Sweet taste receptor affects how glucose is handled metabolically by humans

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The rich research portfolio of the Monell Chemical Senses Center on sweet taste goes way back: Monell scientists were one of four teams in 2001 that found and described the mammalian sweet taste

receptor—TAS1R2-TAS1R3. Twenty years later in 2021, a pair of papers published in Mammalian Genome by Monell researchers covered the genetics of sugar-loving mice.

The sweet taste receptor, expressed in taste bud cells, conveys sweetness from the mouth when it is activated. Earlier this month, a study in PLOS One, led by another Monell researcher, delved into how the sweet-taste receptor might be the first stop in a metabolic surveillance system for sugar. The receptor is also expressed in certain intestinal cells, where it may facilitate glucose absorption and assimilation, as part of this system.

The team found that stimulation and inhibition of TAS1R2-TAS1R3 demonstrates that it helps regulate glucose metabolism in humans and may have implications for managing such metabolic disorders as diabetes. Glucose is the primary type of sugar found in human blood, making it a key source of energy for cells.

"Our objective was to determine whether TAS1R2-TAS1R3 influences glucose metabolism in two directions," said Monell Member Paul Breslin, Ph.D., Professor of Nutritional Sciences, Rutgers University, and senior author on the paper.

They showed that a TAS1R2-TAS1R3 agonist (sucralose, a zero-calorie sweetener) or a TAS1R2-TAS1R3 antagonist (lactisole, a sodium salt that inhibits sweet taste) mixed with a glucose meal acutely altered human glucose tolerance in different ways. Here, an agonist binds to a receptor and stimulates a cell and an antagonist binds to a receptor and prevents stimulation.

"The novelty of our findings is that the receptor we studied in this experiment impacts blood glucose and insulin during a glucose meal differently, depending on whether it is stimulated or inhibited," said Breslin. This work provides further evidence that taste receptors help

regulate metabolism and nutrient handling.

Plasma insulin levels were measured in study participants given an oral glucose tolerance test (OGTT), which follows blood sugar levels before and after a person drinks a liquid meal containing glucose. Participants' ratings of perceived sucralose sweetness correlated with early increases in plasma glucose, as well as increases in plasma insulin levels when sucralose was added to the OGTT. The added sucralose tended to accelerate the release of insulin to the glucose load. On the other hand, participants' sensitivity to lactisole-driven inhibition of sweetness was correlated with decreased plasma glucose levels. Lactisole also tended to slow insulin release.

"When glucose stimulates taste receptors before being absorbed into the body, signals are sent via the mouth and intestine to regulatory organs such as the pancreas. Perhaps, we could devise ways of using TAS1R2-TAS1R3 to help the body handle glucose better by anticipating when glucose will appear in the blood," said Breslin. When the body senses glucose, it speeds up the absorption to deliver glucose to tissues that may need it and possibly also to prevent glucose from moving too far along the intestine, which may not be good for maintaining a healthy gut microbiome.

"This system is elegant in its simplicity," said Breslin. The same taste receptor is all over the body—the mouth, gastrointestinal tract, pancreas, liver, and fat cells, with the last three being major metabolic regulatory tissues, all part of the body's 24/7 metabolic watch.

Is there a relationship between a person's health status and the activity of their TAS1R2-TAS1R3 receptors? Study authors say likely, suggesting that the degree of receptor activation exerts acute influences on plasma glucose and insulin levels and their timing of onset, which is important for metabolic health.

The team maintains that, in general, the current dietary habits of excessive consumption of food and beverages high in sucrose, high fructose corn syrup, and high-potency sweeteners could hyperstimulate TAS1R2-TAS1R3, contributing to the improper regulation of glucose in the blood. This could lead to a diagnosis of metabolic syndrome, a cluster of risk factors including elevated plasma glucose and insulin insensitivity (along with obesity, hypertension, and elevated plasma fats) that increases the risk of heart disease, stroke, and diabetes. The authors say that future studies should examine the effects of TAS1R2-TAS1R3 stimulation and inhibition in people who are at risk for metabolic syndrome to determine the therapeutic potential of manipulating TAS1R2-TAS1R3 for better metabolic control instead of worse.

"Studies like these—using Monell's technical capability and deep expertise in the chemical senses—show that the sweet taste receptor TAS1R2-TAS1R3 helps to regulate glucose differently, depending on the sweetness of the food or beverage," said Breslin. The team's hope is to apply what they learned to make what we eat and drink healthier.

"A small metabolic change for the positive can add a lot more to the life and health of humans when compounded over decades and millions of people," said Breslin.

Along with Breslin, co-authors are Emily C. Hanselman and Matthew C. Kochem, Department of Nutritional Sciences, Rutgers University, New Brunswick, NJ.

More information: Matthew C. Kochem et al, Activation and inhibition of the sweet taste receptor TAS1R2-TAS1R3 differentially affect glucose tolerance in humans, *PLOS ONE* (2024). DOI: 10.1371/journal.pone.0298239

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