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Genetic Predisposition and Taste Preference: Impact on Food Intake and Risk of Chronic Disease

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Abstract Nutritional intake can profoundly impact the development of human disease, mainly by driving the progression of obesity-related conditions such as type 2 diabetes, cardiovascular disease, and cancer. Taste perception can profoundly affect food preference and nutritional intake. Thus, human variation in taste responsiveness to certain foods may play an integral role in these health consequences by influencing nutrient assimilation. Therefore, we review here what is currently known about variation in taste perception, its genetic underpinnings, and how this variation may impact upon nutrient ingestion. We also provide a brief primer on the functional organization of the peripheral gustatory system. Elucidation of the mechanisms underpinning the association between taste perception, eating behavior, and energy regulation could be valuable in predicting who is at greater risk of becoming obese, as well as in finding novel therapeutic targets in the management and mitigation of obesity-related conditions.

Keywords Taste · Genetics · Genetic predisposition · Taste preference · Obesity · Diabetes · Hypertension · Cancer · Food intake · Chronic disease · Peripheral gustatory system · Genetic variation · Sweet · Bitter · Salty · Sour · Umami

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Introduction

Taste impacts food selection, and food intake impacts nutritional status. The taste of food is a major factor in determining food selection. From infancy, we derive pleasure from sweet foods and have an innate dislike for bitter-tasting foods [1]. Taste directs food preferences and plays a role in forming dietary patterns that impact health. Diet impacts risk for many chronic diseases, including cancer, cardiovascular disease (CVD), hypertension, type 2 diabetes mellitus, and obesity. Decades of research suggest that these chronic conditions result in major morbidity and mortality and consume significant health care resources in the United States [2–10]. Collectively, these studies also suggest that a majority of chronic diseases could be prevented or mitigated by the adoption of healthier eating habits. Here, we review the role of taste in modulating nutrient intake as well as what is currently understood with respect to genetic variation in genes involved in chemoreception and their impact on food intake and risk of chronic disease. (Table 1)

Table 1 Genetic variants associated with taste, food preference, and intake

Gene	SNP	Taste quality	Phenotype
GNAT3 [49]	Multiple non-coding SNPs	Sweet	Sensitivity to sucrose
GUSTIN [42, 43, 44••]	A292G (rs2274333)	Bitter	Sensitivity to PROP
TAS1R1 [50, 51]	C329T (not applicable)	Umami	Sensitivity to glutamate
	G1114A (rs142847878)	Umami	Sensitivity to glutamate
TAS1R2 [87]	T572C (rs35874116)	Sweet	Consumption of sugars
TAS1R3 [48, 50, 51]	C2269T (rs307377)	Umami	Sensitivity to glutamate
	Promoter (rs307355)	Sweet	Sensitivity to sucrose
	Promoter (rs35744813)	Sweet	Sensitivity to sucrose
TAS2R3, 4, and *5* haploblock [46]	Not applicable	Bitter	Perceived bitterness of espresso coffee
TAS2R19 [45•, 46]	A895G (rs10772420)	Bitter	Perceived bitterness of grapefruit juice
	Not applicable	Bitter	Perceived bitterness of quinine
TAS2R38 [35, 36, 76–78]	*TASR38* haplotype[a]	Bitter	Perceived bitterness of compounds containing a thiourea moiety and intake of cruciferous vegetables
	TASR38 haplotype[b]	Bitter	Intake of cruciferous vegetables
	G229C (rs713598)	Bitter	Intake of cruciferous vegetables
QTL on Chr 16 [52]	Not applicable	Sweet	Frequency of sweet food intake

SNP single nucleotide polymorphism

[a]Three SNP *TAS2R38* haplotype (rs713598, rs1726866, and rs10246939)

[b]Two SNP *TAS2R38* haplotype (rs713598 and rs1726866)

Sensory systems, particularly taste and olfaction, strongly influence food selection and intake. Chemosensory, thermosensory, and mechanosensory signals arising from specialized receptors positioned in both the oral-pharyngeal and nasal cavities and gastrointestinal tract are transmitted to the central nervous system (CNS), imparting information related to macronutrient composition, caloric density, osmolarity, and potential toxicity of food [11–14]. Chief among these neural signals are those provided by the gustatory system, which is the final guardian of the alimentary tract. It is widely believed that these orosensory inputs, especially taste, integrate with other neural and endocrine signals related to energy, fluid, and electrolyte status and ultimately influence central neural circuits controlling food and fluid intake.

Before we review what is currently known about variation in taste perception, its genetic underpinnings, and how this variation may impact upon nutrient ingestion, we provide a brief primer on the organization of the taste system, with a particular focus on the peripheral gustatory system [15–17].

Functional Organization of the Peripheral Gustatory System

Taste stimuli elicit perceptions that can be categorized into five qualities—sweet, bitter, salty, sour, and umami—each of which is associated with a biologically relevant class of compounds [15, 18]. The detection of these stimuli occurs in taste cells. Taste cells on the tongue are grouped into buds, which in turn are clustered within papillae. Within each taste bud, taste cells fall into three morphological subtypes, types 1, 2, and 3, which seem to correspond to functional classes. Type 2 cells express receptors for sweet, bitter, and umami taste, as well as associated downstream signaling components. These taste cells do not form traditional synapses with afferent nerve fibers but appear to form purinergic connections with nerve fibers and neighboring cells [19–21]. Type 3 cells, by contrast, do form traditional synapses with ascending nerves and are identified by the presence of serotonin and synaptic machinery such as SNAP-25 and NCAM [22, 23]. It appears that at least some type 3 cells are sensors for sour stimuli [24, 25]. Type 1 cells are thought to play more of a supporting, glial-like role, though these cells have recently been implicated in salty taste (Fig. 1) [26–28]. Little is currently known about cell-to-cell communication and its affect on the neural output of the taste bud; therefore, more research is needed to further elucidate details of these mechanisms.

