Beneficial bacteria help repair intestinal injury by inducing reactive oxygen species

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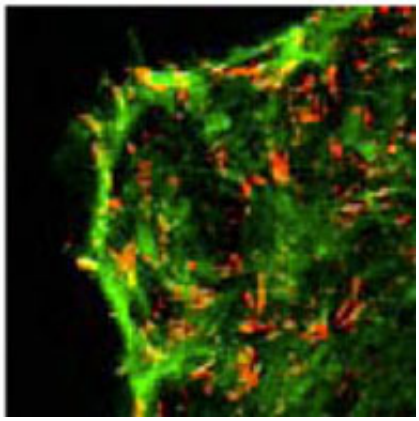

Intestinal epithelial cells exposed to probiotic bacteria. Red indicates focal adhesions that help the cells migrate and repair gaps.

(Medical Xpress) -- The gut may need bacteria to provide a little bit of oxidative stress to stay healthy, new research suggests. Probiotic bacteria promote healing of the intestinal lining in mice by inducing the production of reactive oxygen species, researchers at Emory University School of Medicine have shown.

The results, published online this week in Proceedings of the National Academy of Sciences *Early Edition*, demonstrate a mechanism by which bacterial cultures in foods such as yogurt and kimchi have beneficial effects on intestinal health. The insights gained could also guide doctors to improved treatments for intestinal diseases, such as necrotizing

enterocolitis in premature babies or intestinal injury in critically ill adults.

The laboratories of Andrew Neish, MD and Asma Nusrat, MD, both professors of pathology and laboratory medicine, teamed up for the study. The paper's co-first authors are postdoctoral fellow Philip Swanson, PhD and associate research professor Amrita Kumar, PhD.

"It's been known for years that probiotic bacteria can have these kinds of helpful effects, but it wasn't really clear how this worked," Neish says. "We've identified one example, among many, of how certain kinds of bacteria have specific biochemical functions in the body."

Recent research has shown that the bacteria in our intestines influence our metabolism and immune systems. For example, an imbalance in the proportions of harmful and beneficial bacteria seems to over-activate immune cells in the intestines, driving inflammatory bowel disease.

Intestinal epithelial cells, the cells that line the intestine, live in close contact with bacteria and normally form a barrier that keeps bacteria away from other organs. They can repair small gaps in the barrier, which breaks down in intestinal diseases, by migrating into the gaps.

The researchers showed that Lactobacillus rhamnosus bacteria can accelerate this healing process, both in culture dishes and in mice with intestines damaged by chemicals. Lactobacillus rhamnosus, a species of bacteria found naturally in human intestines and often used as a probiotic, is a relative of other kinds of Lactobacillus bacteria found in fermented foods.

"Unlike most cell types that can not tolerate bacterial contact, intestinal epithelial cells respond to Lactobacillus rhamnosus by increasing their motility," Neish says.

Using a fluorescent dye that is sensitive to reactive oxygen species (ROS), the researchers showed that intestinal epithelial cells produce ROS internally when in contact with Lactobacillus rhamnosus. The ROS induced by the bacteria stimulate the formation of focal adhesions, structures on intestinal epithelial cells that act as anchors for their movement.

“Focal adhesions are where cells attach to the matrix that surrounds them,” Neish says. “The cells lay them down on one side and remove them on the other side, like the tracks of a bulldozer.”

In studying the effect of Lactobacillus rhamnosus on intestines in mice, Neish’s team focused on the small intestine, which normally has fewer bacteria than the colon. This allowed them to avoid using antibiotics to remove naturally existing bacteria beforehand, and to see ROS production in tissue from live animals.

Antioxidants that mop up ROS prevent the bacteria from promoting wound healing in the laboratory, the researchers showed. Neish says his team’s finding suggests that large amounts of antioxidants by humans could interfere with the ability of bacteria to promote intestinal healing.

Previously, it was known that immune cells respond to bacteria by producing ROS, but Neish and his colleagues believe the ROS production they observed stimulates tissue maintenance and is a marker of cohabitation and adaptation, rather than defense.

Oxidative stress, or an imbalance of reactive oxygen species throughout the body, has been linked to diseases such as heart disease and stroke. However, scientists have learned in recent years that cells can also use reactive oxygen species in a controlled, local way to send signals needed for normal functions.

Neish says his team is working to determine which part of the bacteria is responsible for inducing cells to produce ROS. Once identified, this component could be used to encourage intestinal healing in situations where contact with large amounts of live bacteria might be dangerous, such as in premature babies or critically ill adults.

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More information: P.A. Swanson II et al. Enteric commensal bacteria potentiate epithelial restitution via reactive oxygen species-mediated inactivation of focal adhesion kinase phosphatases. *PNAS* Early Edition (2011).

Provided by Emory University