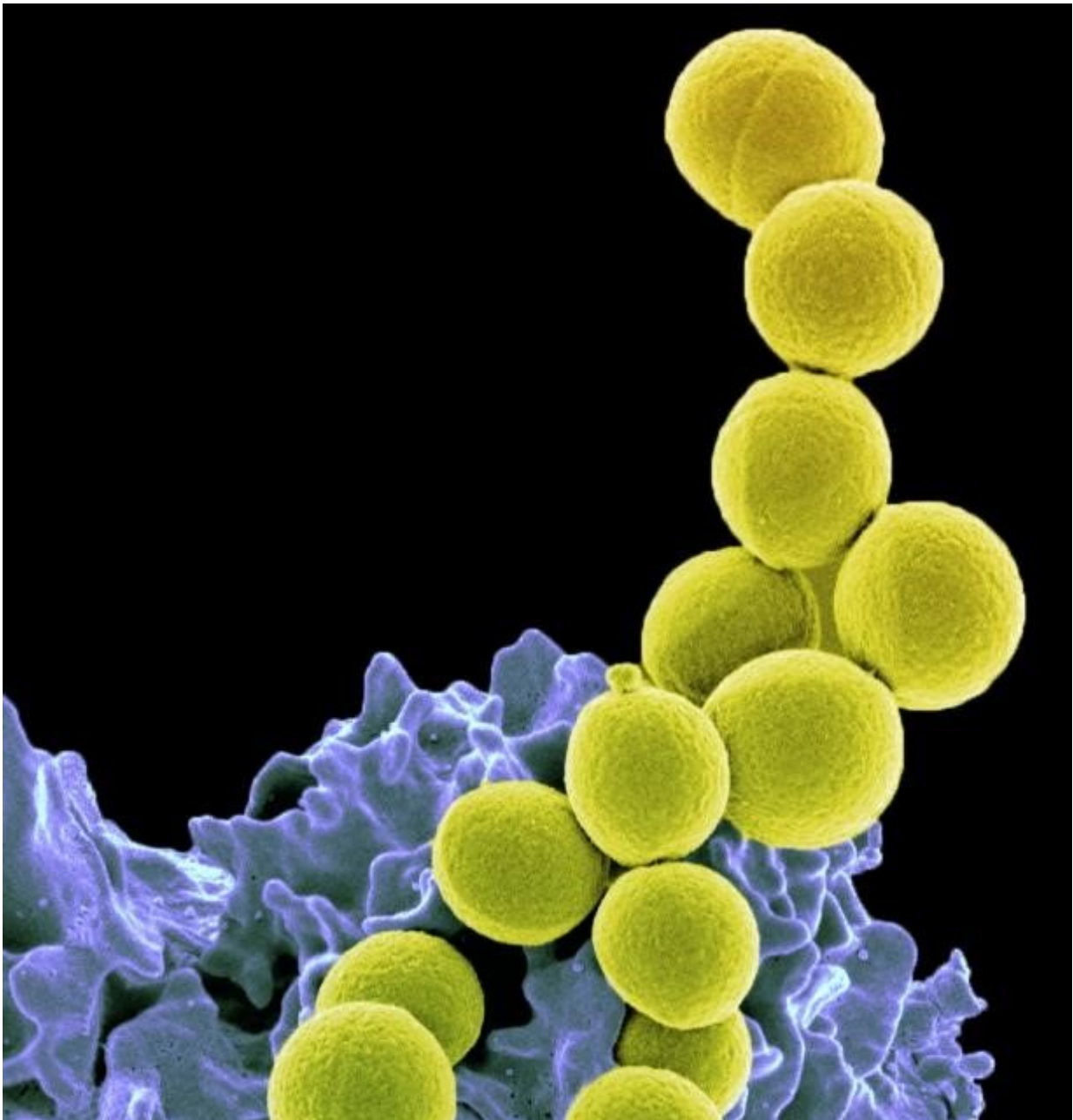


Probiotic markedly reduces *S. Aureus* colonization in phase 2 trial

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Methicillin-resistant *Staphylococcus aureus* bacteria (yellow) being ingested by neutrophil (purplish blue). Credit: NIAID

