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Taste and nutrition

1. Physiological basis of taste perception

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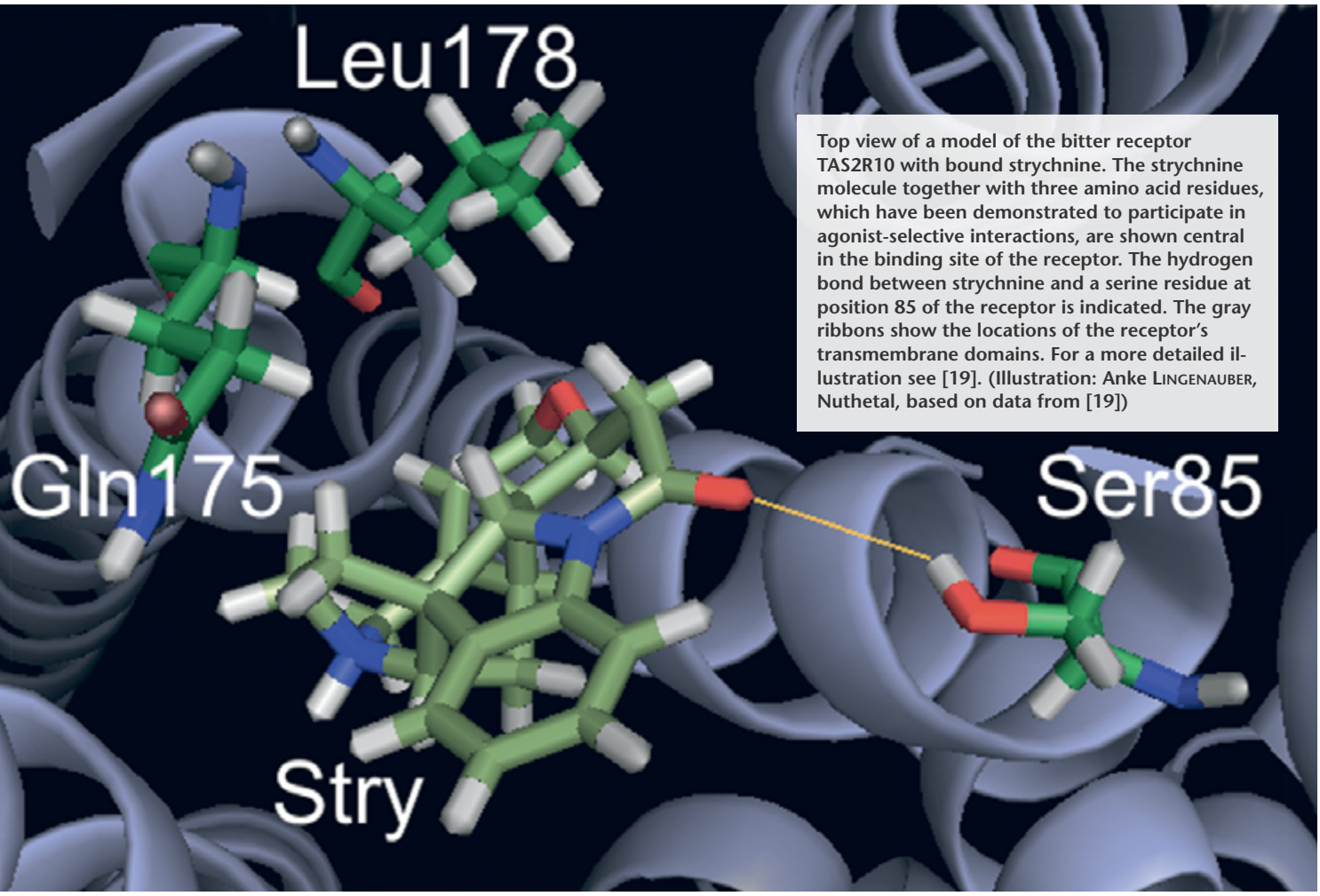

Top view of a model of the bitter receptor TAS2R10 with bound strychnine. The strychnine molecule together with three amino acid residues, which have been demonstrated to participate in agonist-selective interactions, are shown central in the binding site of the receptor. The hydrogen bond between strychnine and a serine residue at position 85 of the receptor is indicated. The gray ribbons show the locations of the receptor's transmembrane domains. For a more detailed illustration see [19]. (Illustration: Anke LINGENAUBER, Nuthetal, based on data from [19])

Taste preferences and aversions determine what subjects eat and drink and thus impact on their health and disease risk. However, we know relatively little about the principles of how taste affects food choice. The present article discusses the physiological basis of gustation. Two future articles explain the influences of genetic variability and environmental factors on taste perception and nutrition and describe the formation of taste preferences and aversions.