Three genes from the *TAS1R* gene family encode three G-protein-coupled receptors (GPCRs), T1R1, T1R2, and T1R3, which are responsible for mediating perceptions of sweet and amino acid tastes. T1R2 and T1R3 combine to from a heteromeric receptor that binds with sugars and a variety of other structurally diverse compounds that give

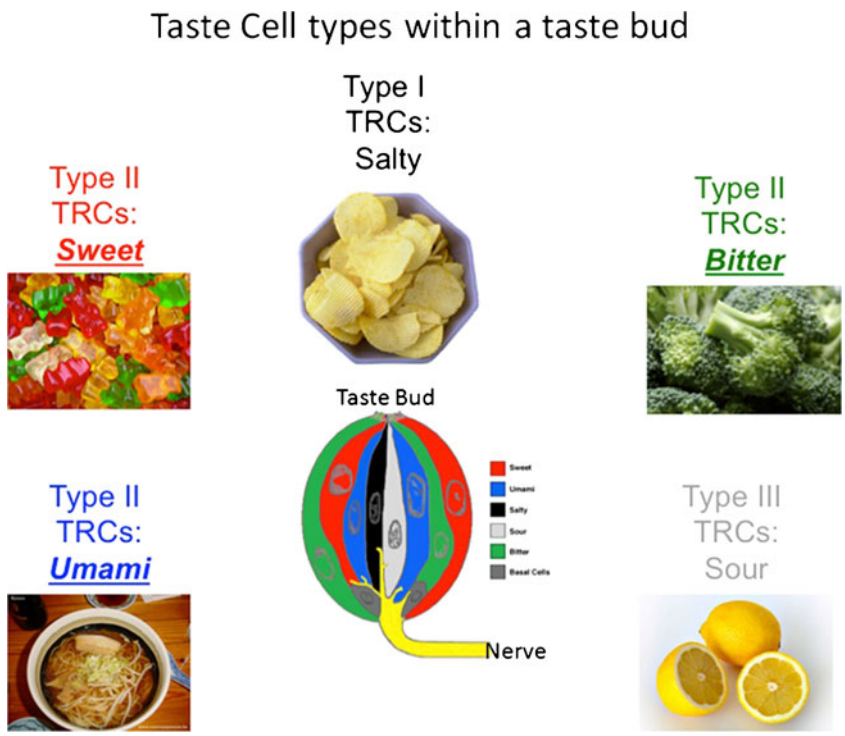

Fig. 1 Schematic description of taste bud with morphologic cell types. *TRC* taste receptor cell

rise to a sweet taste perception [16, 29, 30], while T1R3 in complex with T1R1 forms a heterodimer that responds to L-amino acids. In humans, this receptor is narrowly tuned to the amino acid glutamate [31], the detection of which results in a "savory" perception referred to as umami. The *TAS2R* genes encode bitter taste receptors. It is said that there are about 25 members of this family in humans, which encode broadly tuned GPCRs, allowing for the detection of a large number of structurally diverse bitter compounds [32, 33].

While perceptions of sweet, bitter, and umami tastes are mediated by G-protein-signaling cascades, salty and sour taste detection is mediated via ion channels [34]. Epithelial sodium channels allow for the entrance of Na^+ ions into the cells, leading to a salty taste perception [28]. A subset of type 3 cells appears to be specialized for detecting hydrogen ions released by acidic taste stimuli, leading to a sour perception [24, 25]. Recent work suggests that one pathway in which H^+ ions enter and transduce taste cells is by passing through a specialized proton channel that expresses the polycystic kidney disease 2-like 1 ion channel [24].

Neurophysiologic studies in several mammalian species have shown that four major branches of three cranial nerves innervate taste buds in the oral cavity. These nerves carry gustatory neural signals from the oral cavity to the solitary nucleus in the brainstem. These signals are then propagated up through the gustatory neuroaxis. The chorda tympani branch of the facial nerve innervates taste buds on the anterior two thirds of the tongue. The greater superficial petrosal branch of the facial nerve innervates the taste buds of the soft palate. The lingual–tonsilar branch of the glossopharyngeal nerve innervates taste buds of the posterior third of the tongue. The superior laryngeal branch of the vagus nerve innervates a small number of taste buds located on the laryngeal epithelium.

Genetic Variation Known to Influence Taste Preference

Bitter Taste

The most well-characterized human taste phenotype is the relative sensitivity of individuals to the bitter taste evoked by any variety of compounds containing an N–C = S (thiourea) moiety, such as phenylthiocarbamide (PTC) and 6-n-propylthiouracil (PROP) [35, 36]. As early as the 1930s, investigators found that not everyone can perceive the taste of the bitter compound PTC [37]; the earliest studies of the genetics of taste perception utilized PTC (decades later PROP, another bitter compound to which many people are taste blind, became more widely used when it was found to be less toxic). Early studies on PTC and PROP focused on tasters versus non-tasters. More recently, three categories of tasting ability have emerged: non-tasters, medium tasters, and tasters of PROP. Non-tasters cannot distinguish the taste of solutions containing PROP from that of pure water, whereas tasters characterize PROP as having a distinctively bitter taste [38]. PROP-tasting ability is a heritable trait. Non-tasters were thought to be homozygous for the recessive allele of the PROP-tasting gene, medium tasters heterozygous, and tasters homozygous dominant [38].

