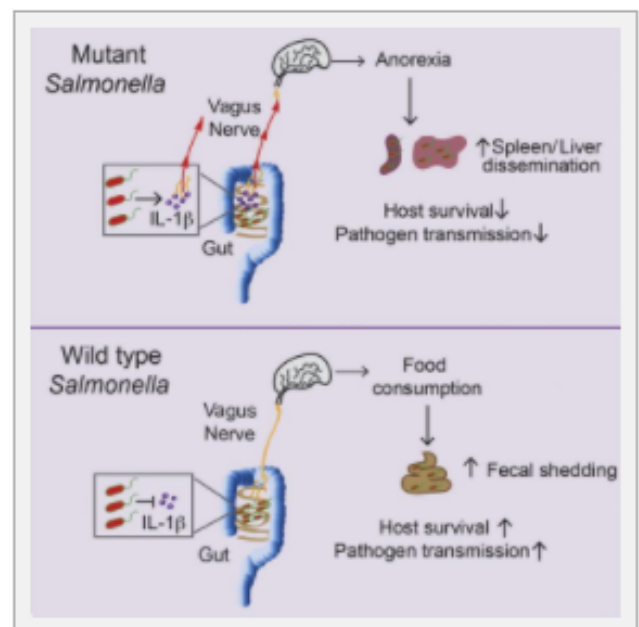


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Anyone who's ever had the flu or a bad cold can relate to the lethargy, sleepiness, and an increased sensitivity to pain that often result when a pathogen infects a host. A Salk Institute study, published January 26 in *Cell*, looked at one of the most well-known sickness behaviors--loss of appetite--in mice and found, surprisingly, that when a bacteria reduces its own virulence (how sick it makes the host) by blocking this anorexic response, it actually increases mouse survival and helps the pathogen spread because more food means more infected feces.

"Traditionally in infectious disease, we think that the stronger a pathogen's ability is to cause disease, the greater its potential is to be transmitted to other hosts," says senior author Janelle Ayres, an assistant professor in immunobiology and microbial pathogenesis at the Salk Institute for Biological Studies. "But we discovered a pathogen that has evolved to become less dangerous to its host. By employing this strategy, it's easier for the pathogen to spread to other hosts."

In the study, the investigators looked at *Salmonella Typhimurium*, a natural intestinal



**IMAGE:** THIS VISUAL ABSTRACT DEPICTS THE FINDINGS THAT PATHOGENS CAN INTERFERE WITH THE GUT-BRAIN CIRCUITS THAT CONTROL HOST ANOREXIA DURING INFECTION TO PROMOTE HOST SURVIVAL WHILE FACILITATING DISEASE TRANSMISSION. [view more >](#)

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In the study, the investigators looked at *Salmonella Typhimurium*, a natural intestinal pathogen in mice (as well as humans) that can easily be transmitted to new hosts. Previous work looking at the connection between *Salmonella* and loss of appetite has mostly involved injecting a microbe or microbial products directly into the circulation of an animal model and studying its effect, but Ayres' group infected the animals orally--thus mimicking the bacteria's route of infection (it spreads from mouse to mouse when the animals eat each other's contaminated feces).

"Host response is only half of the infectious disease equation. We wanted to understand how the bacteria's behavior is affected by the host's loss of appetite, as well," Ayres says. "What a pathogen wants is a steady supply of nutrients, a stable niche so it can replicate, and a reliable mode of transmission." In this case, taming the behavior of the pathogen by enabling the mice to take in more nutrition helped keep the mouse healthy, produce more feces, and then spread infection to other animals.

Further investigation revealed the mechanism by which *Salmonella Typhimurium* inhibits loss of appetite. Sickness behaviors are in large part mediated by a cytokine--a type of molecule involved in cell-to-cell communication--that sends a signal to the hypothalamus, a region of the brain controlling appetite. But this particular *Salmonella* blocks activation of the cytokine in the intestines, preventing the gut from signaling to the brain.

Ayres says she anticipates finding a similar strategy in other microbes, noting that genes similar to the one known to be important in blocking cytokine activation in *Salmonella Typhimurium* also are found in other pathogens. "But a more interesting place to look is at the components of the microbiome, especially the human microbiome," she notes.

"When an infection in the host affects appetite, the microbiome is also potentially compromised by the loss of nutrition. I expect to find that the microbiome has evolved strategies to block this sickness response," Ayres adds.

This is something her research group plans to study.

The researchers hope that one day, their findings may lead to a better understanding of infection transmission and new ways to treat infections by supplementing patients with nutrition rather than treating them with antibiotics. The goal would be to give patients a treatment that would also prevent them from spreading their cold or fever to others.

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*Cell*, Rao et al.: "Pathogen-mediated inhibition of anorexia promotes host survival and

transmission" [http://www.cell.com/cell/fulltext/S0092-8674\(17\)30054-5](http://www.cell.com/cell/fulltext/S0092-8674(17)30054-5)

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