Functional morphology of the peripheral taste system

Flavor

At least tree of our senses contribute to the perception of food. The sense of smell detects the scent of a meal which, through sniffing, reaches the olfactory mucosa via the nostrils or the nasopharynx. Touch and pain report about the texture and temperature of food and the presence of irritants that elicit hot, pungent, astringent, metallic, burning, tingling or electrical sensations. Taste, in the true sense of the word, is restricted to the five basic tastes or taste qualities, sweet, sour, salty, bitter, and umami (savoury). The brain uses all these types of impressions to construct complex flavors. In the following the word taste merely refers to the five basic taste qualities.

Summary

Each taste quality is represented by a specific population of oral chemosensory cells. They are equipped with special receptor molecules which determine the molecular receptive ranges of the sensory cells. Whereas the receptors for salty and sour are, at present, not extensively characterized, a plethora of data exists for sweet, umami and bitter receptors. Although sweet and bitter receptors recognize a broad range of compounds, two different strategies are effective to achieve this goal. In case of the bitter receptors numerous genes have evolved, whereas only two genes code for subunits of the sweet taste receptor. This receptor, however, possesses multiple binding sites to recognize a diversity of sweet substances.

In the taste buds of the tongue sensory cells form assemblies of about 100 cells, which process and integrate taste information with metabolic needs. Sensory afferent nerves transfer gustatory information from the mouth to the brainstem to evoke stereotyped innate attraction or aversion and to prepare the body for digestion. The activity of nerve cells in special areas of the cerebral cortex represents the basic tastes and generates complex flavours by integrating information about taste, smell and texture of food.

Keywords: taste, gustation, physiology, sweet, salty, sour, bitter, umami

Taste organs

Taste buds

The five basic tastes are elicited by substances that are recognized by the taste buds. These principle taste organs are onion-shaped assemblies of ~ 50–100 mostly elongated cells. With their apical tips numerous of these cells contact a depression in the oral epithelium, referred to as taste pore, the contact site between taste molecules and their receptive structures.

Taste papillae

The majority of oral taste buds resides in the lingual taste papillae (◆ Figure 1A). We distinguish fungiform, foliate, and vallate papillae based on their shape, location and number of hosted taste buds. About 300 small, slightly elevated fungiform papillae are distributed about the anterior two thirds of the tongue. In humans, they contain up to five taste buds [1]. The foliate papillae are found at the posterior edges of the tongue and form up to five fissions which contain several hundred taste buds [2]. The posterior tongue displays on average nine vallate papillae which are arranged in a V-shaped manner. They possess most of the lingual taste buds as each of them contains several hundred of these cell assemblies. Further taste buds are embedded in the oral epithelium of the palate, epiglottis, pharynx and larynx.

Chemosensory cells

The chemosensory cells of taste buds differ in shape and function (◆ Figure 1B) [2,3]. They are referred to as secondary sensory cells to indicate the fact that they are specialized epithelial cells and not neurons. The conventional cell typing that is based on morphological criteria is currently being replaced by functional parameters which led recently to the discovery of a fundamental principle in gustation, i. e., the existence of genetically determined, segregated populations of chemosensory cells for the 5 basic tastes [3]. This means the percept of a basic taste is equivalent to the excitation of the cognate population of oral chemosensory cells. This principle explains the existence of only few taste qualities as well as the high discriminatory power across taste qualities and the low discriminatory power with taste qualities. The molecular receptive ranges of the five taste cell populations for taste compounds are defined and separated by the special taste receptor molecules they express. The bitter off-taste of saccharin is thus a result from its ability to potently activate the sweet sensing cells and, at the same time, to weakly excite the sensory cells dedi-

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cated to bitter. Taste cells are very short-lived and replaced by cells that develop from spherical progenitor cells that reside at the base of taste buds [4].

Detection and transmission of taste stimuli

Stimulation of all types of taste receptor cells leads to the excitation of afferent sensory fibers in a manner dependent on the neurotransmitter ATP. This has been demonstrated in mice lacking a special type of ATP receptor [5]. Noteworthy, only the receptor cells dedicated to sour form conventional chemical synapses, i.e., specialized contacts between two cells that propagate the excitation from cell to cell. However, it remains unknown if sour sensing cells synaptically release ATP [2]. The cells for sweet, bitter and umami stimuli do not form synapses. However, they have specializations where afferent fibers come particularly close. It is assumed that these are the sites of ATP release. The use of the same neurotransmitter by all of the 5 receptor cell populations raises the important question of how the brain correctly interprets the taste qualities. The most attractive hypothesis to date assumes that the released ATP is confined to quality specific micro domains in the taste buds [2], yet their existence remains to be demonstrated.

