E. coli more virulent when accompanied by beneficial bacteria

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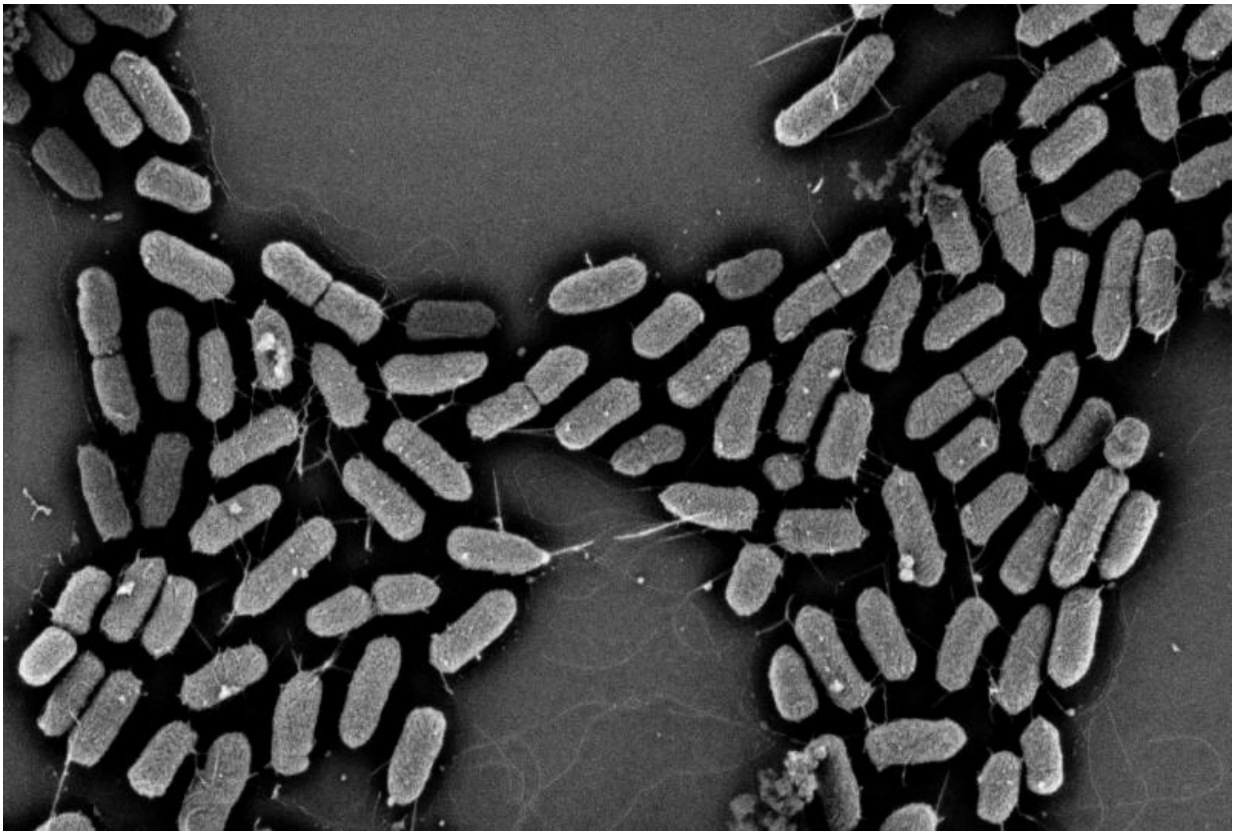

E. coli bacteria sticking to human cell lines seen by an electron microscope. Credit: Edward Dudley, Penn State

Scientists wonder why some people get so sick and even die after being infected by the foodborne pathogen *E.coli* O157:H7, while others

experience much milder symptoms and recover relatively quickly. Now Penn State's College of Agricultural Sciences researchers believe they have discovered an explanation.

Over the course of a four-year study, researchers co-cultured the pathogenic *E. coli* O157:H7 serotype with a nonpathogenic strain of the bacteria and inoculated mice. These mice got much sicker than mice that were infected with the pathogenic strain alone. The finding appears to be especially relevant because people normally have multiple strains of *E. coli* living in their intestines.

Most *E. coli* bacteria are harmless and are an important part of a healthy intestinal tract, noted co-author Edward Dudley, associate professor of food science. However, some *E. coli* are pathogenic, meaning they can cause illness by producing toxins that can result in bloody diarrhea, severe abdominal cramps or other more serious conditions, such as impaired kidney function.

"Within our intestines, each of us carries several hundred different types of bacteria, including *E. coli*, and *E. coli* comes in a large number of varieties. These range from organisms that just naturally colonize our intestines and provide us with benefits to organisms like the ones I focus on that have evolved to be very virulent," he said. "This research suggests that some strains of harmless *E. coli* in our intestines can interact with pathogenic *E. coli* in ways that will either increase or decrease how much toxin the pathogen produces. And that may dictate how sick one gets with an *E.coli* infection, or even if an infection proves to be fatal."

The study, which was published recently in *Infection and Immunity*, may be a significant step toward doctors being able to predict how an *E. coli*-infected patient will fare by evaluating a stool sample and analyzing the presence or absence of various strains of nonpathogenic *E. coli*.

However, an advance like that would first require follow-on studies like those now being conducted in Dudley's laboratory, aimed at determining which nonpathogenic strains of bacteria amplify the production of *E.coli* O157:H7 "Shiga" toxin.

"One of the issues with this particular pathogen is that by the time people are infected, we can't do much for them," said Dudley. "We can't use antibiotics because antibiotics make *E.coli* O157:H7 more virulent—the only treatment is just to monitor the individual and make sure he or she doesn't become dehydrated and be sure the kidneys stay functional."

"What our findings suggest is that by looking carefully at the gut flora of someone who is sick—while we can't necessarily treat them right away—we soon may be able to make a prediction about what the outcome of the disease is going to be. We can see if the patient is going to clear the organisms and have mild symptoms, or if they are likely to have something that is more serious."

To test their hypothesis, lead researchers Kakolie Goswamie and Chun Chen, recent Ph.D.s in food science, cultured multiple strains of *E. coli*, inoculated otherwise germ-free mice and followed the resulting infections. Researchers then examined the animals' kidneys, intestines and livers after their demise, using molecular biology and DNA-sequencing techniques, along with biochemistry procedures. Goswamie is now at Sample6,Cambridge, Massachusetts, and Chen is at Abbott Laboratories, Shanghai, China.

"These findings create a compelling argument to reconsider the appropriateness of assessing the virulence potential of *E. coli* O157:H7 strains solely by quantifying Shiga toxin production in pure cultures, because there are many strains of otherwise harmless *E. coli* present in the human intestine that have the potential to enhance Shiga toxin

production," Goswamie said. "More research on the interactions between *E. coli* O157:H7 and the plethora of bacterial species present in the intestine is needed to appreciate how the gut microbiome affects virulence of this foodborne pathogen."

The next step will be to study how pathogenic and nonpathogenic organisms communicate with each other and how modern medicine might use that information to minimize the course of disease, Dudley said. "We hope these findings have both a diagnostic potential and the promise of leading to information that will make the disease outcome less severe."

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