MedicalXpress

Study identifies mechanism by which intestinal enzyme maintains microbial balance

May 9 2014

Massachusetts General Hospital (MGH) investigators have identified the mechanism by which an enzyme produced in the intestinal lining helps to maintain a healthy population of gastrointestinal microbes. In their report in *American Journal of Physiology – Gastrointestinal and Liver Physiology*, the research team describes finding that intestinal alkaline phosphatase (IAP) promotes the growth of beneficial bacteria by blocking the growth-inhibiting action of adenosine triphosphate (ATP) – an action first described in this paper – within the intestine.

"We found that ATP is a natural inhibitor of bacteria in our intestines and that IAP promotes the growth of 'good' bacteria by blocking ATP," says Richard Hodin, MD, of the MGH Department of Surgery, senior author of the report which has been released online. "By helping to keep these healthy bacteria happy, IAP protects us against dangerous pathogens that can get the upper hand when the balance is disrupted."

The beneficial bacteria and other microbes that normally populate the human digestive system contribute to the digestive process and also prevent the proliferation of any disease-causing bacteria that may be present. A drop in the number of beneficial species – which may be caused by antibiotic treatment, poor nutrition or other health conditions – can allow the population of harmful bacteria to rise, contributing to serious medical problems including chronic diarrhea from pathogenic species such as C. difficile, inflammatory bowel disease, and metabolic

syndrome.

Previous research by Hodin's team found that IAP keeps pathogenic bacteria in the gastrointestinal tract from passing through the intestinal wall, and a 2010 study in mice revealed that the enzyme plays an important role in maintaining levels of beneficial bacteria, including restoring levels reduced by antibiotic treatment. However, that study also showed that IAP does not directly promote bacterial growth, leaving exactly how the enzyme helps maintain the microbial population an open question that the current study was designed to investigate.

A series of experiments first confirmed that mice lacking intestinal IAP had significant reductions in populations of several important bacterial species. Hypothesizing that IAP may act by blocking a growth-inhibiting activity of one of its target molecules, the researchers tested how well bacteria in stool samples would grow in the presence of four known IAP targets. Among the tested targets, only ATP significantly reduced bacterial growth; and ATP's inhibitory effects were reversed by application of IAP. Best known as the primary energy supply within cells, ATP also acts as a signaling molecule both inside and outside of cells, and this study is the first to identify such an activity for ATP within the gastrointestinal system.

Experiments in living mice revealed that IAP knockout animals had 10 times the normal level of ATP within their intestines and that fasting animals, in which IAP levels would be expected to drop, also had elevated intestinal ATP. Adding ATP to the intestines of mice in which IAP activity had been inhibited reduced levels of beneficial E.coli bacteria in the animals' digestive systems. Altogether the results show that ATP inhibits the growth of intestinal bacteria in mice and that IAP's growth-promoting effects result from the enzyme's inactivation of ATP and possibly of related molecules.

"Now we need to find out whether IAP also promotes the growth of beneficial intestinal bacteria in humans," says Hodin, who is a professor of Surgery at Harvard Medical School. "If it does, IAP-based therapies could offer a simple and safe approach to treating the millions of patients who suffer serious health problems caused by disruptions to intestinal microbial balance."

Provided by Massachusetts General Hospital