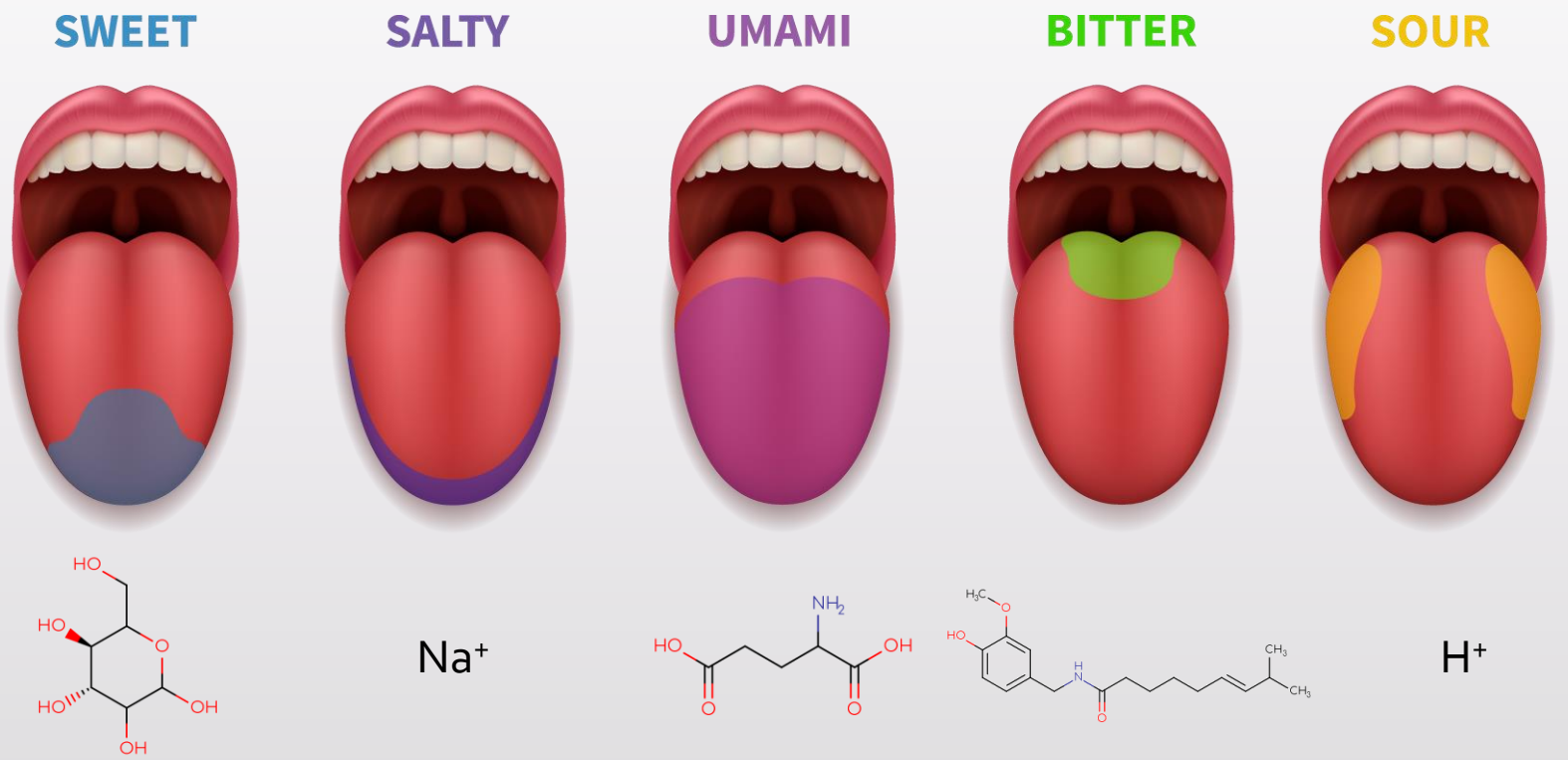
Metabolomics of Taste

Metabolomics of Taste - Human Metabolome Technologies



Recent advances in understanding the molecular basis of taste physiology opens new opportunities to optimize in cellular agriculture. This is particularly relevant at a time when alternative ingredients and processing (e.g. 3D printing) are being increasingly used, potentially altering the digestibility and acceptability of alternative diets, even if they are nutritionally balanced. The molecular characterization of taste receptors reveals common taste discrimination mechanisms, common structures within taste groups leading to predictability of a taste profile from metabolite profiling.

Taste & Taste Receptors

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Taste is an important part of our perception of foods. Taste perception in humans is considered to consist of five canonical basic taste qualities: Sweet, Sour, Salty, Bitter, and Umami. These 5 basic taste qualities interact in almost every consumed food. The primary function of taste is to identify substances that lead to energy and/or electrolyte balance, while avoiding ingestion of toxic substances. Taste can also serve a metabolic function by preparing the body to assimilate ingested nutrients more effectively. Taste interactions can either be enhancing or suppressing, depending on both the taste quality, specific tastants (those metabolites that enduce a flavor response) and tastant concentrations. These interactions are complex and, even though the interactions between tastes have been extensively researched and reviewed, the mechanisms are still not well understood. However, we continue to learn more about tastants and how changes in a tastant profile lends to changes in food flavor.

Skeletal muscle metabolites found in beef, chicken and fish include amino acids and sugars that are precursors of volatile compounds associated with aroma. Muscle metabolites are useful indices to predict or evaluate meat flavor and overall palatability. Metabolic profile comparisons between meats of different animal breeds, feeding conditions, and cellular processes can indicate changes in taste profiles. Studies reveal that metabolomic information is expected to provide indices to predict sensory phenotypes of meat.

