complex can interact with all L-amino acids (Figure 29–15B), but in humans it is preferentially activated by glutamate. Purine nucleotides, such as inosine 5′-monophosphate (IMP), are often added to monosodium glutamate to enhance its pleasurable umami taste. Interestingly, in vitro studies demonstrated that IMP potentiates the responsiveness of T1R1/T1R3 to L-amino acids, acting as a strong positive allosteric modulator of the receptor (Figure 29–15B).

Taste cells with both T1R1 and T1R3 are concentrated in fungiform papillae (Figure 29–16A). Studies in genetically engineered mice in which individual T1R genes have been deleted indicate that the T1R1/T1R3 complex is solely responsible for umami taste, whereas T1R2/T1R3 is solely responsible for sweet taste. As expected, a genetic knockout of T1R1 selectively abolishes umami taste, a knockout of T1R2 specifically abolishes sweet taste, while a knockout of T1R3 eliminates both sweet and umami taste (exactly as predicted, given that it is a common subunit of both the umami and sweet taste receptors).

Sweet and umami receptors differ significantly among different species. Most interestingly, different T1R subunits have been lost in some species, likely reflecting their evolutionary niche and diet. For example, the giant panda, which feeds almost exclusively on a bamboo diet, lacks a functional umami receptor. On the other hand, domestic cats, tigers, and cheetahs do not have a functional sweet receptor, whereas vampire bats that feed on a blood diet have mutations that have eliminated both sweet and umami functional receptors.

Bitter Taste Receptor

Bitter taste is thought to have evolved as an aversive signal of toxic molecules. Bitter taste sensation is elicited by a variety of compounds, including caffeine, nicotine, alkaloids, and denatonium, the most bitter-tasting chemical known (this compound is sometimes added to toxic products that are odorless and tasteless to prevent their ingestion).

Bitter tastants are detected by a family of approximately 30 G protein–coupled receptors called

