Immune cell's role in intestinal movement may lead to better understanding of IBS

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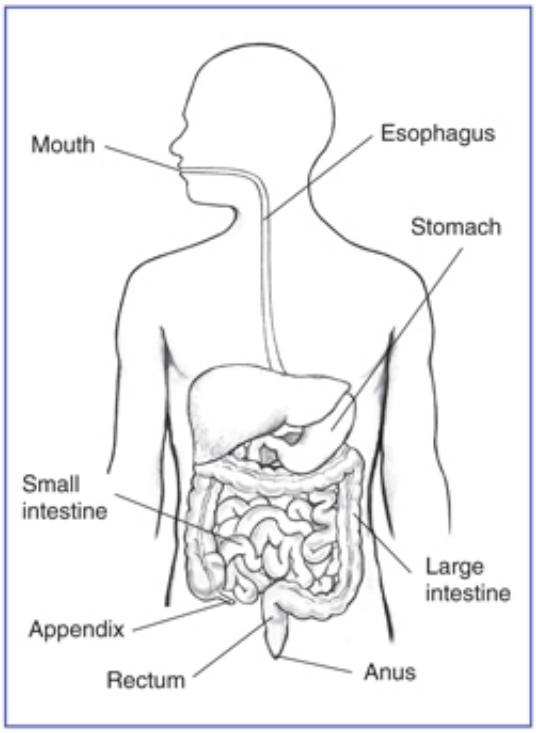

The organs of the GI tract. Credit: National Digestive Diseases Information Clearinghouse

(Medical Xpress)—Learning the role of immune-system cells in healthy digestive tracts and how they interact with neighboring nerve cells may lead to new treatments for irritable bowel syndrome (IBS). Researchers from Penn State College of Medicine, in collaboration with other scientists, have reported the role of macrophages in regulating the contractions of the colon to push digested material through the digestive tract.

The muscular lining of the intestine contains a distinct kind of macrophage, an immune system cell that helps fight infections. The role of these cells in normal colon function is not known, although they have been linked to inflammation after abdominal surgery.

"Very little is known about the function of muscularis macrophages, mainly because these cells are difficult to isolate from intestinal tissue," said Milena Bogunovic, assistant professor of microbiology and immunology.

Digested material is moved through the intestines by the contraction and relaxation of intestinal muscles. The pattern and frequency of these contractions are controlled by the signals from the intestinal nervous system. In patients with diseases like IBS, the signals are overactive and stimulation is exaggerated.

The researchers developed a method to deplete muscularis macrophages in the intestines of mice to determine their function. They report their findings in the journal *Cell*.

"After macrophage depletion, we observed that the normal intestinal movements are irregular, probably because the muscular contractions were poorly coordinated, suggesting that intestinal movements are regulated by macrophages," Bogunovic said.

After confirming the role of the macrophages in the function of the digestive tract, the researchers looked for how the regulation happens. They compared the genetic code of different types of macrophages to find non-immune genes highly active in muscularis macrophages, identifying bone morphogenetic protein 2. BMP2 is one of a family of proteins thought to control organ development.

Blocking the effect of BMP2 mirrored the effects of the macrophage removal, confirming that the protein is used for regulation of intestinal movements. The BMP2 is used by neighboring nerve cells, intestinal neurons, which in turn secrete a protein called colony stimulatory factor 1 (CSF1) that supports macrophages.

"Two completely different cell types help each other to carry one key function, to regulate the physiology

of the gut," Bogunovic said.

The interactions between the two cells types are orchestrated by the "good" bacteria in the intestine that aids in healthy digestion.

By giving mice antibiotics to kill off the bacteria, the communication between macrophages and neurons is interrupted resulting in decreased BMP2 and CSF1 production and disrupted intestinal contractions.

By restoring the "good" bacteria in the mice, the miscommunication between macrophages and neurons is reversed, showing that the dialogue between the macrophages and nervous system is adaptable to the changes in the bacterial environment.

A potential cause of IBS is a change in the bacterial environment in the intestine.

"By better understanding how the nervous system cells, the muscularis macrophages and signals from inside the intestine interact, we may be able to find new treatments for IBS, or even prevent it," Bogunovic said.

Provided by Pennsylvania State University

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