In addition to ATP, several other transmitter substances along with their corresponding receptors have been identified in taste buds. Although not in all cases the specific role of these additional neurotransmitters was demonstrated unambiguously, evidence is mounting that they serve functions in the communication between sensory cells. The released ATP for example, not only elicits action potentials in the afferent nerve fibers, but also stimulates, via a different type of receptor, its own release from sensory cells [6]. Furthermore, adenosine resulting from the enzymatic degradation of ATP, stimulates selectively the responsiveness of sensory cells devoted to the recognition of sweet stimuli [6]. This clearly indicates that taste buds are in fact not just structures which detect and transmit taste stimuli, but rather complex sensory organs that integrate taste information already in the oral cavity [2]. This concept is underscored by the fact that taste sensitivity is dynamically modulated to fit acute metabolic requirements. For example the counter-regulatory roles of the hunger and satiety hormones endocannabinoid and leptin, respectively, modify the sensitivity of sweet taste receptor cells in opposite directions [7].

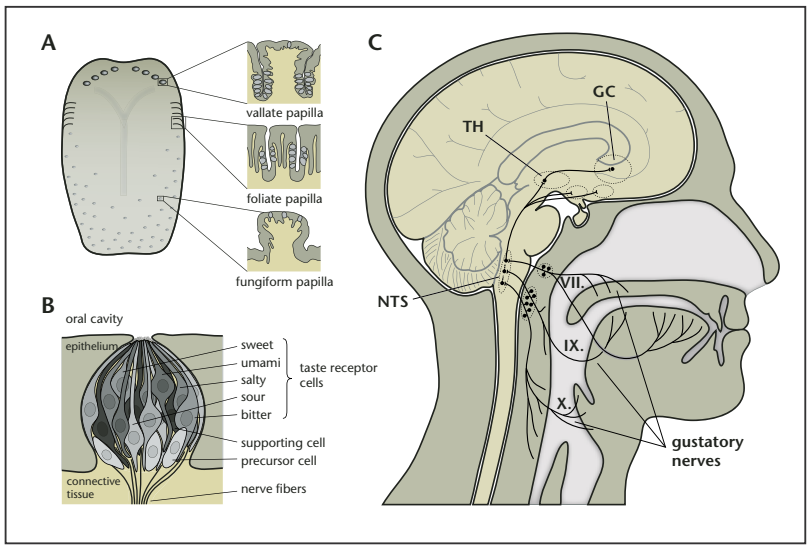

Figure 1: **Anatomy of the taste system**
(A) Schematic of the location and morphology of the three types of taste papillae. The taste buds are embedded in the mucosa of protrusions or invaginations of taste papillae. (B) The onion-shaped appearance of taste buds is caused by numerous elongated cells. Note that for each of the five basic taste qualities a separate cell population exists. (C) Branches of three cranial nerves (VII., IX., X.) innervate the taste buds and transmit taste information to the *Nucleus tractus solitarius* (NTS), a part of the brainstem. The cell bodies of the three nerves are located in ganglia outside the brain. The NTS relays taste information via the thalamus (TH) to the gustatory cortex (GC). (Illustration: Jonas Töle, Nuthetal)

Neuroanatomy

Taste information originating from the oral cavity is transmitted to the brainstem via three cranial nerves (◆ Figure 1C) [8]. Contacts with other nerve cells residing in this brain region mediate muscle contractions coordinating tongue movement, chewing and swallowing to facilitate the ingestion of digestible food items and the disgorging of potentially harmful substances. Furthermore, taste information prepares the alimentary tract in advance for the digestion of the food [9]. The brainstem wires taste information via the midbrain to a specialized area within the cerebrum, the gustatory cortex. Here, the conscious perception of the basic taste qualities is reflected by nerve activity patterns. Together with information about the smell and textural properties of the consumed food a complex flavor percept is generated. Flavor recognition, in turn, is indispensable for the development of food preferences and aversions. Further brain areas involved in the processing of taste information include regions that regulate intake of nutri-

ents and liquids as well as reward systems involved in the generation of addictive behaviors [1].

The receptors for sweet, umami, and bitter taste perception

The tasks for sweet and umami taste receptors on the one hand, and that of bitter taste receptors on the other hand couldn't be more different. Whereas sweet and umami receptors are tailored for the detection of the building blocks for the universal macronutrients, carbohydrates and proteins, bitter taste receptors are required to respond to a large variety of potentially harmful toxic food ingredients. For these very different tasks nature has chosen its perhaps most versatile tools, the G protein-coupled receptors (GPCRs). Numerous hormone and neurotransmitter receptors, but also the visual pigment, rhodopsin, belong to this class of molecules.

