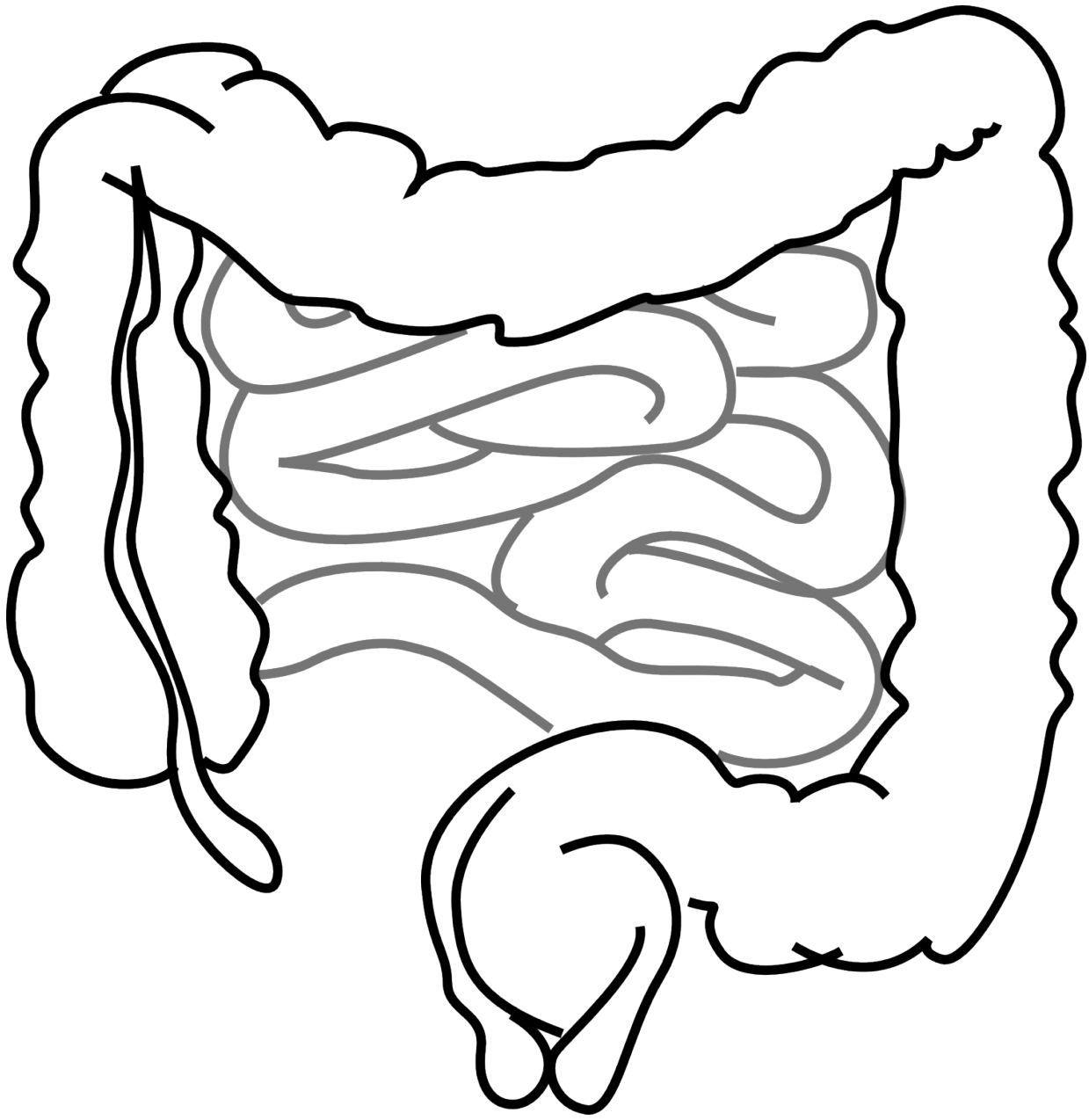
In fighting gut infections, nervous system is key, team finds

January 9 2020



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The peaceful and delicate co-existence of friendly gut bacteria and the immune system relies on highly coordinated information exchange between immune system cells and certain cells lining the intestine. Until now, scientists generally believed these two cell types were also central to the production of antibacterial molecules that fend off dangerous infections.

But scientists at Yale and Harvard medical schools have discovered that, in response to bacterial invaders, nerve cells within the intestine—and not immune cells or cells lining the intestinal wall—release infection-fighting cytokines. They report their findings Jan. 9 in the journal *Cell*.

The findings provide new insights into the body's response to bacterial infections that cause food poisoning and other illnesses.

"We used to believe that the immune system cells and intestinal barrier cells communicated to keep out invading bugs by mobilizing anti-microbial proteins," said co-corresponding author Richard Flavell, Sterling Professor of Immunobiology at Yale and a Howard Hughes Medical Institute investigator. "The story is actually not true—it is the nervous system telling barrier cells what to do."

The foot soldiers in the war against intestinal pathogens, it turns out, are the immune system molecules interleukin-18 or IL-18. Interleukins are part of the immune system's arsenal.

When the researchers deleted IL-18 from both immune cells and cells lining intestinal barriers, mice were still able to fend off intestinal

infection from Salmonella bacteria. This ruled them out as the agents responsible for the immune response, said Flavell. But mice without IL-18 produced by nervous system cells were more susceptible to infection, revealing its key role in fighting infection.

The key role of nerve cells in the defense against pathogens makes sense, given the ability of the nervous system to communicate across long distances, Flavell said.

"The findings offer an opportunity to explore new ways to intervene in infections through the nervous system," he said.

Provided by Yale University

Citation: In fighting gut infections, nervous system is key, team finds (2020, January 9) retrieved 3 May 2024 from https://medicalxpress.com/news/2020-01-gut-infections-nervous-key-team.html

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