Gut Bacteria Help Regulate Blood Pressure

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In a new study, US scientists suggest gut bacteria form part of a complex system that maintains the body's blood pressure. They have discovered a specialized odor-sensing receptor normally present in the nose can also be found in blood vessels throughout the body. In the gut, the receptor reacts to small molecules generated by bacteria by raising blood pressure. The study may aid understanding of how antibiotics, probiotics, and changes in diet affect blood pressure.

The team, led by researchers at The Johns Hopkins University and Yale University, write about their work, which they conducted in mice and lab cultures, in the 11 February online issue of *Proceedings of the National Academy of Sciences*.

First author Jennifer Pluznick, assistant professor of physiology at the Johns Hopkins University School of Medicine, says they were surprised to find that gut microbes contribute to blood pressure regulation and health:

"There is still much to learn about this mechanism, but we now know some of the players and how they interact," she explains in a statement.

Olfactory Receptor 78 Present Throughout the Body

Receptors are proteins usually found on the surfaces of cells. They bind and react to selective molecules, rather like a lock can only be opened by a specific key. The specific molecules are chemical signals that direct the cell to do something, such as divide, die, or allow specific materials to enter or exit the cell.

A few years ago, Pluznick found odor-sensing receptors (thought to exist only in the nose) in the kidneys, an event she describes as a "happy coincidence".

She and her team found one of these, olfactory receptor 78 (Olfr78), was dotted around the major branches of the kidney's artery and also in the small vessels or arterioles that lead into the kidney's filters.

When they looked further, they found Olfr78 throughout the body, sitting in the walls of small blood vessels, with more of them in the heart, diaphragm, skeletal muscle and skin.

Short Chain Fatty Acids Produced by Gut Bacteria Influence Blood Pressure

Intrigued by their find, Pluznick and colleagues set out to determine which molecules bind to Olfr78. They programmed cells to express the receptor on their surfaces, and rigged them so when a molecule bound to it, it triggered the reaction of a light-emitting chemical. So every time the cell "lit up", it meant that particular molecule had bound successfully to Olfr78.

A series of tests with different molecular cocktails revealed that Olfr78 only bound to acetic acid, more commonly known as vinegar.

Further tests revealed that propionate also binds to Olfr78.

Acetic acid, its derivate acetate, and propiniate, are part of a family of molecules called short chain fatty acids (SCFAs). SCFAs are produced in the large bowel as a result of bacterial fermentation of soluble fibre. They are then absorbed into the bloodstream, where they can interact with Olfr78.

When mice missing the Olfr78 gene were given SCFAs, the scientists observed that their blood pressure went down, suggesting SCFAs usually cause it to go up. But when they gave SCFAs to normal mice that had the Olfr78 gene, they were surprised to find this also caused blood pressure to go down, although not as far as with the other mice.

Complex, Contradictory Relationships Between SCFAs and Receptors

The team decided to find out what would happen if they reduced all sources of SCFAs available Olfr78 in the mice, including that produced by the gut bacteria.

So they wiped out the gut bacteria in the mice by putting them on a three-week course of antibiotics, and monitored their blood pressure. The normal mice showed little change, but blood pressure in the mice lacking Olfr78 went up. This suggested the relationship between Olfr78, SCFAs, and blood pressure was a bit more complicated than it looked at first: were other factors involved?

The team eventually discovered a non-odor-related receptor, Gpr41, also plays a role. Gpr41 also binds to SCFAs, and when it does, blood pressure goes down.

So there were two contradictory effects going on: when they bind to Olfr78, SCFAs make blood pressure rise, but when they bind to Gpr41, blood pressure falls. However, the effect of Gpr41 is stronger, so an increase in SCFAs results in an overall decrease in blood pressure.

Pluznick says there are "many players involved in the maintenance of stable levels of blood pressure", and they've found just some of them.

"**We don't know why it would be beneficial for blood pressure to decrease after eating or why gut microbes would play a part in signaling that change**. But our work opens the door for exploring the effects of antibiotic treatments, probiotics and other dietary changes on blood pressure levels in mice, and perhaps eventually people," she adds.

Grants from the National Institute of Diabetes and Digestive and Kidney Diseases, and the Leducq Foundation, financed the study.

An animal study published in the *Journal of Proteome Research* in 2012, suggests that bacteria living in the large bowel may also play a role in obesity by slowing down the activity of energy-burning brown fat.

Written by Catharine Paddock PhD

References

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