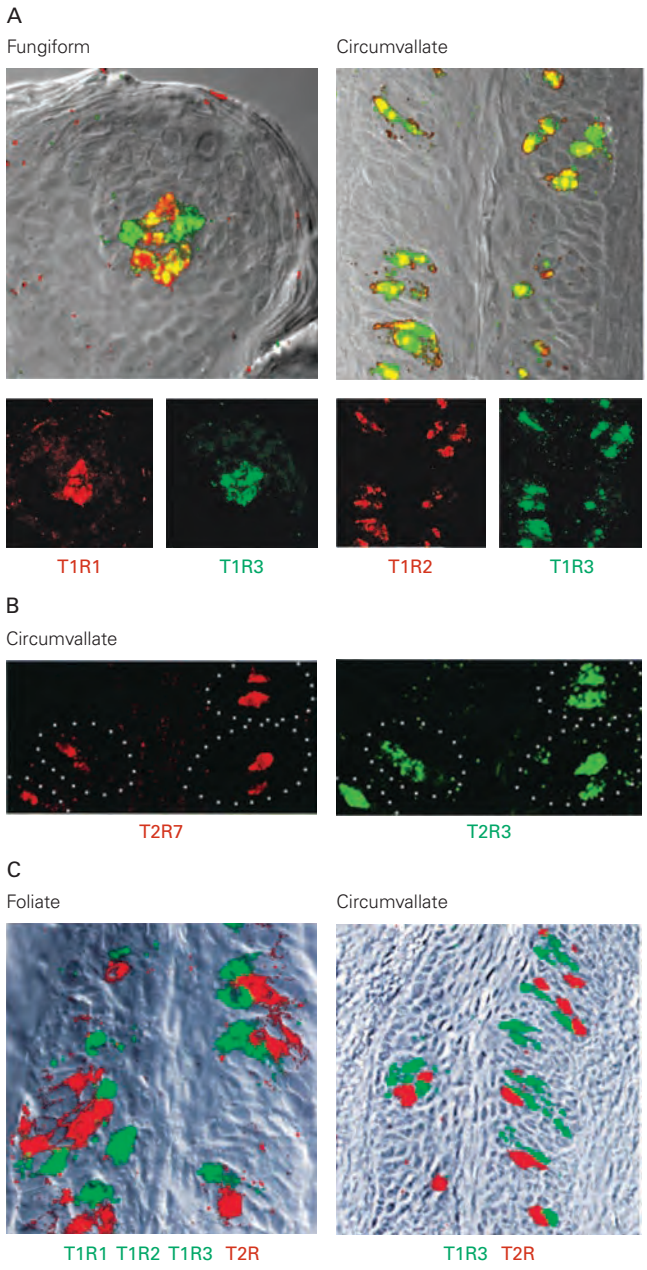

Figure 29–16 (Right) Expression of T1R and T2R receptors on the tongue. Sections of mouse or rat tongue were hybridized to probes that label T1R or T2R mRNAs to detect their sites of expression in taste cells.

A. The T1R3 receptor is expressed in taste cells of all three types of papillae. However, T1R1 is found mostly in fungiform papillae, whereas T1R2 is located predominantly in circumvallate (and foliate) papillae. Overlap between sites of expression appears as yellow cells in the micrographs at the top. The T1R1-T1R3 umami receptor is more frequently found in fungiform papillae, whereas the T1R2-T1R3 sweet receptor is more frequently found in circumvallate and foliate papillae. (Reproduced, with permission, from Nelson et al. 2001.)

B. A taste cell that detects bitter tastants can express several variants of T2R receptors. Here, probes for T2R3 and T2R7 labeled the same taste cells in circumvallate papillae. (Reproduced, with permission, from Adler et al. 2000.)

C. The T1R and T2R receptors are expressed in different taste cells. Taste cells labeled by a T1R3 probe or mixed T1R probes (**green**) did not overlap with cells labeled by a mixture of T2R probes (**red**). (Reproduced, with permission, from Nelson et al. 2001.)

T2Rs (Figure 29–14). However, different animal species contain different numbers of bitter receptors (varying from just a handful in the chicken genome to over 50 in the western clawed frog; humans have 28 T2R genes). These receptors recognize bitter compounds that have diverse chemical structures, with each T2R tuned to detect a small number of bitter compounds (Figure 29–15C). The T2R receptors recognize chemicals with high-affinity binding in the micromolar range, allowing detection of minute quantities of harmful compounds. A single taste cell expresses many, probably most, types of T2R receptors (Figure 29–16B). This arrangement implies that information about different bitter tastants is integrated in individual taste cells. Because different bitter compounds are detected by the same cells, all these compounds elicit the same perceptual bitter taste quality. The degree of bitterness might be caused by a compound's effectiveness in activating bitter taste cells.

Interestingly, genetic differences in the ability to perceive specific bitter compounds have been identified in both humans and mice. For example, humans are either super-tasters, tasters, or taste-blind to the bitter chemical 6-n-propylthiouracil. It was by mapping variation in this trait to specific chromosomal loci, and then by searching for novel G protein–coupled receptor genes within that chromosomal interval, that the T2R receptors were first identified. In the case of 6-n-propylthiouracil detection, the gene responsible for the genetic difference has proven to be a particular T2R gene. Thus, some bitter compounds may be recognized predominantly by only one of the approximately 30 T2R receptor types.

Taste cells expressing T2R receptors are found in both foliate and circumvallate papillae in mice (Figure 29–16C). A given taste cell expresses either T2R or T1R receptors (ie, one taste cell–one receptor class), but a single taste bud can contain taste cells of all types (eg, sweet, umami, bitter). Such mixing of cells accords with the observation that a single taste bud can be activated by more than one class of tastant; for example, sweet as well as bitter.

Salty Taste Receptor

Salt intake is critical to maintaining electrolyte balance. Perhaps because electrolytes must be maintained within a stringent range, the behavioral response to salt is concentration dependent: Low salt concentrations are appetitive, whereas high salt concentrations are aversive. How does the response to salt change based on concentration? It turns out that multiple taste cells detect salt. The essential salt taste receptor cell uses the epithelial sodium channel ENaC (see Figure 29–14). These specialized salt taste receptors are distinct from sweet, bitter, or umami receptors. At much higher salt concentrations, some bitter and sour taste cells also respond to salt, although the molecular details of detection have not been determined. Therefore, appetitive concentrations of salt drive responses via the ENaC salt taste receptor in the salt-sensing cells, whereas high salt concentrations activate the bitter and sour cells and thus trigger behavioral aversion.