TAS1Rs

The family of TAS1R (taste receptor, type 1) genes is responsible for recognizing the taste qualities sweet and umami (for a recent review article see [10]). Based on their amino acid sequence and structural similarities the three members of this gene family, TAS1R1, -R2 and –R3, belong to the class C of GPCRs. This receptor class is characterized by long, amino terminally located extracellular domains. They form a structure resembling the traps of the plant Venus flytrap ("venus flytrap motif"). The carboxy terminal part of these proteins with its 7 transmembrane domains that are connected via 3 intra- and 3 extracellular loops, however, takes the shape of a typical GPCR. Between the amino terminal Venus flytrap motif and the transmembrane region an additional, cystein-rich domain is present.

A functional TAS1-receptor consists of two different subunits. Whereas the TAS1R1 and TAS1R3 subunits assemble to form the umami receptor [11], the sweet taste receptor consists of the TAS1R2 and TAS1R3 subunits [12]. Hence, both receptors share the TAS1R3 subunit and possess one specific subunit each. On a cellular level this principle is evident by the observed co-expression of the TAS1R3 gene with either of the TAS1R1 or TAS1R2 genes, but a strict separation of TAS1R1 and TAS1R2 gene expression.

The sweet taste receptor TAS1R2/3 is the universal sensor for all substances eliciting a sweet taste perception. Given the large number of sweet tasting substances, this is an enormous task to fulfill. On top of the prototypical sweet tastants such as mono- and disaccharides (◆ Table 1), numerous natural and synthetic compounds activate this receptor.
Perhaps one of the most important findings of recent research concerning the sweet taste receptor is the characterization of individual binding sites of various sweet tastants in

Receptor	Agonists
umami	
TAS1R1/R3	L-glutamic acid, enhanced by 5'-ribonucleoside phosphate
sweet	
TAS1R2/R3	Mono-/disaccharides, plant sweet proteins (e.g. brazzein, thaumatin), artificial sweeteners (e.g. saccharin, aspartame), natural sweeteners (e. g. steviosides)
bitter	
TAS2R1	Humulones
TAS2R3	Chloroquine
TAS2R4	Colchicin, L-tryptophane, D-tryptophane
TAS2R5	1,10-Phenanthrolin
TAS2R7	caffeine
TAS2R8	Chloramphenicol
TAS2R9	Ofloxazin
TAS2R10	Parthenolide, denatonium benzoate, strychnine
TAS2R13	Diphenidol, denatonium benzoate
TAS2R14	picrotoxinin, aristolochic acid, caffeine, absinthin
TAS2R16	D-(-)-salicin, D-arbutin, amygdalin
TAS2R20	Cromolyn
TAS2R30	Denatonium benzoate, Picrotoxinin
TAS2R31	Aristolochic acid, saccharin, acesulfame K
TAS2R38	Phenylthiocarbamide (PTC), 6-n-propylthiouracil (PROP)
TAS2R39	Quinine, thiamin, amarogentin
TAS2R40	Humulones, quinine
TAS2R43	Aristolochic acid, saccharin, acesulfame K
TAS2R46	strychnine, absinthin, parthenolide
TAS2R50	Amarogentin, andrographolide

Table 1: **Human taste receptors and some of their activators**
TAS1R/TAS2R = tast receptor, type 1/2

different parts of this receptor (◆Figure 2). A key finding for the successful identification of these binding sites has been the observation of species-specific differences in sweet taste perception. Whereas many artificial sweet compounds activated the human sweet taste receptor, the corresponding rodent receptors do not respond to many of these substances [12,13]. Through the smart combination of subunits from different species or parts thereof and subsequent functional *in vitro* experiments it was possible to locate these binding sites. These experiments demonstrated that the sweet taste receptor possesses several binding sites for sweet compounds distributed over different parts of the molecule and, moreover, provided a convincing explanation for the apparent discrepancy between the number and diversity of sweet compounds and the existence of only a single sensor for these compounds. The identified binding sites are located in the Venus flytrap domains of both subunits, the transmembrane region of the TAS1R3 as well as within the cystein-rich domain.

In contrast to the sweet taste receptor, for the umami receptor, TAS1R1/3, much fewer activating molecules have been identified. Whereas the human umami receptor is specifically tailored for the recognition of L-glutamate, the corresponding rodent receptor is activated by additional L-amino acids [11]. A common hallmark of the human as well as the rodent umami receptor is a strong, ~30-fold enhancement of its sensitivity by inosine monophosphate (IMP) and other 5-ribonucleotides such as GMP.