It was discovered in 2003 that the chief determinant of an individual's responsiveness to PROP/PTC was the inheritance of haplotypes of the gene *TAS2R38* [39, 40]. *TAS2R38* has been extensively characterized in vitro, in vivo, and in human populations, and is responsive to a variety of the bitter-tasting stimuli, all of which contain the N−C = S (thiourea) moiety (eg, PTC and PROP). *TAS2R38* haplotype predicts the majority (55–85 %) of phenotypic variance in PROP sensitivity [39]. Two common haplotypes have been shown to influence perception of these compounds: among individuals of Northern European decent, the nontaster haplotype and taster haplotype represent 47 % and 49 % of all haplotypes, respectively, and 30 % and 70 %, respectively, among individuals of East Asian decent. [39]. Although also studied with respect to bitter taste in general, PROP taster status is not a specific marker for sensitivity to the bitterness of other bitter compounds [41].

As mentioned above, three categories of PROP-tasting ability have been identified: non-tasters, medium tasters, and tasters. However, a subset of tasters are able to perceive the bitterness of PROP at significantly lower concentrations than do typical tasters [38]. These individuals have been dubbed supertasters. Interestingly, supertasters not only do have a heighten sensitivity to PROP but also respond more robustly to a variety of taste compounds, and perceive more burn from oral irritants (alcohol and capsaicin). It was postulated that the supertaster phenotype was due to increased neural "gain" in signals emanating from the oral cavity. This assertion was supported by the fact that the density of taste buds on the anterior tongue was correlated with supertaster status [38]. Additionally, it was recently demonstrated that genetic variation in the taste bud trophic factor gene *GUSTIN* (*CA6*) is also strongly associated with PROP sensitivity [42, 43, 44••].

Although the vast majority of research on the genetic determinants of bitter taste perception has focus, almost exclusively, on the PROP taste sensitivity phenotype, a handful of other studies have attempted to uncover genetic factors associated with taste sensitivity to other prototypical bitter-tasting compounds. Reed et al. [45•] performed a genome-wide association study attempting to discover variants associated with the perceived taste intensity of quinine HCl (QHCl), caffeine, and sucrose octaacetate (SOA). For caffeine and SOA, no single nucleotide polymorphism (SNP) association reached the genome-wide statistical significance criterion. For quinine, however, a peak association was centered in a region that contains the bitter taste receptor *TAS2R19*. It should be noted, however, that the SNP in *TAS2R19* was in tight LD with other bitter receptors, as well as with salivary proline-rich protein genes, which have also been associated with bitter taste responsiveness. In another study, Hayes et al. [46] found, using a candidate gene approach, that a haploblock across *TAS2R3*, *TAS2R4*, and *TAS2R5* was associated with variability in the bitterness of espresso coffee [46]. They also found that variation in *TAS2R19* was associated with the perceived bitterness of grapefruit juice.

It is well-known that a variety of artificial sweeteners possess bitter aftertaste (eg, saccharin). It was discovered that activation of bitter taste receptors mediate this perception [47] and that genetic variation in specific *TAS2R* genes (particularly *TAS2R31*) strongly influenced the perceived bitterness of the artificial sweeteners saccharin and acesulfame K [47].

Sweet and Umami Taste

Although less well-studied than bitter taste, evidence exists suggesting that genetic variation also impacts upon sweet and umami taste perception. For example, Fushan et al. [48] found two SNPs located upstream of the *TAS1R3* coding sequence that were strongly associated with human taste sensitivity to sucrose. This same group also tested if variation in other genes encoding taste-signaling molecules can influence sweet taste perception [49]. Their association analyses revealed a significant correlation between sucrose responsiveness and genetic variation occurring in the *GNAT3* gene. *GNAT3* encodes the taste-specific Gα subunit α-gustducin, a G protein subunit involved in taste cell signal transduction. Raliou et al. [50, 51] showed that variation in monosodium glutamate detection thresholds was also associated with polymorphisms in the *TAS1R1* and *TAS1R3* genes.

Very few studies have attempted to identify whether genetic variation in genes other than those already know to impact the functioning of the peripheral gustatory system can influence sweet and/or umami taste responsiveness. To the best of our knowledge, only one genome-wide study designed to identify genetic factors associated with sweet taste functioning has been published [52]. Keskitalo et al. [52] found a significant association with genetic variation on chromosome 16 and sweet taste preference. It should be noted that these investigators only tested 146 subjects and conducted a genome-wide analysis with only 450 markers. As such, the possibility of type II error was likely high.

