Sensory perception of taste

Jiang, P., May, B.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

The contents of this document may be freely copied and distributed in any media, provided the authors, plus the institutions, are credited, as stated under the terms of Creative Commons Attribution 4.0 International (CC BY 4.0) License. For more information see our license.

28/03/2022
**Introduction**

Reactome is an open-source, open-access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

**Literature references**


Reactome database release: 79

This document contains 4 pathways (see Table of Contents)
**Sensory perception of taste**

**Stable identifier:** R-HSA-9717189

Taste buds contain at least 3 types of cells: type I cells appear to have a support (glial-like) function; type II cells are responsible for tasting sweet compounds, bitter compounds, and umami (savory, amino acid) compounds; and type III cells are responsible for tasting sour (acidic) compounds (reviewed in Liman et al. 2014, Roper and Chaudhari 2017, Kinnamon and Finger 2019, Taruno et al. 2021). Recently identified sodium sensing cells expressing the epithelial sodium channel (ENaC) and POU2F3 are thought to be responsible for tasting low concentrations of salt and may be a subset of type II cells or a novel type of taste cell (Chandrashekar et al. 2010, reviewed in Taruno et al. 2021). High concentrations of salt appear to be detected by both type II and type III cells.

Receptors for sweet compounds, bitter compounds, and umami compounds contain an intracellular domain, transmembrane domains, and an extracellular domain that binds the ligand. The extracellular domains of receptors for sweet and umami ligands have a distinctive "venus flytrap"-shaped domain. Upon binding ligand, sweet taste receptors (TAS1R2:TAS1R3 heterodimers), bitter taste receptors (TAS2R class receptors), and umami receptors (TAS1R1:TAS1R3 heterodimers) then signal through a common downstream pathway: the receptor-ligand complex activates an associated heterotrimeric G protein complex (GNAT3:GNB1 or GNB3:GNG13) to exchange GDP for GTP, the heterotrimeric G protein complex dissociates and the resulting GNB1,3:GNG13 complex activates Phospholipase C beta-2 (PLCB2) which hydrolyzes phosphoinositol 4,5-bisphosphate (PI(4,5)P2) to yield inositol 1,4,5-trisphosphate (I(1,4,5)P3) and diacylglycerol (DAG). I(1,4,5)P3 binds and activates ITPR3 to release calcium ions from the endoplasmic reticulum into the cytosol. Cytosolic Ca2+ causes TRPM5 sodium channels to open and depolarize the cell. SCN2A, SCN3A, and SCN9A sodium channels also appear to augment the depolarization. Depolarization causes opening of CALHM1:CALHM3 channels which transport ATP from the cytosol to the extracellular region. ATP then acts as a neurotransmitter in the taste sensing system.

Alternative pathways exist for sensing sugars and glutamate, as evidenced by residual signaling activity in the absence of TAS1R1 or TAS1R3. Glutamate is sensed by the glutamate receptors GRM1 (mGluR1) and GRM4 (mGluR4) expressed in type II taste cells. GRM1 and GRM4 activate calcium channels by an in-
completely characterized mechanism that probably involves heterotrimeric G proteins. Glucose may be sensed by a pathway comprising transport into type II taste cells via the glucose transporters SGLT1 and GLUT4, generation of ATP, and inhibition of KATP potassium channels by ATP.

Protons (H+ ions) from acidic compounds translocate from the extracellular region to the cytosol of type III taste cells through the OTOP1 channel. Weak acids such as acetic acid and citric acid are also able to enter type III cells by diffusing through the membrane in their protonated, uncharged forms. Once in the cytosol, the H+ ions inhibit KCNJ2 inwardly rectifying potassium channels, depolarizing the cell. The H+ ions may also open unidentified sodium channels to further depolarize the cell. Depolarization causes exocytosis of the neurotransmitters serotonin (5-HT) and gamma-aminobutyric acid (GABA).

Low concentrations of salt appear to be sensed in specific salt-sensing cells that may be a subset of type II cells. Low concentrations of salt are believed to enter the cell through an epithelial sodium channel (ENaC, SCNN) and the ability to taste low concentrations of salt is dependent on the SCNN1A pore-containing subunit of the SCNN complex in mice. Human taste cells express both SCNN1A and SCNN1D pore-containing subunits. The composition of other subunits of the complex is less certain. The transport of sodium ions (Na+) into the cells depolarizes the plasma membrane and eventually leads to opening of CALHM1:CALHM3 channels which transport ATP from the cytosol to the extracellular region.

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Author/Editor Status</th>
<th>Author/Editor Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021-03-05</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2021-08-08</td>
<td>Reviewed</td>
<td>Jiang, P.</td>
</tr>
</tbody>
</table>
Taste receptors for bitter compounds, sweet compounds, and umami compounds (L-glutamate in humans, several amino acids in mice) are G protein-coupled receptors located in type II taste bud cells that signal through a common downstream pathway (reviewed in Margolskee 2002, Kinnamon 2009, Kurihara 2015, Roper and Chauhari et al. 2017, Kinnamon and Finger 2019, Servant et al. 2020). Umami (“savoury”, L-glutamate) taste receptors are heterodimers of the plasma membrane proteins TAS1R1 and TAS1R3. TAS1R1:TAS1R3 heterodimers also bind 5’ nucleotides such as 5’ IMP which synergistically augment umami taste. The glutamate receptors GRM1 (mGluR1) and GRM4 (mGluR4) act in an alternative pathway for sensing glutamate in taste cells (reviewed in Chaudhari et al. 2009). Sweet taste receptors are heterodimers of the plasma membrane proteins TAS1R2 and TAS1R3 (reviewed in Yang et al. 2021). The glucose transporters SGLT1 and GLUT4 are expressed in type II taste cells and may provide an alternative pathway for sensing glucose (reviewed in von Molitor et al. 2020). Bitter receptors are a large family of monomeric plasma membrane proteins, the TAS2R proteins.