Sour Taste Receptor

Sour taste is associated with acidic or fermented foods or drink. As with bitter compounds, animals are innately averse to sour substances, suggesting that the adaptive advantage of sour taste is avoidance of spoiled foods. Sour, like the other 4 taste qualities, is also detected by its own type of taste receptor cells (Figure 29–14). The ion channel Otopetrin-1 (Otop1), a proton-selective channel normally involved in the sensation of gravity in the vestibular system, is the sour-sensing ion channel in the taste system. As expected, a knockout of Otop1 in mice eliminated acid responses from sour taste receptor cells. Furthermore, mice engineered to express Otop1 in sweet taste receptor cells now have sweet cells that also respond to sour stimuli, demonstrating that this channel is sufficient to confer acid sensing.

Molecular-genetic studies have demonstrated that the different taste modalities are detected by distinct subsets of taste cells. As we have seen, a combination of T1R1 and T1R3 is responsible for all umami taste, and a combination of T1R2 and T1R3 is needed for all sweet taste detection except for the detection of high concentrations of sugars, which can be mediated by T1R3 alone. The T1R1 and T1R2 receptors are expressed by separate subsets of taste cells, indicating that the detection of sweet and umami tastants is segregated. Similarly, receptors and molecular markers uniquely define bitter, low salt, and sour taste cells.

A dramatic demonstration that each taste quality is detected by a different category of taste cells comes from studies of mice lacking a specific taste receptor gene or cell type. These studies showed that the loss of one taste modality did not affect the others. For example, mice in which sweet cells have been genetically ablated do not detect sugars but still detect amino acids, bitter compounds, salts, and sour compounds. Similarly, mice engineered to lack specific taste receptors cannot detect the corresponding tastants. For instance, mice lacking selective bitter receptors are not responsive to the corresponding bitter tastants,

and mice lacking ENaC cannot detect the taste of salt. These types of studies have shown that different tastes are detected by different receptors expressed in different classes of taste cells that drive specific behaviors.

Studies in mice further indicate that it is the taste cells rather than the receptors that determine the animal's response to a tastant. The human bitter receptor T2R16 recognizes a bitter tastant that mice cannot detect. When this receptor was expressed in mouse taste cells that normally express T2R bitter receptors, the ligand caused strong taste aversion. However, when that receptor was expressed in cells that express the T1R2/T1R3 sweet complex (ie, sweet cells), the bitter ligand elicited strong taste acceptance. These findings showed that innate responses of mice to different tastants (sweet and bitter in this example) operate via labeled lines that link the activation of different subsets of taste cells to different behavioral outcomes.

Gustatory Information Is Relayed From the Periphery to the Gustatory Cortex

Each taste cell is innervated at its base by the peripheral branches of the axons of primary sensory neurons (Figure 29–13). Each sensory fiber branches many times, innervating several taste cells within taste buds. The release of neurotransmitter from taste cells onto the sensory fibers induces action potentials in the fibers and the transmission of signals to the sensory cell body.

The cell bodies of gustatory sensory neurons lie in the geniculate, petrosal, and nodose ganglia. The peripheral branches of these neurons travel in cranial nerves VII, IX, and X, while the central branches enter the brain stem, where they terminate on neurons in the gustatory area of the nucleus of the solitary tract (Figure 29–17). In most mammals, neurons in this nucleus transmit signals to the parabrachial nucleus of the pons, which in turn sends gustatory information to the ventroposterior medial nucleus of the thalamus. In primates, however, these neurons transmit gustatory information directly to the taste area of the thalamus.

From the thalamus, taste information is transmitted to the gustatory cortex, a region of the cerebral cortex located along the border between the anterior insula and the frontal operculum (Figure 29–17). The gustatory cortex is believed to mediate the conscious perception and discrimination of taste stimuli. The taste areas of the thalamus and cortex also transmit information both directly and indirectly to the hypothalamus, which controls feeding behavior and autonomic responses.