Salty and Sour Taste

Although no genetic variants have been identified that impact upon variation in human salty and sour taste sensitivity, heritability studies suggest that genetic factors do play a part in variation sour taste responsiveness [53]. An investigation by Wise et al. [53] found that sour taste sensitivity displays heritability on par with that of sensitivity to the bitter compounds PROP, strongly suggesting that genetic factors play a large role in variation in this phenotype [54]. Data from a

recent study on acid taste sensitivity in humans suggest the involvement of PKD-like receptors as well as other receptors in the mediation of sour taste. Huque et al. [55] measured the expression level of gene transcripts in taste receptor cells between subjects ageusic to sour tasting stimuli and those with normal sour taste sensitivity. Various ASIC isoforms as well as the channels PKD1L3 and PKD2L1 were readily detectable in subjects with normal taste sensitivity. However, none of these transcripts were detectable in subjects with sour taste ageusia [55]. In the Wise et al. [53] study detailed above, it was also reported that salty taste sensitivity did not show significant genetic heritability. Much more research needs to be conducted on variation in sweet and sour taste perception before it can be ascertained if genetic variation influences taste responsiveness toward these stimuli.

Variation in Taste Responsiveness and its Association with Food Preference and Intake

Although all taste modalities impact upon food selection, the influence of bitter taste perception on food preference has been the most extensively studied [56]. A large body of research indicates that individuals who possess enhanced perception of bitter taste avoid certain foods, including specific fruits and vegetables [57–65]. For example, the perceived bitterness evoked by tasting various types of vegetables (eg, brussels sprouts, kale, asparagus) was shown to predict the preference for those vegetables as well as self-reported measures of vegetable intake [58]. Indeed, bitter taste perception is thought to have evolved to detect toxins in plants, vegetables, and foods and to modulate the ingestion of them [66, 67]. It has been postulated that plants evolved to protect themselves from being eaten by animals by synthesizing phytochemicals such as phenols, flavonoids, isoflavones, terpenes, and glucosinolates, which are almost always bitter, acrid, or astringent [66, 67]. Paradoxically, some of these bitter-tasting phytochemicals, including many flavonoids and polyphenols, have been associated with positive health benefits [68].

Interestingly, as mentioned above, many plants and vegetables synthesize glucosinolates, a class of compounds that also contain the thiourea moiety [69]. It has been proposed by many [58, 70, 71] that taste sensitivity to PROP can be used as a marker for individual differences in taste perception that influence food preferences and intake. For example, it has been demonstrated by multiple laboratories that children identified as insensitive to PROP consumed more vegetables than did the "taster" children during a free-choice intake test [72, 73]. These children also expressed greater "liking" for raw broccoli relative to taster children in a hedonic test [72]. Additionally, in female subjects, sensitivity to the bitterness of PROP was shown to be associated with lower acceptance of cruciferous and selected green and raw vegetables [59–61]. Similarly, female PTC non-tasters reported greater use of cooked turnip and raw watercress than did PTC tasters [64]. Colon cancer patients who tasted PROP as more bitter also reported less vegetable intake [74]. PROP and PTC tasters have also been reported to regard sodium benzoate (a common food preservative) and potassium chloride (a dietary salt substitute) as more bitter than non-tasters [75].

Based on the associations detailed above, one would predict that *TAS2R38* haploypes would also influence the ingestion of certain foods. Indeed, individuals who posses at least one copy of the PROP-sensitive allele of *TAS2R38* eat fewer cruciferous vegetables than do adults who are homozygous for the PROP-insensitive allele [76]. Colares-Bento et al. [77] also reported a similar finding in a cohort of older Brazilian women. Feeney et al. [78] reported that vegetable intake in both men and women was influenced by *TAS2R38* genotype, but in women, the insensitive allele of the *TAS2R38* was also associated with a macro- and micronutrient nutrient intake pattern indicative of healthy eating. Collectively, these data suggest that individuals with a strong sensitivity to bitter taste, along with a concomitant altered perceived taste sensation evoked by certain foods, such as vegetables, reduced their intake of these foods. Intake of fruits and vegetables has been negatively correlated with risk of cancer [79]. Consistent with this observation, bitter taste sensitivity/responsiveness has also been associated with body mass index (BMI), adiposity, and risk factors for CVD [78, 80–84] in adults, as well as with BMI in children [73]. However, there are studies that suggest no links exist [85, 86].

Although less well-studied, variation in sweet taste responsiveness also impacts food preference and intake. Eny et al. [87] found that genetic variation in *TAS1R2* was associated with consumption of sugars, specifically in overweight participants. Moreover, as with the perceived bitterness of certain foods, perceived sweetness was shown to predict the preference for sampled vegetables as well as vegetable intake in adults [58, 60]. In addition, evidence suggests that sweet-tasting substances induce cephalic phase hormonal response reflexes [88–90], providing another route through which sweet taste responsiveness can impact upon health. Indeed, recent evidence suggests that sweet taste receptors in the tongue and palate may be important in initiating preabsorptive metabolic responses to ingested nutrients [91]. However, at least in humans, it appears that sweet taste must be coupled with additional sensory modalities (eg, touch and smell) in order to produce preabsorptive hormone secretions [92, 93]. Be that as it may, it seems clear that variation in sweet taste responsiveness can lead to variation in food intake, as well as in the body's postprandial

hormone response to the ingestion of those nutrients, which could potentially impact upon metabolic health. In support of this contention, multiple investigators have shown that the perceived sweetness of foods is correlated with BMI [94–96]. It has also been demonstrated that a higher preference for sucrose solutions was associated with increased preferences for sweet desserts [60]. These data are particularly compelling considering the recent finding that revealed a positive association between the consumption of sugar-sweetened beverages and blood pressure [97] and with risk of metabolic syndrome and type 2 diabetes mellitus [98].