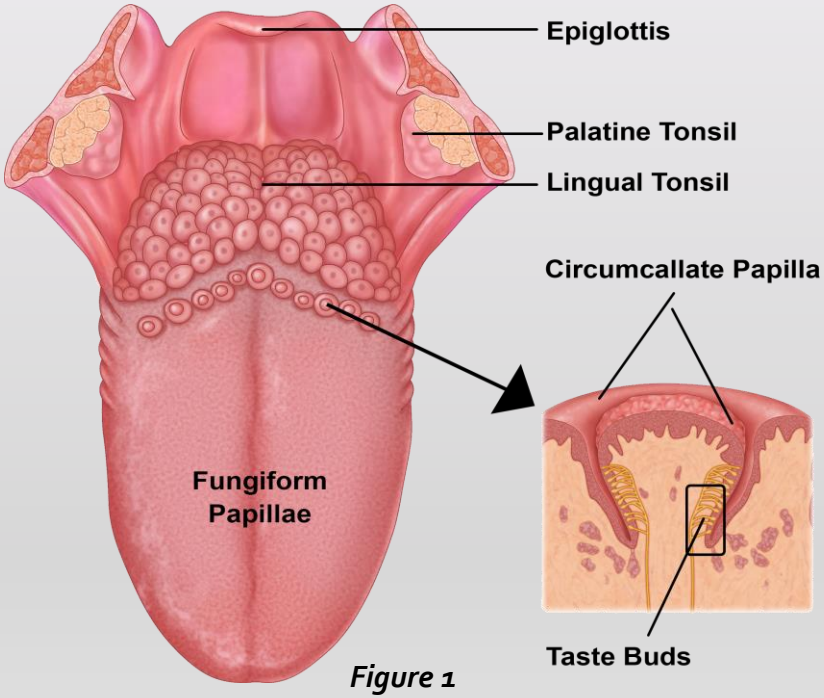

Figure 1

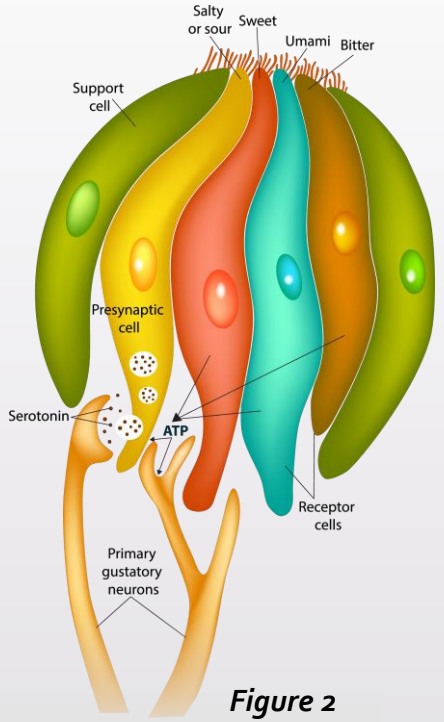

Figure 2

Bitter, sweet, and umami receptors are well understood. The receptors for each of these taste qualities are, by and large, restricted to a single cell types within the taste bud, allowing encoding of information by activation of unique populations of cells. One misconception is that taste receptors are only in the taste buds in the oral cavity (Figure 1). In fact, taste receptors are distributed throughout the body from the nasal cavity to the intestines.

Taste signals are mediated by distinct transduction pathways (Figure 2) expressed in subsets of taste receptor cells. Specifically, sweet and umami tastes are detected by the G protein-coupled receptor (GPCR), T1R family. Umami is detected by metabotropic glutamate receptors. Bitter taste, on the other hand, is detected by GPCR T2R family. Sour and salty tastes are modulated by specialized membrane channels. For sour taste, acid sensing ion channels and for salty taste, epithelial sodium channel facilitates its detection. The out puts of these taste receptors include ATP and neurotransmission through the gustatory nerves.

Sweet, Bitter & Umami Tastants

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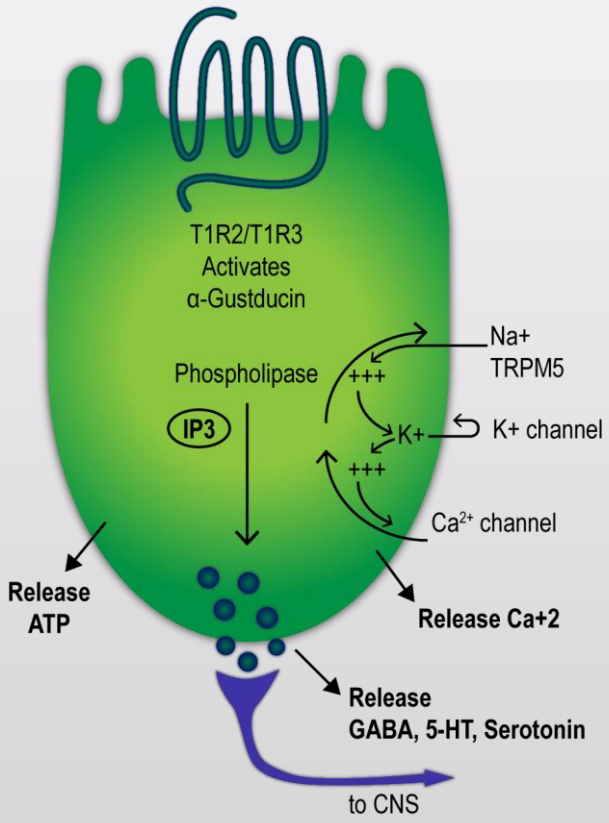
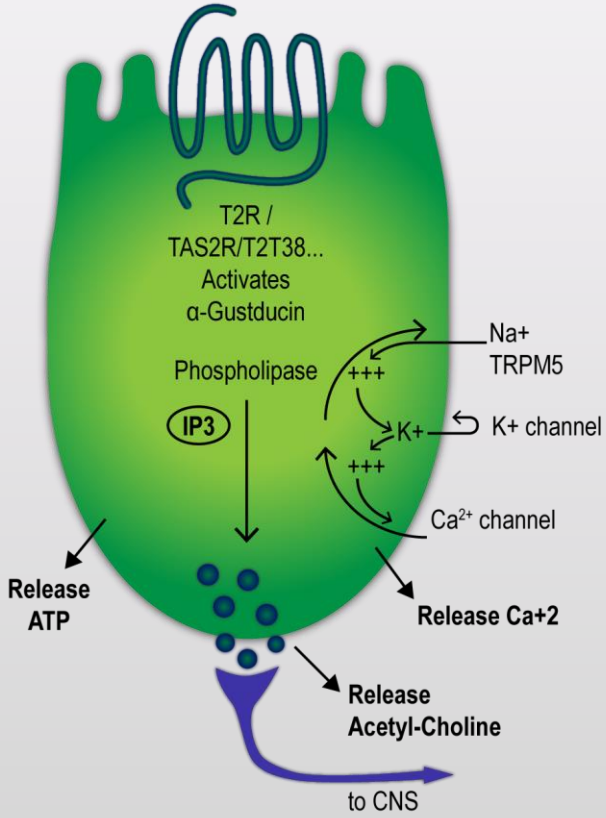
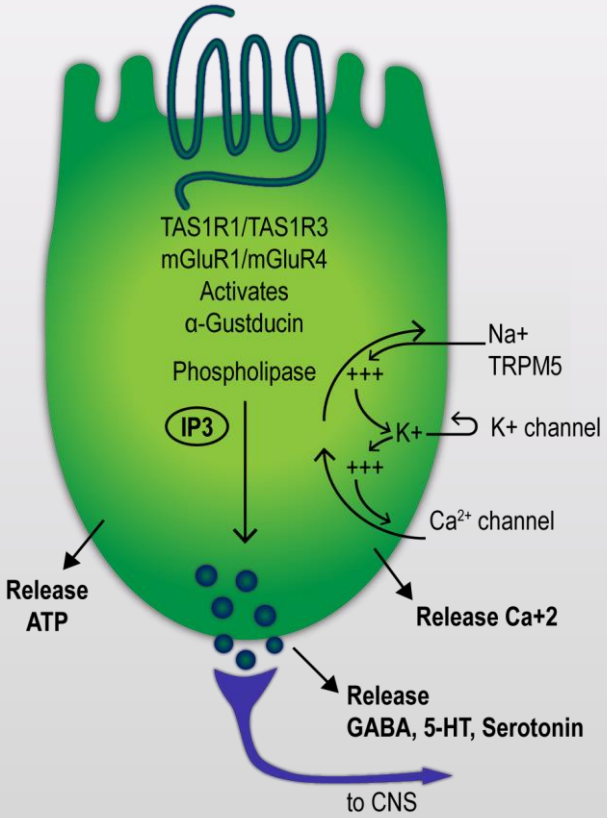
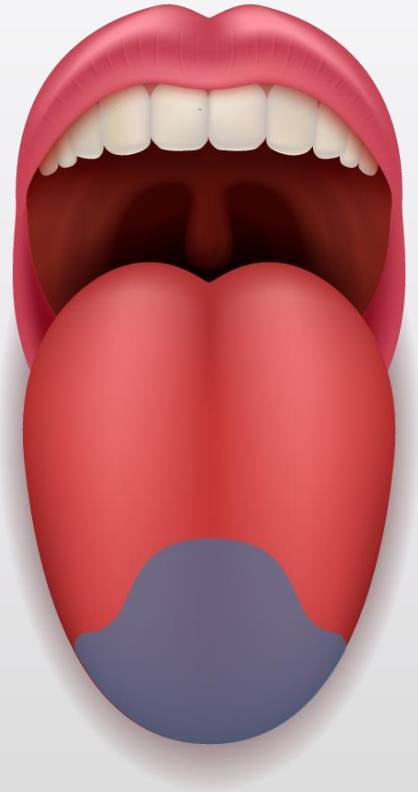




