

Study finds probiotic bacillus eliminates staphylococcus bacteria

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Woman selling vegetable snacks in a Thai market -- a possible source of probiotic Bacillus spores. Credit: NIAID

A new study from National Institutes of Health scientists and their Thai colleagues shows that a "good" bacterium commonly found in probiotic digestive supplements helps eliminate Staphylococcus aureus, a type of bacteria that can cause serious antibiotic-resistant infections. The researchers, led by scientists at NIH's National Institute of Allergy and Infectious Diseases (NIAID), unexpectedly found that Bacillus bacteria prevented S. aureus bacteria from growing in the gut and nose of healthy individuals. Then, using a mouse study model, they identified exactly how that happens. Researchers from Mahidol University and Rajamangala University of Technology in Thailand collaborated on the project.

"Probiotics frequently are recommended as dietary supplements to improve digestive health," said NIAID Director Anthony S. Fauci, M.D. "This is one of the first studies to describe precisely how they may work to provide health benefits. The possibility that oral *Bacillus* might be an effective alternative to antibiotic treatment for some conditions is scientifically intriguing and definitely worthy of further exploration."

Staphylococcus infections cause tens of thousands of deaths worldwide each year. Methicillin-resistant Staphylococcus aureus, or MRSA, is familiar to many people as a cause of serious disease. Less well known is that *S. aureus* often can live in the nose or gut without causing any harm. However, if the skin barrier is broken, or the immune system compromised, these colonizing <u>bacteria</u> can cause serious infections.

One strategy to prevent Staph infections is to eliminate *S. aureus* colonization. However, some decolonization strategies are controversial because they require considerable amounts of topical antibiotics and have limited success, partly because they target only the nose and bacteria quickly recolonized from the gut.

The scientists recruited 200 volunteers in rural Thailand for the study. This population, they speculated, would not be as affected by food sterilization or antibiotics as people in highly developed urban areas. The scientists first analyzed fecal samples from each of the study participants for bacteria correlated with the absence of S. aureus. They found 101 samples positive for Bacillus, primarily B. subtilis-the type found mixed with other bacteria in many probiotic products. Bacillus bacteria form spores that can survive harsh environments and commonly are ingested naturally with vegetables, allowing them to temporarily grow in the intestine. The scientists then sampled the same 200 people for S. aureus in the gut (25 positive) and nose (26 positive). Strikingly, they



found no *S. aureu*s in any of the samples where *Bacillus* were present.

In mouse studies, the scientists discovered an *S. aureus* sensing system that must function for the bacteria to grow in the gut. Intriguingly, all of the more than 100 *Bacillus* isolates they had recovered from the human feces efficiently inhibited that system.

Using chromatography and mass spectrometry techniques, the scientists identified fengycins, a specific class of lipopeptides—molecules that are part peptide and part lipid—as the specific *Bacillus* substance that inhibited the *S. aureus* sensing system. Additional tests showed that fengycins had the same effect on several different strains of *S. aureus*—including high-risk USA300 MRSA which causes most community-associated MRSA infections in the United States and is an increasingly common cause of healthcare-associated MRSA infections.

To further validate their findings, the scientists colonized the gut of mice with *S. aureus* and fed them *B. subtilis* spores to mimic probiotic intake. Probiotic *Bacillus* given every two days eliminated *S. aureus* in the guts of the mice. The same test using *Bacillus* where fengycin production had been removed had no effect, and *S. aureus* grew as expected.

The NIAID and Thai scientists next plan to test whether a probiotic product that contains only *B. subtilis* can eliminate *S. aureus* in people. They plan to enroll more Thai volunteers for the project. Michael Otto, Ph.D., the NIAID lead investigator, says, "Ultimately, we hope to determine if a simple probiotic regimen can be used to reduce MRSA <u>infection</u> rates in hospitals."

More information: Pipat Piewngam et al, Pathogen elimination by probiotic Bacillus via signalling interference, *Nature* (2018). <u>DOI:</u> <u>10.1038/s41586-018-0616-y</u>

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