Conclusions

The ability to detect and discriminate taste stimuli is essential for health and survival and can drive ingestive behaviors. The gustatory system critically influences food preference and food intake. A large body of research clearly suggests a strong link between taste functioning, in particular bitter and sweet taste sensitivity, and food preference and intake. Moreover, a number of genes previously known to influence taste perception have been shown to also impact upon food preference and intake.

However, despite the fact that many other factors in addition to taste receptor biophysiology contribute to the functioning of the gustatory system, genetic association studies of taste functioning have largely been limited to the evaluation of genetic variation in and around taste receptor genes. However, a significant portion of variation in taste preferences likely depends on genes that are not involved in peripheral taste processing [99]. For example, genes involved in central mechanisms of taste processing and reward or motivation are also likely to strongly influence taste perception and food intake [100]. Thus, it is necessary for researchers in chemosensory genetics to expand the breadth and depth of genomic analysis beyond the evaluation of candidate genes to fully understand and explain the greatest proportion of variation in taste perception and its impact of nutritional intake. Indeed, understanding the role of genetics and how genetic variation influences taste functioning and food intake has significant implications for public health. Early ascertainment of heritable risk may facilitate timely implementation of preventive eating strategies that may decrease associated morbidity and mortality.

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References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Rozin P, Vollmecke TA. Food likes and dislikes. Annu Rev Nutr. 1986;6:433–56.
2. Rouse I, Beilin L, Armstrong B, Vandongen R. Blood-pressure-lowering effect of a vegetarian diet: controlled trial in normotensive subjects. Lancet. 1983;1(8314–5):5–10.
3. Appel L, Moore T, Obarzanek E, Vollmer W, Svetkey L, Sacks F, Bray G, Vogt T, Cutler J, Windhauser M, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med. 1997;336(16):1117–24.
4. Brinkworth G, Noakes M, Buckley J, Keogh J, Clifton P. Long-term effects of a very-low-carbohydrate weight loss diet compared with an isocaloric low-fat diet after 12 mo. Am J Clin Nutr. 2009;90(1):23–32.
5. Herder C, Peltonen M, Koenig W, Sütfels K, Lindström J, Martin S, Ilanne-Parikka P, Eriksson J, Aunola S, Keinänen-Kiukaanniemi S, et al. Anti-inflammatory effect of lifestyle changes in the Finnish Diabetes Prevention Study. Diabetologia. 2009;52(3):433–42.
6. Ding E, Mozaffarian D. Optimal dietary habits for the prevention of stroke. Semin Neurol. 2006;26(1):11–23.
7. Hu F, Manson J, Stampfer M, Colditz G, Liu S, Solomon C, Willett W. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med. 2001;345(11):790–7.
8. Lindström J, Peltonen M, Eriksson J, Louheranta A, Fogelholm M, Uusitupa M, Tuomilehto J. High-fibre, low-fat diet predicts long-term weight loss and decreased type 2 diabetes risk: the Finnish Diabetes Prevention Study. Diabetologia. 2006;49(5):912–20.
9. McCarron D, Reusser M. Reducing cardiovascular disease risk with diet. Obes Res. 2001;9 Suppl 4:335S–40S.
10. Swain J, McCarron P, Hamilton E, Sacks F, Appel L. Characteristics of the diet patterns tested in the optimal macronutrient intake trial to prevent heart disease (OmniHeart): options for a heart-healthy diet. J Am Diet Assoc. 2008;108(2):257–65.
11. Morrison C, Berthoud H. Neurobiology of nutrition and obesity. Nutr Rev. 2007;65(12 Pt 1):517–34.
12. Zheng H, Lenard N, Shin A, Berthoud H. Appetite control and energy balance regulation in the modern world: reward-driven brain overrides repletion signals. Int J Obes (Lond). 2009;33 Suppl 2:S8–S13.
13. Ahima R, Antwi D. Brain regulation of appetite and satiety. Endocrinol Metab Clin North Am. 2008;37(4):811–23.
14. Saper C, Chou T, Elmquist J. The need to feed: homeostatic and hedonic control of eating. Neuron. 2002;36(2):199–211.
15. Breslin P, Spector A. Mammalian taste perception. Curr Biol. 2008;18(4):R148–55.
16. Yarmolinsky DA, Zuker CS, Ryba NJ. Common sense about taste: from mammals to insects. Cell. 2009;139(2):234–44.
17. Carleton A, Accolla R, Simon SA. Coding in the mammalian gustatory system. Trends Neurosci. 2010;33(7):326–34.
18. Bartoshuk LM. Taste. In: Stevens SS, Atkinson RC, editors. Stevens' handbook of experimental psychology, vol. 2. New York: Wiley; 1988. p. 461–99.