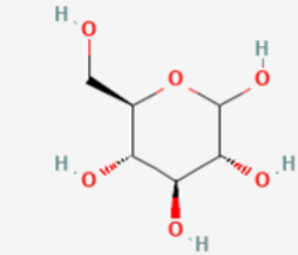


Sweet Taste

SWEET



Sweet taste receptors (Figure 3) are composed of a heterodimer of taste 1 receptor member 2 (T1R2) and taste 1 receptor member 3 (T1R3). Accumulating evidence shows that sweet taste receptors are ubiquitous throughout the body, including the gastrointestinal tract and the hypothalamus. These sweet taste receptors are heavily involved in nutrient sensing, monitoring changes in energy stores, and triggering metabolic and behavioral responses to maintain energy balance. Not surprisingly, these pathways are heavily regulated. Dysfunction in one or more of these pathways may be important in the pathogenesis of common diseases, such as obesity and type 2 diabetes mellitus.



The receptor tastant pathway for sweetness has been extensively studied. Binding of a ligand to the sweet taste receptor leads to activation of the heterotrimeric G-protein α-gustducin. Phospholipase C β2 is subsequently stimulated, leading to release of intracellular Ca2+ and activation of the transient receptor potential cation channel M5 (TRPM5). This sequence results in the release of ATP, which can then activate adjacent sensory afferent neurons that send signals to brain centers involved in taste perception.

Sweet tastants include simple sugars (glucose, fructose, sucrose, maltose and sucralose), artificial sweeteners (e.g., saccharin, aspartame, cyclamate), sweet amino acids (D-tryptophan, D-phenylalanine, D-serine), and sweet proteins (monellin, brazzein, thaumatin). The recognition thresholds for sweet substances are tightly linked with the circulating hormone leptin levels

Endocannabinoids also likely enhance taste cell responses to sweeteners. These findings suggest that endocannabinoids may enhance sweet taste response in sweet taste cells expressing T1R3.

A growing number of studies have demonstrated that sweet taste receptors are expressed throughout the body, including the nasal epithelium, respiratory system and pancreatic islet cells. The function of the sweet taste receptor system in the gastrointestinal tract is likely involved in nutrient sensing, glucose homeostasis, as well as secretion of GI peptides.

The sweet taste is appetitive – meaning sweetness can increase our appetites for calorie rich foods, like sugary carbohydrate containing fruit.

Umami Taste

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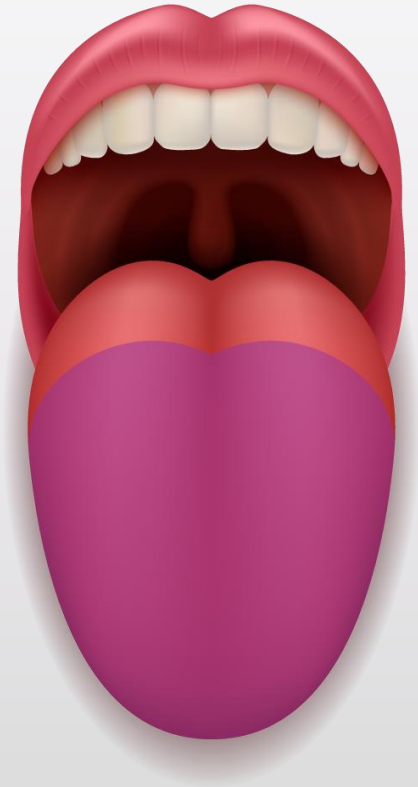
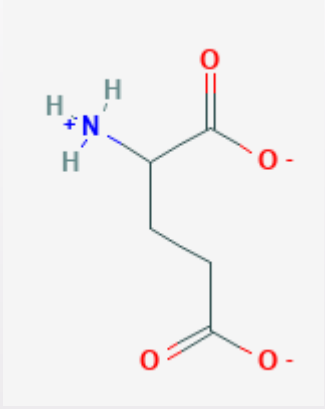
UMAMI





Umami or savoriness taste is elicited by many small molecules, including the amino acid (L-glutamate) and nucleotides (inosine 5-monophosphate (IMP) and guanosine- 5-monophosphate (GMP)) through taste receptors (Figure 4). Umami tastants are widely present in meat broths and fermented products. Some amino acids are sweet or bitter, however, take on an umami flavor when IMP or GMP is present. The umami taste is often described as a meaty, broth-like, or savory taste, and is independent of the four other traditional basic tastes — sweet, sour, salty and bitter. Meaning high levels of umami tastants can be largely independent of other tastants. Meat, fish, and tomatoes have strong umami flavors. As a tomato ripens, the natural content of L-glutamate increases and the tomato becomes more tasty. Similarly, as cheese matures, there is a significant increase in L-Glutamate which contributes to the taste. Kombu (Asian Kelp or brown seaweed) is also high Umami flavor. Kombu is source of L-glutamic acid, iodine and fiber. Umami is thought to evolve as an indicator of healthy food since many of the umami tastants come from protein and a diet high in protein is very desirable.