TAS2Rs

There are countless of structurally diverse bitter compounds present in nature. Many of these possess considerable pharmacological activities and hence could be harmful if ingested. The perception of all these potentially toxic substances is mediated by the bitter taste receptors of the TAS2R (taste receptor, type 2) gene family [14,15]. Humans possess 25 of these receptors, whereas other mammals can have more (e.g. mouse with 35) or fewer (e.g. horses with 19) TAS2R genes.
Bitter taste receptor genes in the oral cavity are expressed in a separate population of taste sensors, the bitter taste receptor cells. Since each of these bitter taste receptor cells express on average only 4–11 different TAS2R genes, the population of human bitter taste receptor cells is highly heterogeneous [16]. In contrast to the already described TAS1Rs, TAS2Rs exhibit only very short extracellular amino termini (◆Figure 2) and, due to their low amino acid sequence relationship with other GPCRs, are difficult to be grouped into existing GPCR-subfamilies.

One of the most burning questions in bitter taste research has been, how a rather small number of TAS2Rs may possibly suffice to detect hundreds of diverse bitter compounds? The enormous progress made in the identification of activators for the 25 human TAS2Rs (a process called "deorphanization" because previously "orphan" receptors become associated with cognate activators) has provided important results to answer this question (◆Table 1).

In the course of these experiments, which resulted in the successful deorphanization of, so far, 21 of the 25 human TAS2Rs, it was shown that the breadth of agonist spectra of these receptors deviate considerably. Some receptors, the "generalist" receptors, exhibit an extremely broad agonist spectrum, the "specialist" receptors respond only to few agonists, whereas the majority of receptors showed an intermediate breadth of tuning [17]. The three most broadly tuned receptors, TAS2R10, -R14, and –R46, each respond to about one-third of all tested bitter compounds and their combined agonist spectra are sufficient for the recognition of already half of all bitter substances. On the other extreme, the receptors TAS2R3, -R5, -R13, -R20, and -R50 are activated by only very few bitter substances. Intriguingly, even the most broadly tuned TAS2Rs possess only a single ligand binding pocket (◆cover illustration), which accommodates all the diverse

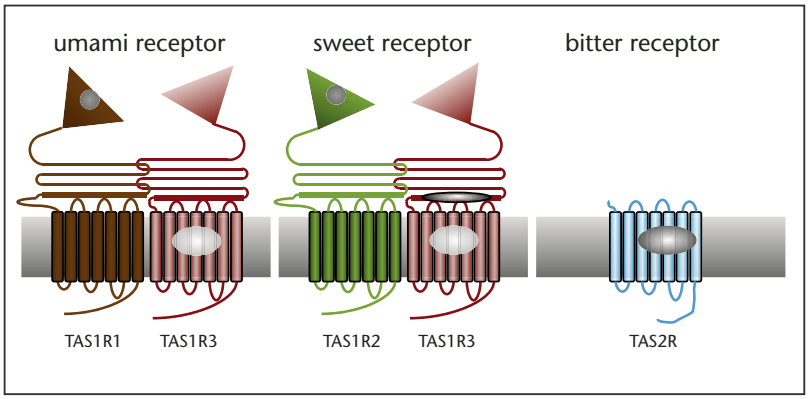

Figure 2: **Schematic of sweet, umami, and bitter receptor structures**
The extracellular Venus flytrap motifs of the TAS1R are shown. The cystein-rich domains of TAS1Rs are highlighted as bold lines. Transmembrane helices are shown as cylinders traversing the plasma membrane. Identified binding sites for activators are indicated by gray spheres. (Illustration: Authors' own schematic)
TAS1R/TAS2R = taste receptor, Type 1/2

bitter compounds via different contact points between receptor and agonists [18].

Moreover, it has been demonstrated that the ligand binding pockets are tailored to accommodate numerous compounds at the expense of possibly higher affinities for each of the single substances [19]. Two of the 25 human TAS2Rs exhibit pronounced selectivity for distinct large classes of bitter compounds. One of them is the TAS2R16, which responds almost exclusively to stimulation with β-D-glucopyranosides, the other receptor, the TAS2R38, is activated only by molecules possessing isothiocyanate or thioamide groups. All other receptors exhibit intermediate tuning properties.