19. Eddy MC, Eschle BK, Barrows J, Hallock RM, Finger TE, Delay ER. Double P2X2/P2X3 purinergic receptor knockout mice do not taste NaCl or the artificial sweetener SC45647. Chem Senses. 2009;34(9):789–97.
20. Finger TE, Danilova V, Barrows J, Bartel DL, Vigers AJ, Stone L, Hellekant G, Kinnamon SC. ATP signaling is crucial for communication from taste buds to gustatory nerves. Science. 2005;310 (5753):1495–9.
21. Hayato R, Ohtubo Y, Yoshii K. Functional expression of ionotropic purinergic receptors on mouse taste bud cells. J Physiol. 2007;584(Pt 2):473–88.
22. DeFazio RA, Dvoryanchikov G, Maruyama Y, Kim JW, Pereira E, Roper SD, Chaudhari N. Separate populations of receptor cells and presynaptic cells in mouse taste buds. J Neurosci. 2006;26 (15):3971–80.
23. Clapp TR, Medler KF, Damak S, Margolskee RF, Kinnamon SC. Mouse taste cells with G protein-coupled taste receptors lack voltage-gated calcium channels and SNAP-25. BMC Biol. 2006;4:7.
24. Huang A, Chen X, Hoon M, Chandrashekar J, Guo W, Tränkner D, Ryba N, Zuker C. The cells and logic for mammalian sour taste detection. Nature. 2006;442(7105):934–8.
25. Kataoka S, Yang R, Ishimaru Y, Matsunami H, Sévigny J, Kinnamon J, Finger T. The candidate sour taste receptor, PKD2L1, is expressed by type III taste cells in the mouse. Chem Senses. 2008;33(3):243–54.
26. Yoshida R, Horio N, Murata Y, Yasumatsu K, Shigemura N, Ninomiya Y. NaCl responsive taste cells in the mouse fungiform taste buds. Neuroscience. 2009;159(2):795–803.
27. Vandenbeuch A, Clapp TR, Kinnamon SC. Amiloride-sensitive channels in type I fungiform taste cells in mouse. BMC Neurosci. 2008;9:1.
28. Chandrashekar J, Kuhn C, Oka Y, Yarmolinsky DA, Hummler E, Ryba NJ, Zuker CS. The cells and peripheral representation of sodium taste in mice. Nature. 2010;464(7286):297–301.
29. Zhao GQ, Zhang Y, Hoon MA, Chandrashekar J, Erlenbach I, Ryba NJ, Zuker CS. The receptors for mammalian sweet and umami taste. Cell. 2003;115(3):255–66.
30. Nelson G, Hoon MA, Chandrashekar J, Zhang Y, Ryba NJ, Zuker CS. Mammalian sweet taste receptors. Cell. 2001;106(3):381–90.
31. Li X, Staszewski L, Xu H, Durick K, Zoller M, Adler E. Human receptors for sweet and umami taste. Proc Natl Acad Sci U S A. 2002;99(7):4692–6.
32. Chandrashekar J, Mueller KL, Hoon MA, Adler E, Feng L, Guo W, Zuker CS, Ryba NJ. T2Rs function as bitter taste receptors. Cell. 2000;100(6):703–11.
33. Meyerhof W. Elucidation of mammalian bitter taste. Rev Physiol Biochem Pharmacol. 2005;154:37–72.
34. Lindemann B. Receptors and transduction in taste. Nature. 2001;413(6852):219–25.
35. Wooding S. Phenylthiocarbamide: a 75-year adventure in genetics and natural selection. Genetics. 2006;172(4):2015–23.
36. Tepper B. Nutritional implications of genetic taste variation: the role of PROP sensitivity and other taste phenotypes. Ann Rev Nutr. 2008;28:367–88.
37. Fox AL. The relationship between chemical constitution and taste. Proc Natl Acad Sci U S A. 1932;18(1):115–20.
38. Bartoshuk LM, Duffy VB, Miller IJ. PTC/PROP tasting: anatomy, psychophysics, and sex effects. Physiol Behav. 1994;56 (6):1165–71.
39. Kim UK, Jorgenson E, Coon H, Leppert M, Risch N, Drayna D. Positional cloning of the human quantitative trait locus underlying taste sensitivity to phenylthiocarbamide. Science. 2003;299 (5610):1221–5.
40. Bufe B, Breslin PA, Kuhn C, Reed DR, Tharp CD, Slack JP, Kim UK, Drayna D, Meyerhof W. The molecular basis of individual differences in phenylthiocarbamide and propylthiouracil bitterness perception. Curr Biol. 2005;15(4):322–7.
41. Delwiche JF, Buletic Z, Breslin PA. Covariation in individuals' sensitivities to bitter compounds: evidence supporting multiple receptor/transduction mechanisms. Percept Psychophys. 2001;63 (5):761–76.
42. Cabras T, Melis M, Castagnola M, Padiglia A, Tepper BJ, Messana I, Tomassini Barbarossa I. Responsiveness to 6-n-propylthiouracil (PROP) is associated with salivary levels of two specific basic proline-rich proteins in humans. PLoS One. 2012;7(2):e30962.
43. Calò C, Padiglia A, Zonza A, Corrias L, Contu P, Tepper BJ, Barbarossa IT. Polymorphisms in TAS2R38 and the taste bud trophic factor, gustin gene co-operate in modulating PROP taste phenotype. Physiol Behav. 2011;104(5):1065–71.
44. •• Padiglia A, Zonza A, Atzori E, Chillotti C, Calò C, Tepper BJ, Barbarossa IT. Sensitivity to 6-n-propylthiouracil is associated with gustin (carbonic anhydrase VI) gene polymorphism, salivary zinc, and body mass index in humans. Am J Clin Nutr. 2010;92 (3):539–45. *This explains some of the hidden variance in PROP taste responsiveness: The GUSTIN (CA6) gene is a trophic factor for taste bud development. This study investigated the role of this gene in PROP tasting. These researchers showed that a polymorphism in the GUSTIN gene results in a loss of full functionality of the protein. Variation in this gene was associated with PROP taster status (the genotype associated with a disruption in the protein was more frequent in nontasters). These data suggest that variation in GUSTIN may be associated with differences in papillae densities and oral chemosensory abilities across PROP phenotypic groups*.
45. • Reed DR, Zhu G, Breslin PA, Duke FF, Henders AK, Campbell MJ, Montgomery GW, Medland SE, Martin NG, Wright MJ. The perception of quinine taste intensity is associated with common genetic variants in a bitter receptor cluster on chromosome 12. Hum Mol Genet. 2010;19(21):4278–85. *This is only one of the only genome-wide evaluations of taste responsiveness: The perceived taste intensities of quinine HCl, caffeine, sucrose octaacetate (SOA), and PROP were examined. To identify genes involved in these phenotypes, a genome-wide association study was performed with 1,457 twins and their siblings using approximately 610,000 SNPs. For caffeine and SOA, no SNP association reached a genome-wide statistical significance. For PROP, the peak association was within TAS2R38, which accounted for 45.9% of the trait variance. For quinine, the peak association was centered in a region that contained the bitter taste receptor, TAS2R19, as well as salivary protein genes and explained 5.8% of the trait variance (this association was confirmed in a replication sample)*.
46. Hayes JE, Wallace MR, Knopik VS, Herbstman DM, Bartoshuk LM, Duffy VB. Allelic variation in TAS2R bitter receptor genes associates with variation in sensations from and ingestive behaviors toward common bitter beverages in adults. Chem Senses. 2011;36(3):311–9.
47. Pronin A, Xu H, Tang H, Zhang L, Li Q, Li X. Specific alleles of bitter receptor genes influence human sensitivity to the bitterness of aloin and saccharin. Curr Biol. 2007;17(16):1403–8.
48. Fushan A, Simons C, Slack J, Manichaikul A, Drayna D. Allelic polymorphism within the TAS1R3 promoter is associated with human taste sensitivity to sucrose. Curr Biol. 2009;19(15):1288–93.
49. Fushan AA, Simons CT, Slack JP, Drayna D. Association between common variation in genes encoding sweet taste signaling components and human sucrose perception. Chem Senses. 2010;35(7):579–92.
50. Raliou M, Wiencis A, Pillias AM, Planchais A, Eloit C, Boucher Y, Trotier D, Montmayeur JP, Faurion A. Nonsynonymous single