The taste receptors (Figure 4) responsible for the sense of umami include glutamate receptors mGluR4, mGluR1, and taste receptor type 1 (TAS1R1 + TAS1R3), all of which have been found in all regions of the tongue bearing taste buds. These receptors are also found in some regions of the duodenum.

Receptors mGluR1 and mGluR4 are specific to L-Glutamate whereas TAS1R1 + TAS1R3 are responsible for the synergistic responses. However, the specific role of each type of receptor in taste bud cells remains unclear. They are G protein-coupled receptors (GPCRs) with similar signaling molecules that include G proteins beta-gamma, PLCB2 and PI3-mediated release of calcium (Ca2+) from intracellular stores. Calcium activates a so-called transient-receptor-potential cation channel that leads to membrane depolarization and the consequent release of ATP and secretion of neurotransmitters including serotonin. Cells responding to umami taste stimuli do not possess typical synapses, but ATP conveys taste signals to gustatory nerves and in turn to the brain that interprets and identifies the taste quality via the gut-brain axis.

In 2006, a Japanese research team found the glutamate receptor type 1 variant (mGluR1), in stomach tissue. As the umami taste sends signals to the brain through the taste nerves after activation of its receptors on the tongue, umami receptors in the stomach also send signals to the brain via the vagus nerve. The vagus nerve is the nerve that transfers sensory information of ingested foods from various alimentary organs, including the stomach, to the brain to regulate digestion of food. Upon receiving those signals, the brain responds by preparing the stomach for the digestion of food taken into the body via other nerve fibers of the vagus.

While L-Glutamate is associated with umami flavor, the optical isomer, D-Glutamate, is more associated with sour taste. L-Glutamate containing peptides have also been associated with umami flavor depending upon amino acid sequence. However, gamma-Glu dipeptides are associated with Kokumi flavor and para-glutamate peptides with sweet.

Umami is appetitive encouraging consumption of savory, protein rich meat sources.

Bitter Taste

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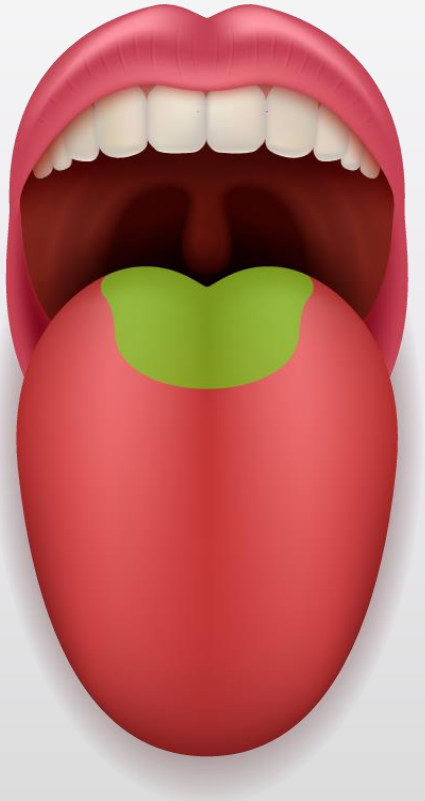
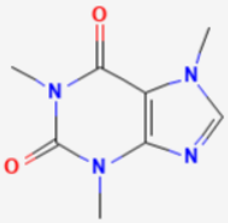
BITTER



Bitter taste is thought to guide organisms to avoid harmful toxins, noxious substances, unsafe or unripe foods and thus is critical to human survival. Bitterness could suggest rotten meat. The T2R bitter receptors also play in processes as diverse as innate immunity, secretion, contraction, and reproduction. Like other unpleasant tastes (sour, salty), some bitter taste is acceptable and part of healthy diet flavor, however, high levels of bitterness would suggest unsafe or rotten food.

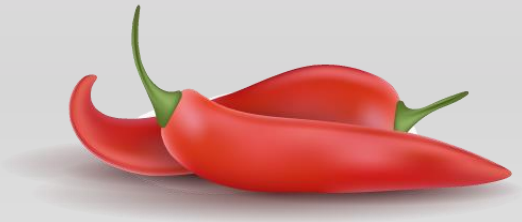


The sensors for bitter compounds (T2Rs or TAS2Rs), are a class of GPCRs originally identified in type II taste receptor cells in the taste bud (Figure 5). Humans possess 40 to 80 different types of bitter taste receptors.

The bitter receptor, T2R38, is also expressed in the cilia of human sinus epithelium. It is activated by microbe-derived quorum-sensing molecules (e.g., acyl-homoserine lactones [AHLs]) generating nitric oxide, a potent bactericide and releases anti-microbial peptides. Hence bitterness warns of both rotten food, as well as, food with high amounts of bacteria.

Alkaloids, quinine, sulfamides, and caffeine are among the most of bitter substances with extremely low taste thresholds and are detectable in very low concentrations. The size of such molecules is one aspect to account for degree of bitterness. An increase in length of chains of carbon atoms in organic molecules tends to be associated with increased bitterness Due to the number and complexity of bitter related receptors, bitter chemicals cover a large range of chemical classes.

Because drugs are often bitter to the taste, quite a bit has been studied to understand bitterness. In fact, a bitter database exists (//bitterdb.agri.huji.ac.il) and a bitterness prediction tool (*Sci Rep* **7,** 12074 (2017). BitterPredict suggests that about 40% of random molecules, and a 66% of clinical and experimental drugs, and of 77% natural products have bitterness. The high percentage of predicted bitter compounds in this set suggests that bitter taste may be among the most abundant tastes encountered in nature. Food ingredients represented in the food data base, (https://foodb.ca) are predicted to include 38% bitter compounds suggesting bitterness as a critical factor in a healthy diet.



Aside from alkyloids and important bitter tastants, peptides represent a large and growing list of bitter tastants. Bitter peptides are a structurally diverse group of oligopeptides often generated in fermented, aged, and hydrolyzed food products that make them unfavorable for consumption. Knowledge of the structural features of bitter receptors and of the factors that stimulate bitter receptors will aid in understanding the mechanism responsible for bitter taste perception.