Large-scale calcium imaging revealed that some neurons in the gustatory cortex respond preferentially to one taste modality, such as bitter or sweet. These neurons are localized in segregated cortical fields or hot spots. Interestingly, using a light-activated ion channel to activate neurons in the sweet hot spot elicits innately attractive responses. In contrast, activation of the bitter hot spot evokes suppression of licking and strong aversive orofacial responses, mimicking what is often seen in response to bitter tastants. These experiments showed that direct control of primary taste cortex can evoke specific, reliable, and robust behaviors that mimic responses to natural tastants. They also illustrated that the gustatory pathway can activate innate, immediate responses to sweet and bitter chemicals. To demonstrate that these cortically triggered behaviors are innate (ie, independent of learning or experience), similar stimulation experiments were performed in mutant mice that had never tasted sweet or bitter chemicals (the mutation abolished all sweet and bitter signal transduction). Even in these animals, activation of the corresponding cortical fields triggered the expected behavioral response, thus substantiating the predetermined nature of the sense of taste.

Perception of Flavor Depends on Gustatory, Olfactory, and Somatosensory Inputs

Much of what we think of as the flavor of foods derives from information provided by the integration of the taste and olfactory systems. Volatile molecules released from foods or beverages in the mouth are pumped into the back of the nasal cavity ("retronasal passage") by the tongue, cheek, and throat movements that accompany chewing and swallowing. Although the olfactory epithelium of the nose clearly makes a major contribution to sensations of flavor, such sensations are localized in the mouth rather than in the nose.

The somatosensory system is also thought to be involved in this localization of flavors. The coincidence between taste, somatosensory stimulation of the tongue, and the retronasal passage of odorants into the nose is assumed to cause odorants to be perceived as flavors in the mouth. Sensations of flavor also frequently have a somatosensory component that includes the texture of food as well as sensations evoked by spicy or minty foods and by carbonation.

Insects Have Modality-Specific Taste Cells That Drive Innate Behaviors

Insects have a specialized gustatory system that evaluates potential nutrients and toxins in food. Taste neurons are found on the proboscis, internal mouthparts, legs, wings, and ovipositor, allowing insects to sample