nucleotide polymorphisms in human tas1r1, tas1r3, and mGluR1 and individual taste sensitivity to glutamate. Am J Clin Nutr. 2009;90(3):789S–99S.
51. Raliou M, Grauso M, Hoffmann B, Schlegel-Le-Poupon C, Nespoulous C, Débat H, Belloir C, Wiencis A, Sigoillot M, Bano SP, et al. Human genetic polymorphisms in T1R1 and T1R3 taste receptor subunits affect their function. Chem Senses. 2011;36(6):527–37.
52. Keskitalo K, Knaapila A, Kallela M, Palotie A, Wessman M, Sammalisto S, Peltonen L, Tuorila H, Perola M. Sweet taste preferences are partly genetically determined: identification of a trait locus on chromosome 16. Am J Clin Nutr. 2007;86(1):55–63.
53. Wise P, Hansen J, Reed D, Breslin P. Twin study of the heritability of recognition thresholds for sour and salty taste. Chem Senses. 2007;32(8):749–54.
54. Kaplan AR, Fischer R, Karras A, Griffin F, Powell W, Marsters RW, Glanville EV. Taste thresholds in twins and siblings. Acta Genet Med Gemellol (Roma). 1967;16(3):229–43.
55. Huque T, Cowart B, Dankulich-Nagrudny L, Pribitkin E, Bayley D, Spielman A, Feldman R, Mackler S, Brand J. Sour ageusia in two individuals implicates ion channels of the ASIC and PKD families in human sour taste perception at the anterior tongue. PLoS One. 2009;4(10):e7347.
56. Garcia-Bailo B, Toguri C, Eny K, El-Sohemy A. Genetic variation in taste and its influence on food selection. OMICS. 2009;13 (1):69–80.
57. Drewnowski A, Henderson S, Shore A. Taste responses to naringin, a flavonoid, and the acceptance of grapefruit juice are related to genetic sensitivity to 6-n-propylthiouracil. Am J Clin Nutr. 1997;66(2):391–7.
58. Dinehart M, Hayes J, Bartoshuk L, Lanier S, Duffy V. Bitter taste markers explain variability in vegetable sweetness, bitterness, and intake. Physiol Behav. 2006;87(2):304–13.
59. Drewnowski A, Henderson S, Shore A, Barratt-Fornell A. Sensory responses to 6-n-propylthiouracil (PROP) or sucrose solutions and food preferences in young women. Ann N Y Acad Sci. 1998;855:797–801.
60. Drewnowski A, Henderson S, Levine A, Hann C. Taste and food preferences as predictors of dietary practices in young women. Public Health Nutr. 1999;2(4):513–9.
61. Drewnowski A, Henderson S, Hann C, Berg W, Ruffin M. Genetic taste markers and preferences for vegetables and fruit of female breast care patients. J Am Diet Assoc. 2000;100 (2):191–7.
62. Fischer R, Griffin F, England S, Garn S. Taste thresholds and food dislikes. Nature. 1961;191:1328.
63. Glanville EV, Kaplan AR. Food preference and sensitivity of taste for bitter compounds. Nature. 1965;205(4974):851–3.
64. Jerzsa-Latta M, Krondl M, Coleman P. Use and perceived attributes of cruciferous vegetables in terms of genetically-mediated taste sensitivity. Appetite. 1990;15(2):127–34.
65. Tepper B, Williams T, Burgess J, Antalis C, Mattes R. Genetic variation in bitter taste and plasma markers of anti-oxidant status in college women. Int J Food Sci Nutr. 2009;60 Suppl 2:35–45.
66. Ames B, Profet M, Gold L. Dietary pesticides (99.99% all natural). Proc Natl Acad Sci U S A. 1990;87(19):7777–81.
67. Drewnowski A, Gomez-Carneros C. Bitter taste, phytonutrients, and the consumer: a review. Am J Clin Nutr. 2000;72(6):1424–35.
68. Hollman PC, Katan MB. Dietary flavonoids: intake, health effects and bioavailability. Food Chem Toxicol. 1999;37(9–10):937–42.
69. Sandell MA, Breslin PA. Variability in a taste-receptor gene determines whether we taste toxins in food. Curr Biol. 2006;16 (18):R792–4.
70. Duffy V, Bartoshuk L. Food acceptance and genetic variation in taste. J Am Diet Assoc. 2000;100(6):647–55.