Salty & Sour Taste

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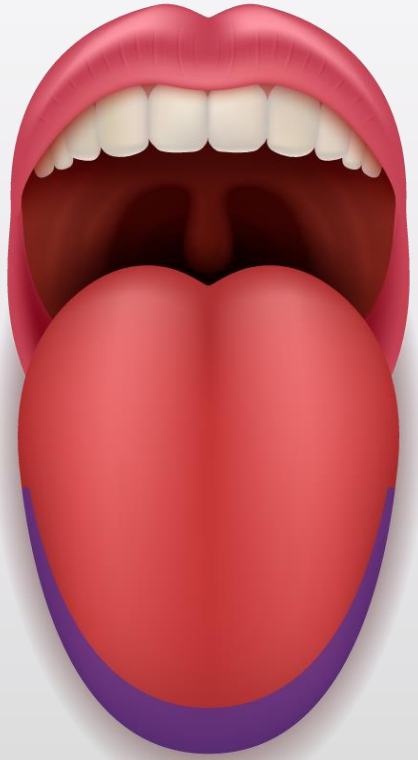
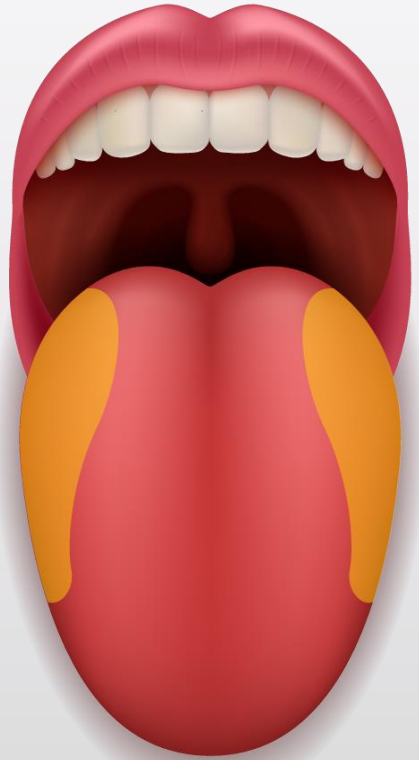
SALTY



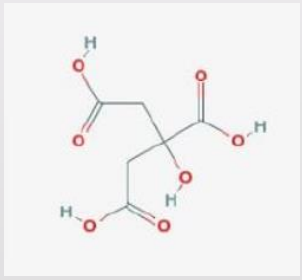
The **salty taste** is mitigated through the epithelial sodium channel, ENaC, which serves as the salty receptor. ENaC is co-expressed with the voltage-activated ATP release channel CALHM1/3 in a subset of taste cells and that these cells mediate the salty taste. The degree of saltiness decreases in the following order: ammonium (most salty), potassium, calcium, sodium, lithium, and magnesium (least salty).

The degree of saltiness is evolved as either a good or unpleasant taste. Sodium is an essential nutrient, so some saltiness is necessary and sought in flavor. Our bodies use salt (largely as sodium chloride) to regulate fluids and to create nerve impulses. Yet unlike other vital minerals, such as calcium (which we store in our bones), we can't store salt for later use. However, too high saltiness is unpleasant and acts as a consumption warning. Too high salt is not healthy. Drinking sea water will kill you, and a diet with consistently too much salt has been linked to heart attacks, stroke, and high blood pressure. A high salt diet also puts heavy a burden on your kidneys and can lead to painful kidney stones.

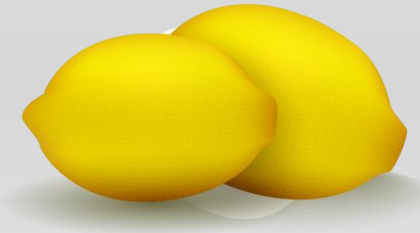
SOUR



Sour taste is considered the simplest of the basic tastes because it is elicited only by hydrogen ions. However, there is not a clear understanding of that relationship to allow sour taste intensity to be predicted and rationally modified in foods. The intensity of sour taste perception is related to the molar concentration of all organic acid species. Acids are detected by the type III taste receptor cells (TRCs). The first step in sour taste transduction is believed to be entry of protons into the taste bud cell, which leads to acidification and the generation of action potentials.



While sour receptors are yet to fully delineated, studies suggest that 4 carbon diacids (Fumarate, Succinate, Itaconate, D/L-Malate and Tartaric) have a higher sourness score than smaller or larger common acids (Citrate, lactate, Levulinate, Sorbate) and higher scores than D-Glutamate and N-AcetylGlutamate. The sugar (Galactouronate) has a higher sourness score than lactones Gluconolactone, D/L-Ascorbate, Ribonolactone and Galactononlactone.



Sourness has also evolved as a test of food value. Ripe fruit has just the right amount of sourness when ready for consumption. Sour taste is acceptable when mild, but becomes unpleasant when strong. It helps us to avoid unripe fruit and damage our tissue with acids. For example, too much lactic acid may suggest milk has gone bad or spoiled.

Other Candidates for Flavor Sensors

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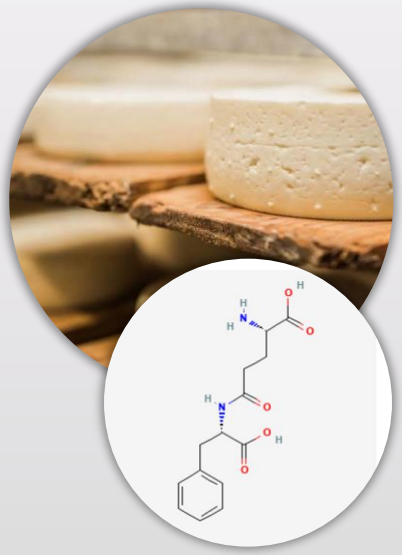
OLEOGUSTUS, OILY OR FATTY TASTE

Lipid sensors have been identified on the tongue which suggests that fat can be considered as the sixth taste. People can identify the distinct taste of fat as something totally separate from its texture. While the pure flavor of fat might sound delicious, it's not. Oleogustus is described as "unpalatable," "rancid" and "irritating." when it's tasted on its own. However, combined with other flavors, oleogustus can be delicious. Fatty taste itself is not pleasant. When concentrations of fatty acids are high in a food it is typically rejected, as would be the case when a food is rancid. Long chain nonesterified fatty acids (LC-NEFA) are proposed as stimuli for "fat taste". While shorter chain fatty acids (2 to 5 carbons) stimulate a sensation similar to sour and middle chain fats (6 to 12 carbons) to provide a more complex flavor. In general, as chain length increases to long chain (13 to 21 Carbons) this sensation changes to an oleogustus taste.



