How a touch-sensing protein could stop constipation

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When we eat food, our gut somehow senses its presence to begin shifting it along our digestive tract, but the question has always been—how?

Now, new Flinders University research using both human gut samples

and mice has discovered that a touch-sensing protein that was a focus of a 2021 Nobel Prize, called Piezo2, is not just in our fingers, but also in our gut, with its presence likely playing a key role in constipation. This work has recently been published in the leading international journal *Gastroenterology*.

"Many people suffer from digestive issues on a daily basis, such as chronic constipation, however we still don't understand the cause which underlies most of them," says Lauren Jones, lead author and final year Ph.D. student in the College of Medicine and Public Health.

"Our research identified Piezo2 in cells that line the human digestive tract, allowing them to sense physical stimuli, such as touch or pressure, that would occur when food is present. The cells then respond by releasing serotonin to stimulate gut contractions and push the food along."

Last year, international researchers Ardem Patapoutian and David Julius were awarded the Nobel Prize in Physiology or Medicine for their research on receptors responsible for the perception of touch and temperature, including the discovery of Piezo2, now known to be responsible for sensing light touch on our skin.

Of potential clinical importance, the Flinders research team also discovered that the levels of Piezo2 decrease in the gut with age, and found that if the protein was removed only from gut serotonin cells, gut motility slowed down in mice, causing constipation.

The authors say this could be a potential contributing factor to age-related constipation and provide a possible path to treatment.

"Age-related constipation affects 1 in 2 adults over the age of 80, whilst constipation generally affects almost everyone at some point throughout

their life," says Ms. Jones.

"It's therefore extremely important we increase our understanding of the underlying mechanisms, so that we can find targeted solutions to improve the quality of life of the many people who suffer daily from various gut disorders, including constipation.

"This research provides the building blocks for both further research and the development of highly specific treatments to reduce the impacts of constipation."

While further research is needed to definitively link Piezo2 to constipation, the authors say overall the research is an important advancement into our understanding of gut physiology, opening up new targets for the treatment of digestive issues.

"More specifically, we now have the potential to create treatments that are taken orally and only directly impact these cells that line the gut, therefore significantly reducing side effects typically seen with many of the current medications," says Ms. Jones.

More information: Lauren A. Jones et al, Diminished Piezo2-Dependent Tactile Sensitivity Occurs in Aging Human Gut and Slows Gastrointestinal Transit in Mice, *Gastroenterology* (2022). DOI: 10.1053/j.gastro.2022.01.043

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