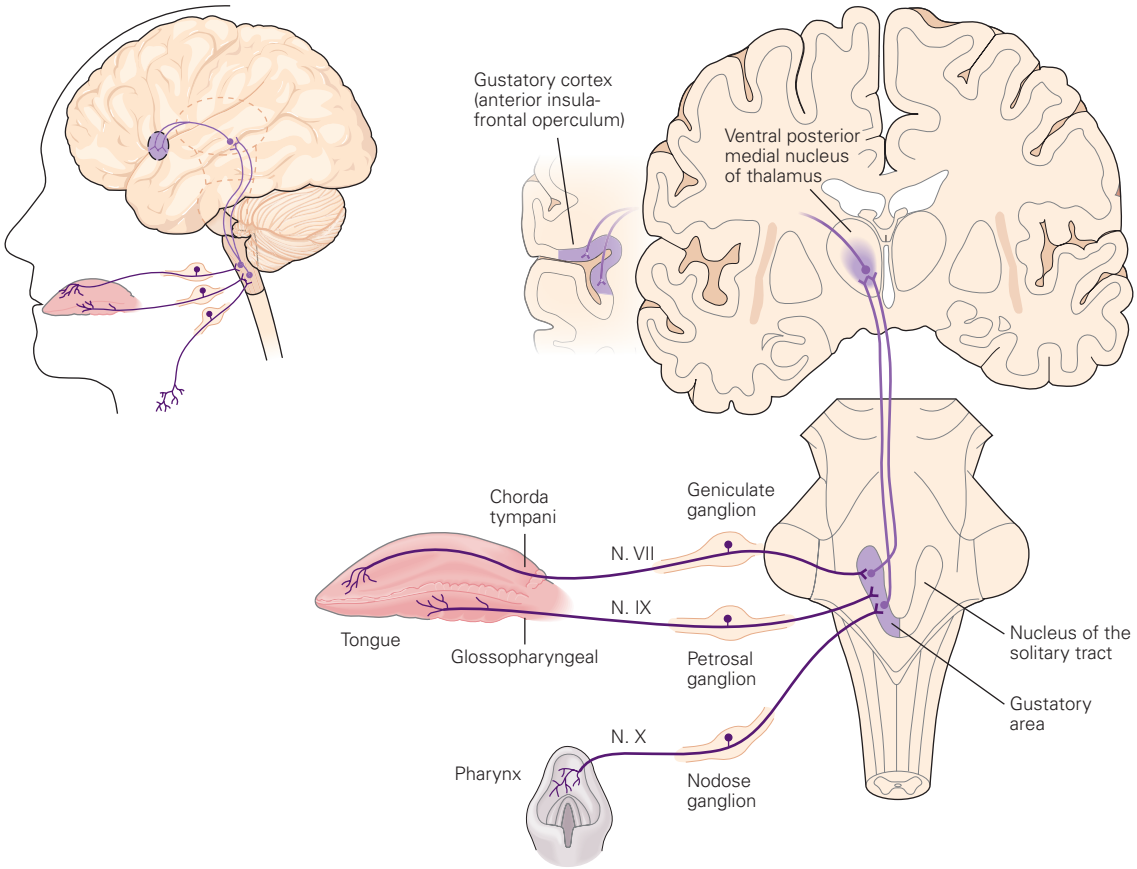

Figure 29–17 The gustatory system. Tastants are detected in taste buds in the oral cavity. Taste buds on the tongue and pharynx are innervated by the peripheral fibers of gustatory sensory neurons, which travel in the glossopharyngeal, chorda tympani and vagus nerves and terminate in the nucleus of the solitary tract in the brain stem. From there, taste information is relayed through the thalamus to the gustatory cortex as well as to the hypothalamus.

the local chemical environment prior to ingestion. As in mammals, only a few different types of taste cells detect different tastes. In the *Drosophila* fly, the different taste cell classes include those that sense sugars, bitter compounds, water, and pheromones. As in mammals, activation of these different taste cells drives different innate behaviors; for example, activation of sugar cells drives food acceptance behavior, whereas activation of bitter cells drives food rejection. Thus, the basic organization of taste detection is remarkably similar in insects and mammals, despite divergent evolutionary histories.

The taste receptors in insects are not related to vertebrate receptors. Members of the gustatory receptor (GR) gene family participate in the detection of sugars and bitter compounds. The GRs are membrane-spanning receptors that are distantly related to the odorant receptors of the fly. The fly has approximately 70 GR genes, a surprisingly large number considering it has approximately 60 olfactory receptor genes. Different GRs are found in sugar cells versus bitter cells, with many GRs present in a single neuron. In addition to GRs, other gene families participate in insect taste, including variants of ionotropic glutamate receptors and other ion channel classes. Similar to olfactory detection, the gene families involved in taste recognition differ across phyla, demonstrating that the gene families for chemical recognition have evolved independently.

Highlights

1. Odor detection in the nose is mediated by a large family of odorant receptors that number approximately 350 in humans and 1,000 in mice. These receptors vary in protein sequence, consistent with an ability to detect structurally diverse odorants.