KOKUMI TASTE

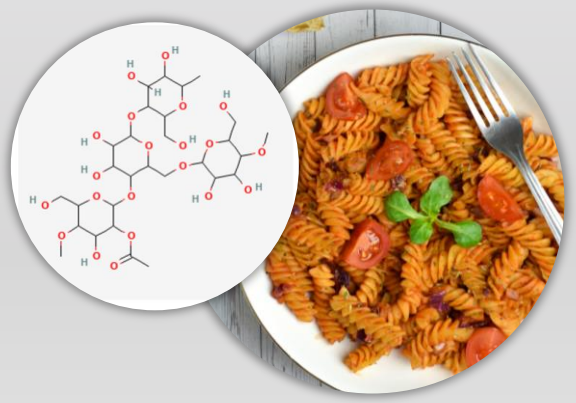
Kokumi is another putative taste quality gaining interest in the field of sensory sciences. Kokumi is a well-accepted taste sensation in Asian cuisine. It is described as a sensation of enhancement of sweet, salty and umami tastes when associated with specific compounds

The human Calcium Sensing Receptor (CaSR) has been designated as the putative kokumi taste receptor for humans. CaSR is a member of the same receptor class as the T1R receptors for umami and sweet taste, the class C of GPCRs. CaSR has been found to be expressed in most tissues involved in calcium homeostasis e.g. the parathyroid glands, kidneys, thyroid and the brain, as well as the gastrointestinal tract and taste papillae (Figure 1). It is also known to be involved in many physiological processes including, gastric acid secretion, insulin release from beta-cells in the pancreas and promoting glucose tolerance, as well as, pathophysiological processes such as vascular calcification and osteoporosis.

γ-glutamyl peptides have been identified as a primary tastant for Kokumi and for agonist activity against hCaSR. Like Umami, kokumi is an important taste modality for carnivores that enhances the palatability of meat-derived compounds such as peptides and amino acids.

STARCHINESS OR STARCHY TASTE

It is widely accepted that humans can taste mono- and disaccharides as sweet substances, but they cannot taste longer chain oligo- and polysaccharides. From the evolutionary standpoint, the ability to taste starch or its oligomeric hydrolysis products would be highly adaptive, given their high nutritional value. Glucose oligomer detection (7 to 14 glucose units) is found to be independent of the T1R2/ T1R3 sweet taste receptor. Because starch is one of the primary sources of energy that enables the body to perform its function, its gustatory detection would be highly beneficial. Large glucose oligomers and polymers (e.g. starch) can be detected through the gustatory system, independent of the sweet taste, when starch is broken down into smaller glucose oligomers by an enzyme in our saliva called alpha-amylase. These smaller glucose oligomers can be tasted by specific receptors. The taste of these glucose oligomers is cereal-like, bread-like or rice-like and generally referred to as "starchy".



Tastomics of Meats

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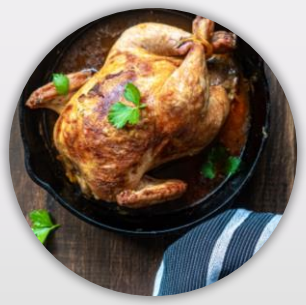
Skeletal muscle characteristics are designed by a functionally cooperative set of genes specific to the spatiotemporal requirement in each muscle. Gene expression is further modulated at levels of transcription, post-transcription, translation, and protein modification during development, growth, and maturation stages of the muscle or muscle cultivate. Accordingly, muscle metabolites determine the physiological muscle characteristics and meat quality traits as the major phenotypic components. Hence each type of meat muscle (e.g. Fish, chicken, beef) has its own metabolic, nutrient and tastant profile conditional to its source and generation. Although often meats are cooked and seasoned as food, the end product is heavily influenced by the raw muscle tastant combinations and metabolic profiles.

TASTOMICS OF FISH

Fish live in a totally foreign environment than beef and chicken. High levels of osmolytes are required to maintain cellular osmotic pressure which can bring a bitter taste. High levels of fats are required for thermal homeostasis bringing in a fishy or fatty taste. The taste active components of fish also include high amounts of amino acids like glutamate (umami), glycine (sweet), alanine, arginine and proline and nucleic acids like nucleotides inosine 5′-monophosphate (IMP), adenosine 5′-monophosphate (AMP), guanosine 5′-monophosphate (GMP) are also in fish muscle. Acids (sour) such as lactate and succinate are important contributors to the taste of raw and processed fish products. L-Glutamate contributes to *umami* taste intensified by the co-existence of IMP, GMP and AMP. However, a large amount of alanine or glutamate can suppress the sweetness effect of glycine through antagonistic effects. Hence a balance of these amino acids, nucleotides and fats lends to the taste perception in fish products.

TASTOMICS OF BEEF

When you are craving meat, most likely what you're really craving is fat. The unique mixture of fat and umami, a savory taste, creates a particular texture of creaminess and juiciness within meat. Inosinate (a nucleoside found in meat and fish) and guanylate (like in dried mushrooms) contribute to that umami taste. When a number of these substances combine, the umami taste intensifies to what chefs are calling a "u-bomb." Beef muscle is also high in fat content, that can contribute a fatty taste or oleogustus flavor. Alanine, Glutamate and Ser are the major amino acids that can also contribute to flavor in beef products.



TASTOMICS OF CHICKEN

Chicken has a higher level of D-amino acids than beef and fish adding a higher sweet contribution from these amino acids than the more bitter amino acid levels found in beef and fish. Studies have suggested that chicken breast muscle taste differences are caused by the altered metabolism of carbohydrates, protein and amino acids, combined with fatty acid oxidation products. Discriminators in chicken meat flavors may include branched chain amino acids, histidine, creatine, beta-alanine, long chain fatty acids, carnitine, carnosine and anserine. Increases of alanine, serine, glutamate, taurine, and leucine are particularly notable for adding favorable taste through combination of sweet and umami flavors.

