## TASTE IN THE MOUTH

of salty, sour, bitter, sweet, and umami (the taste of glutamate). While sweet, umami, and salty foods provide pleasurable sensations that drive the intake of carbohydrates, amino acids, and sodium, the tastes of bitter and sour inhibit intake of Sweet or Na⁺ Sensory nerve fiber glutamaterushes in rich foods sends signal to brain Taste cell 2 4 (1)Ca TrpM5 channel TIR Endoplasmic reticulum (ER) ATP Purinergic receptors 3 Pannexin ATP channel

Taste-bud receptors, primarily on the tongue, sense the qualities

### THE TASTE SIGNALING CASCADE IN THE MOUTH

The binding of molecular components of sweet or glutamate-rich foods to T1R-class receptors and bitter substances to T2R receptors stimulates the release of  $Ca^{2+}$  into the cytosol from the endoplasmic reticulum (ER) via G protein signaling and the second messenger molecule inositol trisphosphate (IP<sub>3</sub>) The  $Ca^{2+}$  activates the TrpM5 channel to allow the entry of sodium ions (Na<sup>+</sup>), depolarizing the cell 2. The combination of depolarization resulting from the influx of Na+ and rise in intracellular Ca<sup>2+</sup> opens pannexin channels in the taste-cell membrane, releasing ATP from the cell 3. This in turn activates purinergic receptors on the sensory nerve fibers innervating the taste buds, thereby sending a signal to the brain 4.

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# TASTE IN THE GUT

In contrast to taste receptors in the mouth, T1R and T2R receptors in the gut do not induce sensations of taste, but rather initiate molecular pathways that help guide the digestion or rejection of food substances traveling through the intestines. The underlying pathways, however, have many similarities.

### FOODS IN THE GUT

Specialized endocrine cells of the small intestine, known as enteroendocrine cells, display T2R bitter receptors on their cell membranes. When bitter compounds bind to the T2R receptors, the cells release the peptide hormone cholecystokinin (CCK), which acts on CCK2 receptors located on enterocytes, or intestinal absorptive cells. This increases the expression of the transporter ABCB1, which pumps toxins or unwanted substances out of the cell and back into the intestinal lumen. CCK also binds to CCK1 receptors on sensory fibers of the vagus nerve, sending signals to the brain to cease food intake.

 $\textcircled{3} T1R-class receptors on enteroendocrine cells lining the small intestine detect sweet substances and respond by secreting the glucagon-like peptide GLP-1. GLP-1 then travels to the pancreas via the bloodstream, where it boosts the release of insulin from pancreatic <math>\beta$ -cells, promoting the uptake of glucose by diverse tissues. Additionally, GLP-1 diffuses to neighboring enterocyte cells in the small intestine, driving the insertion of the glucose transporters SGLT-1 and GLUT2, which facilitates the uptake of glucose from the intestines.

**(**In the colon, bitter ligands bind to T2R receptors on epithelial cells, where they induce the secretion of anions and water, which leads to fluid rushing into the intestine, resulting in diarrhea that flushes out the colon.





## TASTE IN THE AIRWAYS

Scientists have also recently identified the existence of taste pathways in human airway cells, where they likely mediate defensive responses to inhaled foreign and potentially toxic substances.



#### IN THE UPPER AIRWAY

In the upper airways (nasal passages and trachea), T2R receptors on chemosensory cells sense bitter compounds, releasing secondary messengers that spur the release of Ca<sup>2+</sup> from the ER. The increase in cytoplasmic Ca<sup>2+</sup> activates the TrpM5 transduction channel, allowing the influx of Na<sup>+</sup> and the depolarization of the cell. This in turn activates voltage-gated Ca<sup>2+</sup> channels, which permit even more Ca<sup>2+</sup> to flood into the cell. This initiates the fusion of synaptic vesicles with the plasma membrane, releasing the neurotransmitter acetylcholine to activate nearby nerve fibers and induce protective reflexes such as sneezing A.

cell

causes cilia to move

#### IN THE LOWER AIRWAY

In airway smooth muscle cells Bitter of the lungs, the same T2R foods pathway is initiated by the Airway binding of bitter compounds. smooth Increases in cytoplasmic Ca2+ muscle likely cause nearby calcium-B T2R activated potassium channels to open, allowing the outflow of K<sup>+</sup>, which causes hyperpolarization and subsequent relaxation of the muscle cells **B**. Also in the FR lungs, T2R receptors on ciliated airway epithelial cells bind bitter compounds, initiating the same G protein-mediated pathway that results in the release of Ca2+ from Ŧ intracellular stores and thereby an Calciumincrease in ciliary beat frequency, • activated which researchers suspect serves potassium channel to sweep irritants away from the surface of the cell **C**. K++ Bitter rush out foods Cilia on airway epithelial cells C 2R Ca<sup>2+</sup> release