2. Individual odorant receptors can detect multiple odorants, and different odorants activate different combinations of receptors. This combinatorial strategy explains how we can discriminate a multitude of odorants and how nearly identical odorants can have different scents.
3. Each olfactory sensory neuron in the nose expresses a single type of receptor. Thousands of neurons with the same receptor are dispersed in the olfactory epithelium and intermingled with neurons expressing other receptors.
4. In the olfactory bulb, the axons of the sensory neurons expressing the same receptor converge in a few receptor-specific glomeruli, generating a map of odorant receptor inputs that is similar among individuals.
5. The axons of olfactory bulb projection neurons project broadly to multiple areas of the olfactory cortex, generating a highly distributed organization of cortical neurons responsive to individual odorants. The olfactory cortex transmits information to many other brain areas.
6. In mice, pheromones can be detected in the nose or in the vomeronasal organ, a structure absent in humans. Signals from the nose and vomeronasal organ travel through different neural pathways in the brain.
7. The olfactory system of the fruit fly *Drosophila melanogaster* resembles that of mammals in many aspects. It uses a large number of diverse olfactory receptors, with one or a few olfactory receptors expressed by each olfactory sensory neuron. Moreover, neurons with the same receptor synapse in a few specific glomeruli in the antennal lobe of the brain. From there, olfactory signals are transmitted to two major brain areas involved in innate versus learned odor responses. The ease of using genetic approaches in fruit flies has enabled rapid study of mechanisms underlying odor coding and behavior.
8. The gustatory system detects five basic tastes: sweet, sour, bitter, salty, and umami (amino acids). Tastants that activate these taste qualities are detected by taste receptor cells located primarily in taste buds on the tongue and palate epithelium. The detection of the five different taste modalities is mediated by different taste receptor cells, each dedicated to one modality.
9. Sweet tastants are detected by a single type of receptor, which is composed of two subunits, T1R2 and T1R3. Umami receptors are related but comprise a combination of T1R1 and T1R3 subunits.
10. Bitter taste receptors constitute a family of approximately 30 related but diverse receptors that vary in ligand specificity. Individual taste receptor cells express many or all bitter receptors.
11. In contrast to sweet, umami, and bitter receptors, which are all G protein–coupled receptors, salty and sour tastes are detected by ion channels: ENaC for salt taste and Otopetrin-1 for sour taste.
12. Taste signals travel from taste buds through cranial nerves from gustatory sensory neurons in the geniculate, petrosal, and nodose ganglia via labeled lines (sweet taste receptor cells to sweet neurons, bitter taste cells to bitter neurons, etc.). They then travel to the gustatory area of the nucleus of the solitary tract and parabrachial nucleus, and from there to the taste area of the thalamus and then the gustatory cortex. The gustatory cortex, in turn, projects to many brain areas, including those involved in motor control, feeding, hedonic value, learning, and memory.
13. The gustatory cortex contains hot spots for sweet and bitter taste, which, when directly stimulated, can elicit behavioral responses similar to those obtained with tastants applied to the tongue.
14. The fruit fly *Drosophila* also has a specialized gustatory system that evaluates potential nutrients and toxins in food. Different classes of taste cells sense sugars, bitter compounds, pheromones, or water. Activation of these different peripheral sensors drives different innate behaviors, such as food acceptance or rejection.

Linda Buck
Kristin Scott
Charles Zuker

Selected Reading

Bargmann CI. 2006. Comparative chemosensation from receptors to ecology. Nature 444:295–301.

Giessel AJ, Datta SR. 2014. Olfactory maps, circuits and computations. Curr Opin Neurobiol 24:120–132.

Stowers L, Kuo TH. 2015. Mammalian pheromones: emerging properties and mechanisms of detection. Curr Opin Neurobiol 34:103–109.

Touhara K, Vosshall LB. 2009. Sensing odorants and pheromones with chemosensory receptors. Annu Rev Physiol 71:307–332.

Wilson DA, Sullivan RM. 2011. Cortical processing of odor objects. Neuron 72:506–519.
Yarmolinsky DA, Zuker CS, Ryba NJ. 2009. Common sense about taste: from mammals to insects. Cell 139: 234–244.