Amino Acids & Taste Reference Chart

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Amino Acids	D Taste	L Taste	L form with IMP/GMP Enhancement
Arginine	Bitter	Bitter	
Isoleucine	Bitter	Bitter	
Lysine	Bitter	Bitter	
Ornirine	Bitter	Bitter	
Methionine	Bitter	Bitter	
Tyrosine	Bitter	Bitter	
Proline	Bitter	Sweet	
Hydroxy proline	Bitter	Sweet	
Glycine	Na	Sweet	Added Umami
Asparagine	Sweet	Bitter	
Histidine	Sweet	Bitter	
Leucine	Sweet	Bitter	
Phenylalanine	Sweet	Bitter	
Tryptophan	Sweet	Bitter	
Valine	Sweet	Bitter	
Aminobutyric (abu)	Na	Sweet	
Alanine	Sweet	Sweet	Added Umami (Only L)
b-Alanine	Sweet	Sweet	
Glutamine	Sweet	Sweet	Added Umami
Serine	Sweet	Sweet-umami	Added Umami
Threonine	Sweet	Sweet	
Aspartic acid	Sour, Salty	Sour, Bitter	Added Umami
Cysteine	Sour, Bitter	Sulphurous	
Glutamic acid	Sour	Umami	Enhanced Umami
Succinyl-Arg		Umami	
Succinyl-Glu		Umami	
GABA		Bitter	
Carboxymethyllysine (CML)		Bitter	
Frucosyl-Val		Bitter	

Peptides & Taste Reference Chart

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Peptides	Taste
Glu-Trp	Bitter
Glu-Tyr	Bitter
Glu-Phe	Bitter
Glu-Gly	Bitter
Glu-Thr	Bitter
Glu-Val	Bitter
Gly-Val	Bitter
Gly-Gly-Val	Bitter
Gly-Val-Val	Bitter
Val-Val-Val	Bitter
Val-Leu	Bitter
Val-Ile	Bitter
Val-Phe	Bitter
Val-Ile-Phe	Bitter
Leu-Val	Bitter
Ile-Val	Bitter
Phe-Val	Bitter
Phe-Ile-Val	Bitter
Met-Ile	Bitter
Arg-Leu	Bitter To Sour
Phe-Thr	Bitter To Sour
Phe-Gln	Bitter To Sour
Pro-Leu	Bitter
Gly-Gly	Flat
Ala-Gly	Flat
Gly-Ala	Flat
Gly-Val-Gly	Flat
Val-Val-Gly	Flat
Glutathione	Bitter
Anserine	Bitter
Acyl-hSer-Lactones	Bitter
Carnosine	Bitter

Peptides	Taste
Val-Asp	Bitter/Umami/Sour
Val-Glu	Bitter/Umami/Sour
Glu-Glu	Umami
Glu-Asp	Umami
Glu-Ser	Umami
Glu-Asp-Glu	Umami
Glu-Gly-Ser	Umami
Asp-Glu-Ser	Umami
Thr-Glu	Umami
Ala-Glu	Umami
Val-Gly	Umami
Val-Gly-Gly	Umami
Val-Val	Umami
Glu-Gln-Glu	Umami
Ser-Glu-Glu	Umami
Frucosyl-Glu	Umami
Asp-Val	Sour
Gly-Val	Sour
<Glu-Gln	Sweet
<Glu-Gly	Sweet
Leu-Gln	Sweet
Ile-Gln	Sweet
Thr-Phe	Sweet
Pro-Lys	Sweet
ile-Glu	Sweet
Ala-Ala	Sweet
Ala-Gly-Gly	Sweet
Val-Gly-Val	Sweet
g-Glu-Glu	Kokumi
g-Glu-Phe	Kokumi
g-Glu-Gly	Kokumi
g-Glu-Cys-Gly	Kokumi
g-Glu-Val-Gly	Kokumi

Common Acids and Others & Taste Reference Chart

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Others	Taste
Vit C	Sour, Acidic
Vit D2	Tasteless
Vit E	Fatty Distasteful
Vit K1	Tasteless, Mild Sweet
Vit A	Stale, Weak
Vit B1	Sour, Bitter
Vit B2	Strong Bitter
Vit B12	Tasteless Flat
Butanoic acid 4:0	Rancid, Sour
Caproic Acid 6:0	Sour, Sweaty
Caprylic acid 8:0	Sour, Yeasty
Capric Acid 10:0	Rancid Sour Fatty Citrus
Palmitoic Acid C16:0	Bitter Obnoxious
Linolenic Acid C18:3) OMEGA 3	Salty Pungent
Linoleic Acid (C18:2) OMEGA 6	Bitter, Metallic
Oleic Acid (C18:1) OMEGA 9	Soapy
Stearic Acid C18:0)	Waxy Fatty
Lutein	Bitter
Zeazanthin	Bitter
Plant alkyloids	Bitter
Plant carotenoids (xanthophylls)	Bitter
Plant Flavanoids	Bitter
Glycosides	Bitter
Urea	Cooling Saline Metallic
Glycerol	Sweet
Galactosylglycerol	Sweet
TMAO	Bitter
IMP GMP AMP	Umami Enhancing
Hypoxanthine	Bitter

Common Acids	Taste
D/L-Malic Acid	Sour
Fumaric Acid	Sour
Itaconic Acid	Sour
L-Tartaric Acid	Sour
Succininic Acid	Sour
Citric Acid	Sour
D/L-Ascorbic Acid	Sour
Lactic Acid	Sour
Levulinic Acid	Sour
Sorbic Acid	Sour
Cis-Aconitic Acid	Sour
D-Glutamic Acid	Sour
D-Gluconic Acid	Sour
D-Glucuronic Acid	Sour
Gluconolactone	Sour
Gluconolactone	Sour
Glutaric Acid	Sour
L-Threonic Acid	Sour
N-Acetyl-L-Glutamic Acid	Sour
Ribononlactone	Sour

Summary & References

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Taste is a complex sense based on a combination of all of our senses. The 5 taste receptors (sour, salty, umami, sweet and bitter) have been identified, while others (Starchy, Oleogustus, Kokumi) are becoming more accepted as unique tastes in themselves. Each taste bud recognizes different tastants, while some tastants interact with others for a complex flavor response. Metabolomic profiling of raw meat muscle and muscle cell products can allow for fine tuning taste, cell line optimization and nutrient assessment.