In summary, the deorphanization process allowed to clarify the question of how so few receptors can possibly be responsible to facilitate recognition of so many different bitter compounds. In fact, the question can now be turned around and one may ask why do humans possess so many receptors with, in part, clearly overlapping agonist spectra? The recent identification of naturally occurring bitter taste receptor inhibitors may provide an explanation for this phenomenon [20]. These inhibitors are present in the same plants synthesizing typical bitter compounds, however, unlike agonists they block bitter receptor responses instead of activating them. The presence of multiple receptors with overlapping agonist interaction patterns may prevent the complete inhibition of bitter taste recognition by such substance and thus, prevent the accidental ingestion of those plants with possibly fatal consequences.

Intracellular signaling cascades of TAS1Rs and TAS2Rs

Despite of the obvious differences in structure, number, activation mechanisms and their strict separation in different cell populations among sweet and umami receptors on the one hand, and bitter receptors on the other hand, the signal transduction mechanism is similar (◆ Figure 3). Activation of the receptors is transmitted via a specific heterotrimeric guanine nucleotide binding protein onto the enzyme phospholipase C 2. The resulting inositol-1,4,5-trisphosphate stimulates the type 3 IP3-receptor in the endoplasmic reticulum causing elevation of intracellular calcium levels. The calcium-induced opening of the ion channel TRPM5 initiates a kation current through the plasma membrane, resulting in the depolarization of taste receptor cells and the concurrent release of the neurotransmitter ATP through pannexin-hemichannels.

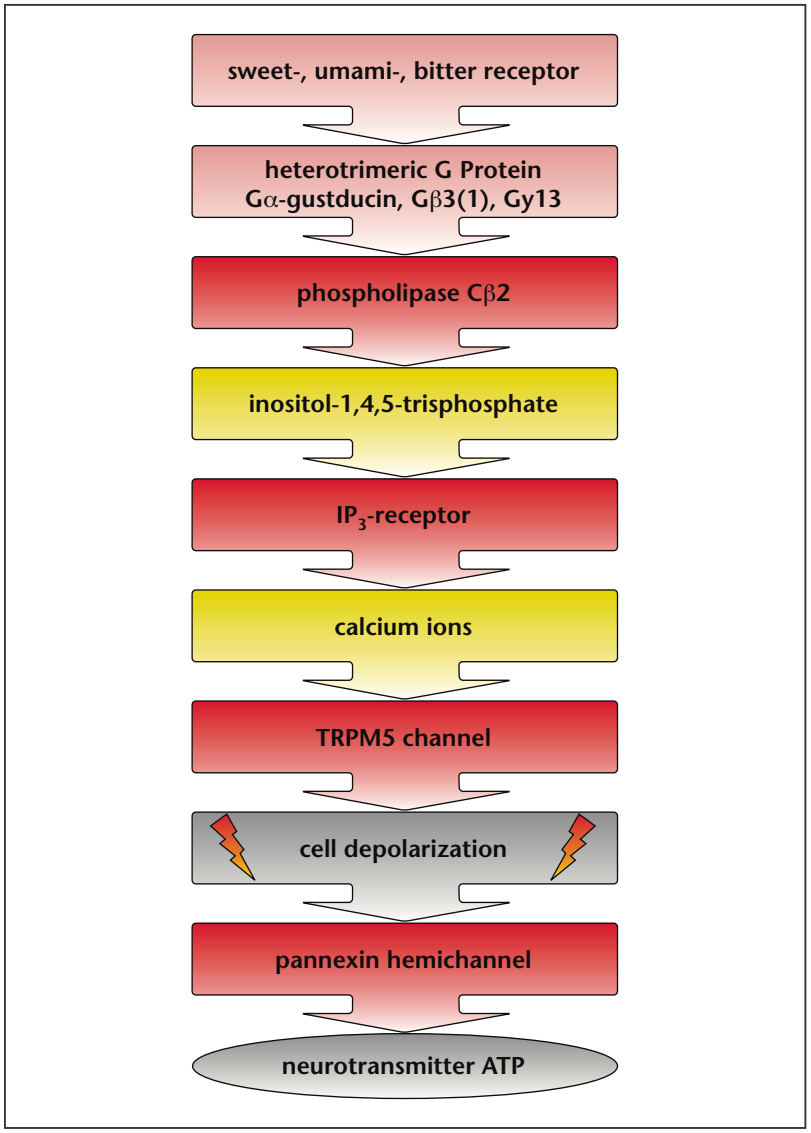

Figure 3: **Flow diagram of the cellular signal transduction cascade in taste receptor cells**
The single components are shown following the sequence of their activation. Abbreviations: IP3-receptor, inositol-1,4,5-trisphosphate receptor; TRPM5, transient receptor potential cation channel subfamily M, member 5; ATP, adenosine trisphosphate (Authors' own diagram).

