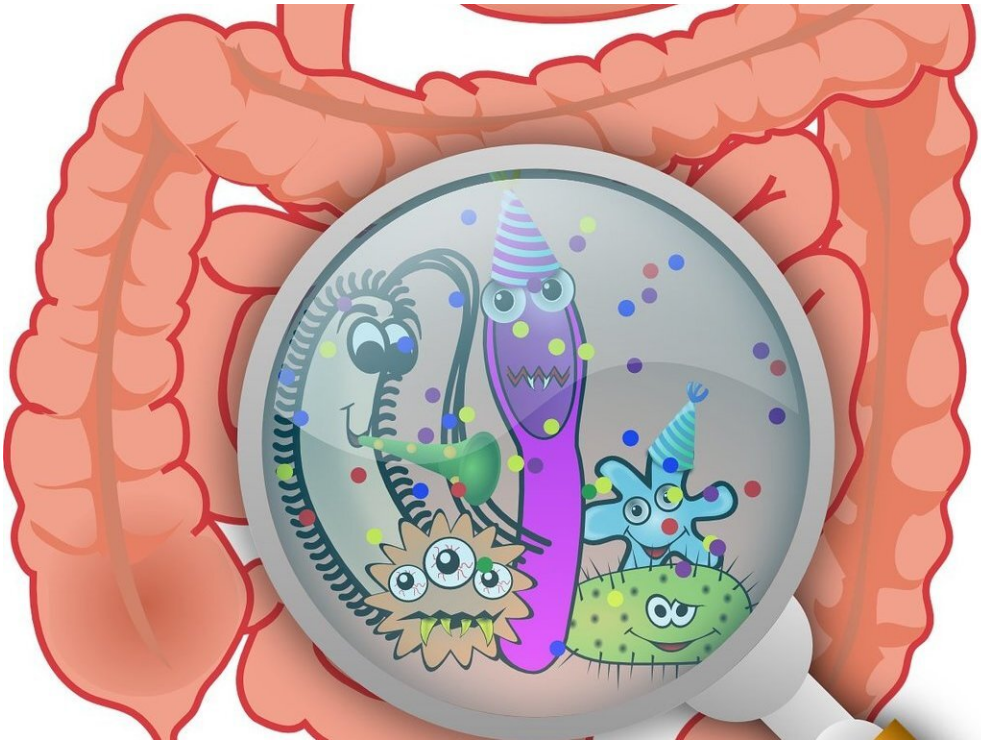
Next frontier in study of gut bacteria: mining microbial molecules

April 19 2019, by Ziba Kashef



Credit: CC0 Public Domain

The human gut harbors trillions of invisible microbial inhabitants, referred to as the microbiota, that collectively produce thousands of unique small molecules. The sources and biological functions of the vast majority of these molecules are unknown. Yale researchers recently applied a new technology to uncover microbiota-derived chemicals that

affect human physiology, revealing a complex network of interactions with potentially broad-reaching impacts on human health.

Led by immunobiologist Noah Palm, the research team used a chemical screening technology, known as PRESTO-Tango, that simultaneously tests thousands of human receptors at once. With it, they identified human gut bacteria that release small molecules that activate a specific group of receptors. Since these receptors regulate a wide range of physiological functions, the authors reasoned that the small-molecule-producing bacteria would also impact various aspects of human biology.

The team cultured and screened over 100 diverse gut bacteria for production of molecules that activated host receptors, and uncovered multiple chemical interactions between microbes and their human hosts. Their discoveries shed new light on the following:

- Drug responses: A number of gut microbes produce small molecules that activate receptors for dopamine. One molecule made by a unique gut microbe can reach the brain and potentially impact how different individuals respond to antidepressants.
- Treatment targets: Gut bacteria from patients with inflammatory bowel disease produce the inflammatory compound histamine. By blocking histamine receptors in mice colonized with these bacteria, the researchers reversed symptoms of this condition, suggesting a potential treatment strategy.
- Diet-microbe-host and microbe-microbe-host interactions: Multiple "orphan" receptors—ones with no previously known small-molecule activators—are stimulated by compounds produced by gut bacteria or derived from diet. This suggests that further screening could identify previously hidden interactions between bacteria, our diet, and human health, say researchers.

These findings demonstrate the potential of activity-based, small-

molecule screening approaches to illuminate the diverse physiological effects of molecules produced by gut bacteria, note the researchers.

"Understanding the ultimate impact of the gut microbial community on human health and disease will require an in-depth understanding of the complex chemical communication and exchanges between microbes, the host, and our diet," said Palm.

The full study is published in *Cell*.

More information: Haiwei Chen et al. A Forward Chemical Genetic Screen Reveals Gut Microbiota Metabolites That Modulate Host Physiology, *Cell* (2019). DOI: 10.1016/j.cell.2019.03.036

Provided by Yale University