A promising approach to control *Staphylococcus aureus* bacterial colonization in people—using a probiotic instead of antibiotics—was safe and highly effective in a Phase 2 clinical trial. The new study, reported in *The Lancet Microbe*, found that the probiotic *Bacillus subtilis* markedly reduced *S. aureus* colonization in trial participants without harming the gut microbiota, which includes bacteria that can benefit people. The research was conducted by researchers at the National Institutes of Health led by Michael Otto, Ph.D., an NIH senior investigator at the National Institute of Allergy and Infectious Diseases (NIAID).

Methicillin-resistant *S. aureus*, or MRSA, is familiar to many people as a cause of serious disease. Less well known is that *S. aureus* often lives in the nose, on the body and in the gut without causing any harm. However, if the skin barrier is broken, or the [immune system](#) compromised, these colonizing bacteria can cause serious skin, bone, lung, and blood infections.

The prevention of *S. aureus* infections using approaches to "decolonize" the body has gained increased attention as the spread of antibiotic resistance limits treatment options. Some decolonization strategies are controversial because they also require large amounts of antibiotics, raising concerns about damage to the microbiota and the development of antibiotic resistance. So far, it appears that only nasal *S. aureus* colonization can be targeted with topical antibiotics without doing too much harm, but bacteria quickly can recolonize in the nose from the gut.

Probiotics, digestive supplements containing live microorganisms, may be a way to complement or replace antibiotics. Probiotic Bacillus is especially promising because it is administered orally as spores that can survive passage through the stomach and then temporarily grow in the intestine.

In prior studies, Dr. Otto's group discovered an *S. aureus* sensing system needed for *S. aureus* to grow in the gut. They also found that fengycins, Bacillus lipopeptides that are part peptide and part lipid, prevent the *S. aureus* sensing system from functioning, thereby eliminating the bacteria.

In the clinical trial, conducted in Thailand, the research team tested whether this approach works in people. They enrolled 115 healthy participants, all of whom were colonized naturally with *S. aureus*. A group of 55 people received *B. subtilis* [probiotic](#) once daily for four weeks; a control group of 60 people received a placebo.

After four weeks researchers evaluated the participants' *S. aureus* levels in the gut and nose. They found no changes in the [control group](#), but in the probiotic group they observed a 96.8% *S. aureus* reduction in the stool and a 65.4% reduction in the nose.

"The probiotic we use does not 'kill' *S. aureus*, but it specifically and strongly diminishes its capacity to colonize," Dr. Otto said. "We think we can target the 'bad' *S. aureus* while leaving the composition of the microbiota intact."

The researchers also found that levels of *S. aureus* bacteria in the gut far exceeded *S. aureus* in the nose, which for decades has been the focus of staph infection prevention research. This finding adds to the potential

importance of *S. aureus* reduction in the gut.

"Intestinal *S. aureus* colonization has been evident for decades, but mostly neglected by researchers because it was not a viable target for antibiotics," Dr. Otto said. "Our results suggest a way to safely and effectively reduce the total number of colonizing *S. aureus* and also call for a categorical rethinking of what we learned in textbooks about *S. aureus* colonization of the human body."

More information: Pipat Piewngam et al, Probiotic for pathogen-specific *Staphylococcus aureus* decolonisation in Thailand: a phase 2, double-blind, randomised, placebo-controlled trial, *The Lancet Microbe* (2023). [DOI: 10.1016/S2666-5247\(22\)00322-6](https://doi.org/10.1016/S2666-5247(22)00322-6)

Pipat Piewngam et al, Pathogen elimination by probiotic *Bacillus* via signalling interference, *Nature* (2018). [DOI: 10.1038/s41586-018-0616-y](https://doi.org/10.1038/s41586-018-0616-y)

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