Sour transduction

Acids are the principle stimuli of sour taste. Since strong inorganic acids such as hydrochloric acid dissociate completely in protons and anions, we have to assume that protons themselves serve as sour stimulus. But also weak organic acids taste sour. Paradoxically, at constant pH the weak acetic acid appears to be sourer than the strong hydrochloric acid [6]. This led to the assumption that, in addition to protons, the undissociated organic acids serve as adequate sour stimuli [21]. In the protonated state organic acids are capable of permeating plasma membranes. In the cytosol they dissociate into protons and anions which leads to intracellular acidification.

Receptor candidates for sour have repeatedly been reported about in the literature. To date, none of them matches all of the necessary criteria that a true sour receptor should fulfill. Despite this lack of knowledge we have to assume that at least two transduction pathways are involved in the recognition of acids [2]. Plasma membrane proton channels enable the influx of protons into the cytosol of sour-detecting receptor cells in the taste bud. Together with those protons released from the organic acids in the cytosol they activate intracellular target sites. Eventually this leads to calcium influx in the sour-detecting sensory cells and release of neurotransmitter substances. This hypothesis is also supported by the observation that all taste cells are accessible to organic acids and show the drop in pH but only in the sour receptor cells low pH is coupled to calcium influx and neurotransmitter release [6].

Salt taste transduction

We continuously loose electrolytes through excretion. In this context salty taste can be considered a control element ensuring electrolyte homeostasis. The recognition of salt and its intrinsic pleasant taste at low to moderate concentrations promotes salt uptake compensating the continued loss.

Salty taste is mostly elicited by NaCl, table salt, but other sodium salts elicit a very similar taste. The taste of other mineral salts does not compare to the taste of NaCl, it is clearly different.

In rodents two salt tastes have been described. One of them is pleasant and specifically elicited by sodium ions. This taste is induced by low stimulus concentrations and blocked by the diuretic drug amiloride. The other is repulsive, depends on high sodium concentration, is also elicited by various other mineral salts including calcium, magnesium, ammonium and potassium salts, and insensitive to amiloride. The observation that rodents are unable to distinguish NaCl from KCl in the presence of amiloride illustrates the dualism of salty taste [22].

A well-known target for amiloride in the kidney is ENaC, the epithelial sodium channel which is composed of two alpha, a beta and a gamma subunit. The ENaC is highly selective for sodium ions and mediates the recovery of sodium from the primary urine. These findings led to the assumption that ENaC in oral taste tissues is involved in salt transduction. Various circumstantial evidence supported this assumption, yet only very recent direct evidence demonstrated that α-ENac is part of the salt transduction machinery [23]. However, the precise channel composition remains unknown. The amiloride-insensitive salt taste involves other transduction mechanisms. Apparently, high-salt-reception recruits sour and bitter transduction pathways [24] which impressively explains the unpleasant sensation that is evoked by high sodium concentrations and other mineral salts.

Comparatively, little is known about salt taste in humans. It is true that the ENaC subunits are present in human taste buds but salt taste in humans is amiloride insensitive [25] challenging a potential role for ENaC in human salt transduction. Perhaps the insensitivity of human salt taste to amiloride can be explained by a different channel composition. Humans possess an additional ENaC gene which is absent in rodents and which encodes the δ-subunit. Delta-ENaC is also present in human taste buds and can functionally replace the α-subunit. However, δ-ENaC is far less sensitive to amiloride than the α-subunit [26] which could explain the amiloride-insensitivity of human salty taste. However, future research has to clarify this and other open questions regarding sour and salty transduction.

Outlook

We have seen that important concepts and basic principles in taste perception have been worked out quite recently. However, new knowledge raises new questions. Thus, we have to register unexpected large gaps in our knowledge about sour and salty taste and about fundamental principles of gustatory information transmission from mouth to brain. Moreover, taste receptors have recently been found in numerous extraoral sites where they probably exert hitherto unknown functions.

Numerous laboratories worldwide aim at filling the gaps in knowledge. In particular, elucidating the molecular and cellular basis of gustatory transmission and processing in the brain is indispensable for understanding of how taste impacts on ingestive behavior. The to-do-list for taste researcher is long and complex and hopefully can be worked off quick in order to solve public health issues in nutrition some of which will be targeted in the next articles.

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Conflict of Interests
Maik Behrens has filed patents and patent applications on human bitter taste.

Anja Voigt declares no conflict of interest in accordance with the guidelines of the International Committee of Medical Journal Editors.