1. **Changes in the perception of bitter constituents in thermally treated yeast extract,** *Aygul Alim, Huanlu Song, Chao Yang, Ye Liu, Tingting Zou, Yu Zhang and Songpei Zhang,* J Sci Food Agric. Aug 15;99(10):4651-4658 (2019).
2. **Taste receptors for umami: the case for multiple receptors1–4,** *Nirupa Chaudhari, Elizabeth Pereira, and Stephen D Roper,* Am J Clin Nutr 90(suppl):738S–42S (2009).
3. **Mammalian taste perception,** *Paul A.S. Breslin and Alan C. Spector*, Current Biology Vol 18 No 4 (2008).
4. **Human gustation and flavour**, *Breslin, P.A.S.*, Flav. Fragr. J. *16*, 439–456 (2001).
5. **The receptors and cells for mammalian taste,** *Chandrashekar, J., Hoon, M.A., Ryba, N.J.P., and Zuker, C.S.*, Nature 444, 288–294 (2006).
6. **Anatomy of the peripheral gustatory system**, *Miller, I.J. Jr.*, In Handbook of Olfaction and Gustation, R.L. Doty, ed. (New York: Marcel Dekker), pp. 521–547 (1995).
7. **The representation of taste quality in the mammalian nervous system,** *Spector, A.C., and Travers, S.P.*, Behav. Cogn. Neurosci. Rev. *4*, 143–191 (2005).
8. **Breadth of tuning and taste coding in mammalian taste buds,** *Tomchik, S.M., Berg, S., Kim, J.W., Chaudhari, N., and Roper, S.D.*, J. Neurosci. *27*, 10840–10848 (2007).
9. **The eating paradox: How we tolerate food,** *Woods, S.C.* Psychol. Rev. *98*, 488–505 (1991).
10. **Taste producing components in fish and fisheries products: A review,** *Mohammed Golam Sarower, Abul Farah Md. Hasanuzzaman, Bhabananda Biswas and Hiroki Abe, Intl. J. of Food. Ferment. Technol. 2(2): 113-121, December, (2012).*
11. **The physiology of taste in fish: potential implications for feeding stimulation and gut chemical sensing,** *Sofia Morais*, Reviews in Fisheries Science & Aquaculture, 25:2 (2017).
12. **Taste of nutrients: Amino acids, vitamins, and fatty acids,** *Susan S. Schiffman and Charles Dackis, Perception & Psychophysics Vol. 17 (2).140-146 (1975).*
13. **Is fat the sixth taste primary? Evidence and implications,** *Russell SJ Keast and Andrew Costanzo*, Flavour 4:5 (2015).
14. **Sugars, Sweet Taste Receptors, and Brain Responses,** *Allen A. Lee and Chung Owyang,* Nutrient. Jul; 9(7): 653 (2017).
15. **Humans Can Taste Glucose Oligomers Independent of the hT1R2/hT1R3 Sweet Taste Receptor,** *Trina J. Lapis, Michael H. Penner and Juyun Lim* Chemical Senses, Vol 41, 755–762 (2016).
16. **Cellular and Neural Responses to Sour Stimuli Require the Proton Channel Otop1,** *Bochuan Teng, Courtney E. Wilson, Yu-Hsiang Tu, Narendra R. Joshi, Sue C. Kinnamon, Emily R. Liman Teng et al.*, Current Biology 29, 3647–3656 November 4, (2019).
17. **Taste Interactions between Sweetness of Sucrose and Sourness of Citric and Tartaric Acid among Chinese and Danish Consumers,** *Jonas Yde Junge , Anne Sjoerup Bertelsen, Line Ahm Mielby, Yan Zeng, Yuan-Xia Sun, Derek Victor Byrne and Ulla Kidmose*, Foods , 9, 1425 (2020).
18. **Ratio scales of acid sourness**, *Howard R. Moskowitz,* Perception & Psychophysics, , Vol. 9 (3B) (1971).
19. **Mammalian Taste Bud Cells Utilize Extragemmal 5-Hydroxy-L-Tryptophan to Biosynthesize the Neurotransmitter Serotonin,** *Pan Hong-Ru, Tian Miao, Xue Jian-Bo, Li Song-Min, Luo Xiao-Cui, Huang Xiao, Chen Zhen-Huang, Huang Liquan*, Frontiers in Cellular Neuroscience VOLUME 12 (2018).
20. **Role of the Hydrophobic Amino Acid Residue in the Bitterness of Peptides**, *Norio Ishibashi, Ichiro Ono, Kuniki Kato, Toshiaki Shigenaga, Ichizo Shinoda, Hideo OKAi & Sakuzo Fukui,* Agricultural and Biological Chemistry, 52:1, 91-94 (1988).
21. **Structural basis for perception of diverse chemical substances by T1r taste receptors,** *Nipawan Nuemket,W, Norihisa Yasui, Yuko Kusakabe, Yukiyo Nomura, Nanako Atsumi, Shuji Akiyama, Eriko Nango, Yukinari Kato, Mika K. Kaneko, Junichi Takagi, Maiko Hosotani & Atsuko Yamashita,* Nature Communications volume 8, Article number:15530 (2017).
22. **Active taste compounds in juice from oranges symptomatic for Huanglongbing (HLB) citrus greening disease,** *Bruno M. Dala Paula, Smita Raithore, John A. Manthey, Elizabeth A. Baldwin, Jinhe Bai, Wei Zhao, M. Beatriz A. Glória, Anne Plotto*, Food Science and Technology 91 518–525 (2018).
23. **MEATabolomics: Muscle and Meat Metabolomics in Domestic Animals** *Susumu Muroya, Shuji Ueda, Tomohiko Komatsu , Takuya Miyakawa and Per Ertbjerg*, Metabolites, 10, 188 (2020).
24. **Kokumi taste perception is functional in a model carnivore, the domestic cat (*Felis catus*)** *A. Laffitte1,6, M. Gibbs1,6, C. Hernangomez de Alvaro1, J. Addison1, Z. N. Lonsdale1, M. G. Giribaldi, A. Rossignoli, T. Vennegeerts, M. Winnig, B. Klebansky, J. Skiles, D. W. Logan & S. J.* McGrane Scientific Reports 11:10527 (2021).
25. **Taste Enhancements Between Various Amino Acids and IMP,** *Misako Kawai, Atsushi Okiyama and Yoichi Ueda,* Chem Senses 27 739-745 (2002).
26. **L-Amino Acids Elicit Diverse Response Patterns in Taste Sensory Cells: A Role for Multiple Receptors,** *Shreoshi Pal Choudhuri, Rona J. Delay, Eugene R. Delay*, PLoS ONE 10(6) (2015).
27. **Review Metabolomics for Evaluating Flavor-Associated Metabolites in Plant-Based Products,** *Shruti Pavagadhi 1,2 and Sanjay Swarup*, Metabolites, 10, 197 (2020).
28. **The Examination of Fatty Acid Taste with Edible Strips,** *Sahbina Ebbaa,c, Ray A. Abarintosa, Dae G. Kima, Melissa Tiyouha, Judith C. Stullb, Ankur Movaliaa, and Gregory SmutzeraPhysiol Behav.*, July 16; 106(5): 579–586 (2012).
29. **Is There a Fatty Acid Taste?,** *Richard D. Mattes*, *Annu Rev Nutr*; 29: 305–327 (2009).
30. **Accumulating Evidence Supports a Taste Component for Free Fatty Acids in Humans,** *Richard D. Mattes,* RDPhysiol Behav. September 26; 104(4): 624–631 (2011).
31. **Oleogustus: The Unique Taste of Fat,** *Cordelia A. Running, Bruce A. Craig, and Richard D. Mattes, Chemical Senses*, Vol 40, 507–516 (2015).