References

Adler E, Hoon MA, Mueller KL, Chandrashekar J, Ryba NJ, Zuker CS. 2000. A novel family of mammalian taste receptors. Cell 100:693–702.
Bachmanov AA, Bosak NP, Lin C, et al. 2014. Genetics of taste receptors. Curr Pharm Des 20:2669–2683.
Buck L, Axel R. 1991. A novel multigene family may encode odorant receptors: a molecular basis for odor recognition. Cell 65:175–187.
Chandrashekar J, Kuhn C, Oka Y, et al. 2010. The cells and peripheral representation of sodium taste in mice. Nature 464:297–301.
Chandrashekar J, Mueller KL, Hoon MA, et al. 2000. T2Rs function as bitter taste receptors. Cell 100:703–711.
Chen X, Gabitto M, Peng Y, Ryba NJ, Zuker CS. 2011. A gustotopic map of taste qualities in the mammalian brain. Science 333:1262–1266.
Dulac C, Axel R. 1995. A novel family of genes encoding putative pheromone receptors in mammals. Cell 83:195–206.
Dulac C, Torello AT. 2003. Molecular detection of pheromone signals in mammals: from genes to behaviour. Nat Rev Neurosci 7:551–562.
Glusman G, Yanai I, Rubin I, Lancet D. 2001. The complete human olfactory subgenome. Genome Res 1:685–702.
Godfrey PA, Malnic B, Buck LB. 2004. The mouse olfactory receptor gene family. Proc Natl Acad Sci U S A 101:2156–2161.
Greer PL, Bear DM, Lassance JM, et al. 2016. A family of non-GPCR chemosensors defines an alternative logic for mammalian olfaction. Cell 165:1734–1748.
Hallem EA, Carlson JR. 2006. Coding of odors by a receptor repertoire. Cell 125:143–160.
Herrada G, Dulac C. 1997. A novel family of putative pheromone receptors in mammals with a topographically organized and sexually dimorphic distribution. Cell 90:763–773.
Hoon MA, Adler E, Lindemeier J, Battey JF, Ryba NJ, Zuker CS. 1999. Putative mammalian taste receptors: a class of taste-specific GPCRs with distinct topographic selectivity. Cell 96:541–551.
Johnson BA, Farahbod H, Leon M. 2005. Interactions between odorant functional group and hydrocarbon structure influence activity in glomerular response modules in the rat olfactory bulb. J Comp Neurol 483:205–216.
Keller A, Zhuang H, Chi Q, Vosshall LB, Matsunami H. 2007. Genetic variation in a human odorant receptor alters odour perception. Nature 449:468–472.
Kondoh K, Lu Z, Ye X, Olson DP, Lowell BB, Buck LB. 2016. A specific area of olfactory cortex involved in stress hormone responses to predator odours. Nature 532:103–106.
Liberles SD, Buck LB. 2006. A second class of chemosensory receptors in the olfactory epithelium. Nature 442:645–650.
Liberles SD, Horowitz LF, Kuang D, et al. 2009. Formyl peptide receptors are candidate chemosensory receptors in the vomeronasal organ. Proc Natl Acad Sci U S A 106:9842–9847.
Malnic B, Godfrey PA, Buck LB. 2004. The human olfactory receptor gene family. Proc Natl Acad Sci U S A 101:2584–2589.
Malnic B, Hirono J, Sato T, Buck LB. 1999. Combinatorial receptor codes for odors. Cell 96:713–723.
Matsunami H, Buck LB. 1997. A multigene family encoding a diverse array of putative pheromone receptors in mammals. Cell 90:775–784.
Matsunami H, Montmayeur JP, Buck LB. 2000. A family of candidate taste receptors in human and mouse. Nature 404:601–604.
Mombaerts P, Wang F, Dulac C, et al. 1996. Visualizing an olfactory sensory map. Cell 87:675–686.
Montmayeur JP, Liberles SD, Matsunami H, Buck LB. 2001. A candidate taste receptor gene near a sweet taste locus. Nat Neurosci 4:492–498.
Morrison E, Constanzo R. 1990. Morphology of the human olfactory epithelium. J Comp Neurol 297:1–13.
Mueller KL, Hoon MA, Erlenbach I, Chandrashekar J, Zuker CS, Ryba NJ. 2005. The receptors and coding logic for bitter taste. Nature 434:225–229.
Nelson G, Chandrashekar J, Hoon MA, et al. 2002. An amino-acid taste receptor. Nature 416:199–202.
Nelson G, Hoon MA, Chandrashekar J, et al. 2001. Mammalian sweet taste receptors. Cell 106:381–390.
Neville KR, Haberly LB. 2004. The olfactory cortex. In: GM Shepherd (ed). *The Synaptic Organization of the Brain*, pp. 415–454. New York: Oxford University Press.
Niimura Y, Nei M. 2005. Evolutionary changes of the number of olfactory receptor genes in the human and mouse lineages. Gene 14:23–28.
Northcutt RG. 2004. Taste buds: development and evolution. Brain Behav Evol 64:198–206.
Oka Y, Butnaru M, von Buchholtz L, Ryba NJ, Zuker CS. 2013. High salt recruits aversive taste pathways. Nature 494:472–475.
Peng Y, Gillis-Smith S, Jin H, Tränkner D, Ryba NJ, Zuker CS. 2015. Sweet and bitter taste in the brain of awake behaving animals. Nature 527:512–515.
Ressler KJ, Sullivan SL, Buck LB. 1993. A zonal organization of odorant receptor gene expression in the olfactory epithelium. Cell 73:597–609.
Ressler KJ, Sullivan SL, Buck LB. 1994. Information coding in the olfactory system: evidence for a stereotyped and highly organized epitope map in the olfactory bulb. Cell 79:1245–1255.
Riviere S, Challet L, Fluegge D, Spehr M, Rodriguez I. 2009. Formyl peptide receptor-like proteins are a novel family of vomeronasal chemosensors. Nature 459:574–577.
Root CM, Denny CA, Hen R, Axel R. 2014. The participation of cortical amygdala in innate, odour-driven behaviour. Nature 515:269–273.