Prof. Dr. Wolfgang Meyerhof filed several patents and patent applications on bitter receptors. Parts of his research are funded by industrial partners.

References

1. *Smith DV, Boughter JD, Jr. Neurochemistry of the Gustatory System. In: Lajtha A, Johnson DA (ed). Handbook of Neurochemistry and Molecular Neurobiology. Springer, New York (2007), S. 109–135*
2. *Roper SD (2007) Signal transduction and information processing in mammalian taste buds. Pflugers Arch 454: 759–776*
3. *Chandrashekar J, Hoon MA, Ryba NJ et al. (2006) The receptors and cells for mammalian taste. Nature 444: 288–294*
4. *Beidler LM, Smallman RL (1965) Renewal of cells within taste buds. J Cell Biol 27: 263–272*
5. *Finger TE, Danilova V, Barrows J et al. (2005) ATP signaling is crucial for communication from taste buds to gustatory nerves. Science 310: 1495–1499*
6. *Roper SD (2013) Taste buds as peripheral chemosensory processors. Semin Cell Dev Biol 24: 71–79*
7. *Jyotaki M, Shigemura N, Ninomiya Y (2010) Modulation of sweet taste sensitivity by orexigenic and anorexigenic factors. Endocr J 57: 467–475*
8. *Hamilton RB, Norgren R (1984) Central projections of gustatory nerves in the rat. J Comp Neurol 222: 560–577*
9. *Spector AC (2000) Linking gustatory neurobiology to behavior in vertebrates. Neurosci Biobehav Rev 24: 391–416*
10. *Behrens M, Meyerhof W, Hellfritsch C et al. (2011) Sweet and umami taste: natural products, their chemosensory targets, and beyond. Angew Chem Int Ed Engl 50: 2220–2242*
11. *Nelson G, Chandrashekar J, Hoon MA et al. (2002) An amino-acid taste receptor. Nature 416: 199–202*
12. *Nelson G, Hoon MA, Chandrashekar J et al. (2001) Mammalian sweet taste receptors. Cell 106: 381–390*
13. *Li X, Staszewski L, Xu H et al. (2002) Human receptors for sweet and umami taste. Proc Natl Acad Sci U S A 99: 4692–4696*
14. *Adler E, Hoon MA, Mueller KL et al. (2000) A novel family of mammalian taste receptors. Cell 100: 693–702*
15. *Chandrashekar J, Mueller KL, Hoon MA et al. (2000) T2Rs function as bitter taste receptors. Cell 100: 703–711*
16. *Behrens M, Foerster S, Staehler F et al. (2007) Gustatory expression pattern of the human TAS2R bitter receptor gene family reveals a heterogenous population of bitter responsive taste receptor cells. J Neurosci 27: 12630–12640*
17. *Meyerhof W, Batram C, Kuhn C et al. (2010) The molecular receptive ranges of human TAS2R bitter taste receptors. Chem Senses 35: 157–170*
18. *Brockhoff A, Behrens M, Niv MY et al. (2010) Structural requirements of bitter taste receptor activation. Proc Natl Acad Sci U S A 107: 11110–11115*
19. *Born S, Levit A, Niv MY et al. (2012) The Human Bitter Taste Receptor TAS2R10 Is Tailored to Accommodate Numerous Diverse Ligands. J Neurosci 33: 201–213*
20. *Brockhoff A, Behrens M, Roudnitzky N et al. (2011) Receptor agonism and antagonism of dietary bitter compounds. J Neurosci 31: 14775–14782*
21. *Lyall V, Alam RI, Phan DQ et al. (2001) Decrease in rat taste receptor cell intracellular pH is the proximate stimulus in sour taste transduction. Am J Physiol Cell Physiol 281: C1005–C1013*
22. *Eylam S, Spector AC (2005) Taste discrimination between NaCl and KCl is disrupted by amiloride in inbred mice with amiloride-insensitive chorda tympani nerves. Am J Physiol Regul Integr Comp Physiol 288: R1361–R1368*
23. *Chandrashekar J, Kuhn C, Oka Y et al. (2010) The cells and peripheral representation of sodium taste in mice. Nature 464: 297–301*
24. *Oka Y, Butnaru M, von Buchholtz L et al. (2013) High salt recruits aversive taste pathways. Nature 494: 472–475*
25. *Staehler F, Riedel K, Demgensky S et al. (2008) A Role of the Epithelial Sodium Channel in Human Salt Taste Transduction? Chem Percept 1(1): 78–90*
26. *Halpern BP (1998) Amiloride and vertebrate gustatory responses to NaCl. Neurosci Biobehav Rev 23: 5–47*

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