TAS1R-containing sweet and umami receptors and TAS2R bitter receptors are each physically associated with a particular heterotrimeric G protein complex, the gustducin complex, containing GNAT3 (gustducin), GNB1 or GNB3, and GNG13. Upon binding an agonist ligand, the receptor activates the alpha subunit, GNAT3, to exchange GDP for GTP, which results in a conformational change in GNAT3 that causes the receptor-gustducin complex to dissociate, yielding GNAT3:GTP, GNB1,3:GNG13, and the receptor:ligand. The GNB1,3:GNG13 complex binds and activates Phospholipase C beta-2 (PLCB2), which then hydrolyzes phosphoinositol 4,5-bisphosphate (PI(4,5)P2) to yield diacylglycerol and inositol 1,4,5-trisphosphate (I(1,4,5)P3). I(1,4,5)P3 binds and activates the calcium channel IP3-gated Ca-channel type 3 (ITPR3) and ITPR3 then releases calcium ions from the endoplasmic reticulum into the cytosol. The increased cytosolic calcium activates the TRPM5 cation channels, which then transport sodium ions along the concentration gradient from the extracellular region to the cytosol (reviewed in Aroke et al. 2020). The depolarization activates SCN2A, SCN3A, and SCN9A channels, which transport further sodium ions from the extra-
cellular region to the cytosol. The depolarization of the plasma membrane opens CALHM1:CALHM3 channels, which transport ATP, a neurotransmitter in the olfactory system, from the cytosol to the extracellular region.

Taste receptors were initially discovered in taste buds of the tongue and have now been found in several other tissues including nasal epithelium (Barnham et al. 2015, inferred from rodent homologs in Tizzano et al. 2011), the respiratory system, pancreatic islet cells, sperm (Governini et al. 2020), leukocytes (Malki et al. 2015), and enteroendocrine cells of the gut (inferred from rat and mouse homologs in Wu et al. 2002).

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Edition</th>
<th>Author/Editor</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021-03-05</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2021-08-08</td>
<td>Reviewed</td>
<td>Jiang, P.</td>
</tr>
</tbody>
</table>
Sensory perception of sour taste

Location: Sensory perception of taste

Stable identifier: R-HSA-9729555

The sour taste channel OTOP1 is located in type III taste bud cells where it transports H+ ions from the extracellular region into the cytosol (reviewed in Liman and Kinnamon 2021). Organic acids such as acetic acid and citric acid are believed to also enter type III taste bud cells by passive diffusion of the protonated (uncharged) form of the acid across the plasma membrane. The increase in cytosolic H+ ions inhibits the KCNJ2 potassium channel and may also open unidentified sodium channels to further depolarize the cell. The resulting depolarization is adequate to generate an action potential which eventually results in release of the neurotransmitters serotonin (5-HT) and gamma-butyric acid (GABA) (inferred from mouse type III cells in Huang et al. 2005, Huang et al. 2009, Huang et al. 2011). Mice lacking both P2x2 and P2x3 ATP receptors do not produce nerve activity in response to sour tastants so ATP may play a role in transmission of sour taste (Eddy et al. 2009).

Literature references


Editions

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021-04-28</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2021-08-08</td>
<td>Reviewed</td>
<td>Jiang, P.</td>
</tr>
</tbody>
</table>

https://reactome.org
Initially, type I taste bud cells were suggested to be responsible for tasting low concentrations of salt, however a subset of type II taste bud cells are now thought to be responsible (Nomura et al. 2020). The identity of salt-tasting cells remains a subject of current research. The ability to taste low concentrations of salt is at least partially due to an amiloride-sensitive sodium channel believed to be an SCNN channel (ENaC channel). SCNN complexes contain the pore-forming subunit SCNN1A or SCNN1D, and the modulatory subunits SCNN1B and SCNN1G, all of which have been detected in human taste buds (Rossier et al. 2004, Stähler et al. 2008). Knockout of SCNN1A in mice abolished amiloride-sensitive salt taste and attraction to low concentrations of salt, however SCNN1B and SCNN1G do not colocalize with SCNN1A in taste cells of mice (Lossow et al. 2020), raising the question of the subunit composition of the SCNN complex. SCNN1D is present in human taste buds but not in mouse taste cells.

In humans, a SCNN channel containing SCNN1A or SCNN1D located in the plasma membrane is believed to transport sodium ions from the extracellular region into the cytosol, resulting in depolarization that causes CALHM1:CALHM3 channels to open and release ATP, a neurotransmitter, from the cytosol to the extracellular region.

**Literature references**


**Editions**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021-05-07</td>
<td>Authored, Edited</td>
<td>May, B.</td>
</tr>
<tr>
<td>2021-08-08</td>
<td>Reviewed</td>
<td>Jiang, P.</td>
</tr>
</tbody>
</table>
# Table of Contents

- Introduction 1
- Sensory perception of taste 2
  - Sensory perception of sweet, bitter, and umami (glutamate) taste 4
  - Sensory perception of sour taste 6
  - Sensory perception of salty taste 7

Table of Contents 9