Royer SM, Kinnamon JC. 1991. HVEM Serial-section analysis of rabbit foliate taste buds. I. Type III cells and their synapses. J Comp Neurol 306:49–72.

Sarafi-Reinach TR, Sengupta P. 2000. The forkhead domain gene *unc*-130 generates chemosensory neuron diversity in *C. elegans*. Genes Dev 14:2472–2485.

Shepherd GM, Chen WR, Greer CA. 2004. The olfactory bulb. In: GM Shepherd (ed). *The Synaptic Organization of the Brain*, 5th ed., pp. 164–216. New York: Oxford Univ. Press.

Shepherd GM, Greer CA. 1998. The olfactory bulb. In: GM Shepherd (ed). *The Synaptic Organization of the Brain*, 4th ed., pp. 159–203. New York: Oxford Univ. Press.

Stettler DD, Axel R. 2009. Representations of odor in the piriform cortex. Neuron 63:854–864.

Sullivan SL, Adamson MC, Ressler KJ, Kozak CA, Buck LB. 1996. The chromosomal distribution of mouse odorant receptor genes. Proc Natl Acad Sci U S A 93: 884–888.

Teng B, Wilson CE, Tu YH, Joshi NR, Kinnamon SC, Liman ER. 2019. Cellular and neural responses to sour stimuli require the proton channel Otop1. Curr Biol 4:3647–3656.

Troemel ER, Kimmel BE, Bargmann CI. 1997. Reprogramming chemotaxis responses: sensory neurons define olfactory preferences in *C. elegans*. Cell 91:161–169.

Vassar R, Ngai J, Axel R. 1993. Spatial segregation of odorant receptor expression in the mammalian olfactory epithelium. Cell 74:309–318.

Vosshall L, Amrein H, Morozov PS, Rzhetsky A, Axel R. 1999. A spatial map of olfactory receptor expression in the *Drosophila* antenna. Cell 96:725–736.

Vosshall LB, Stocker RF. 2007. Molecular architecture of smell and taste in *Drosophila*. Annu Rev Neurosci 30:505–533.

Vosshall LB, Wong AM, Axel R. 2000. An olfactory sensory map in the fly brain. Cell 102:147–159.

Wang JW, Wong AM, Flores J, Vosshall LB, Axel R. 2003. Two-photon calcium imaging reveals an odor-evoked map of activity in the fly brain. Cell 112:271–282.

Wilson RI. 2013. Early olfactory processing in *Drosophila*: mechanisms and principles. Annu Rev Neurosci 36:217–241.

Zhang X, Firestein S. 2002. The olfactory receptor gene superfamily of the mouse. Nat Neurosci 5:124–133.

Zhang Y, Hoon MA, Chandrashekar J, et al. 2003. Coding of sweet, bitter, and umami tastes: different receptor cells sharing similar signaling pathways. Cell 112:293–301.

Zhang J, Jin H, Zhang W, et al. 2019. Sour Sensing from the Togue to the Brain. Cell 179:392–402.

Zhao GQ, Zhang Y, Hoon MA, et al. 2003. The receptors for mammalian sweet and umami taste. Cell 115:255–266.

Part V

Preceding Page

Fresco of dancing Peucetian women from the Tomb of the Dancers in the Corso Cotugno necropolis of Ruvo di Puglia, 4th–5th century BC. The tomb has a semichamber design. Its six painted panels depict 30 dancing women, moving from left to right with arms interlocked as though they were dancing in a circle around the interior of the tomb. The skeletal remains of the deceased in the tomb clearly belonged to a distinguished male warrior. The tomb is named after the dancing women that appear on the frescoes in the tomb. The panels with the frescoes are now exhibited in the Naples National Archaeological Museum, inv. 9353. (Source: https://en.wikipedia.org/wiki/Tomb_of_the_Dancers.)