71. Tepper B. Nutritional implications of genetic taste variation: the role of PROP sensitivity and other taste phenotypes. Annu Rev Nutr. 2008;28:367–88.
72. Bell K, Tepper B. Short-term vegetable intake by young children classified by 6-n-propylthoiuracil bitter-taste phenotype. Am J Clin Nutr. 2006;84(1):245–51.
73. Negri R, Di Feola M, Di Domenico S, Scala MG, Artesi G, Valente S, Smarrazzo A, Turco F, Morini G, Greco L. Taste perception and food choices. J Pediatr Gastroenterol Nutr. 2012;54(5):624–9.
74. Basson M, Bartoshuk L, Dichello S, Panzini L, Weiffenbach J, Duffy V. Association between 6-n-propylthiouracil (PROP) bitterness and colonic neoplasms. Dig Dis Sci. 2005;50(3):483–9.
75. Bartoshuk LM. Bitter taste of saccharin related to the genetic ability to taste the bitter substance 6-n-propylthiouracil. Science. 1979;205(4409):934–5.
76. Sacerdote C, Guarrera S, Smith GD, Grioni S, Krogh V, Masala G, Mattiello A, Palli D, Panico S, Tumino R, et al. Lactase persistence and bitter taste response: instrumental variables and mendelian randomization in epidemiologic studies of dietary factors and cancer risk. Am J Epidemiol. 2007;166(5):576–81.
77. Colares-Bento FC, Souza VC, Toledo JO, Moraes CF, Alho CS, Lima RM, Cordova C, Nobrega OT. Implication of the G145C polymorphism (rs713598) of the TAS2r38 gene on food consumption by Brazilian older women. Arch Gerontol Geriatr. 2012;54(2):e13–8.
78. Feeney E, O'Brien S, Scannell A, Markey A, Gibney ER. Genetic variation in taste perception: does it have a role in healthy eating? Proc Nutr Soc. 2011;70(1):135–43.
79. Riboli E, Norat T. Epidemiologic evidence of the protective effect of fruit and veges on cancer risk. Am J Clin Nutr. 2003;78(3 Suppl):559S–69S.
80. Duffy VB. Associations between oral sensation, dietary behaviors and risk of cardiovascular disease (CVD). Appetite. 2004;43(1):5–9.
81. Goldstein GL, Daun H, Tepper BJ. Adiposity in middle-aged women is associated with genetic taste blindness to 6-n-propylthiouracil. Obes Res. 2005;13(6):1017–23.
82. Tepper BJ, Ullrich NV. Influence of genetic taste sensitivity to 6-n-propylthiouracil (PROP), dietary restraint and disinhibition on body mass index in middle-aged women. Physiol Behav. 2002;75(3):305–12.
83. Tepper B. Does genetic taste sensitivity to PROP influence food preferences and body weight? Appetite. 1999;32(3):422.
84. Tepper B, Koelliker Y, Zhao L, Ullrich N, Lanzara C, d'Adamo P, Ferrara A, Ulivi S, Esposito L, Gasparini P. Variation in the bitter-taste receptor gene TAS2R38, and adiposity in a genetically isolated population in Southern Italy. Obesity (Silver Spring). 2008;16(10):2289–95.
85. Drewnowski A, Henderson S, Cockroft J. Genetic sensitivity to 6-n-propylthiouracil has no influence on dietary patterns, body mass indexes, or plasma lipid profiles of women. J Am Diet Assoc. 2007;107(8):1340–8.
86. Yackinous C, Guinard J. Relation between PROP (6-n-propylthiouracil) taster status, taste anatomy and dietary intake measures for young men and women. Appetite. 2002;38 (3):201–9.
87. Eny KM, Wolever TM, Corey PN, El-Sohemy A. Genetic variation in TAS1R2 (Ile191Val) is associated with consumption of sugars in overweight and obese individuals in 2 distinct populations. Am J Clin Nutr. 2010;92(6):1501–10.
88. Bernstein I, Woods S. Ontogeny of cephalic insulin release by the rat. Physiol Behav. 1980;24(3):529–32.
89. Woods S, Bernstein I. Cephalic insulin response as a test for completeness of vagotomy to the pancreas. Physiol Behav. 1980;24(3):485–8.

90. Berthoud H, Trimble E, Siegel E, Bereiter D, Jeanrenaud B. Cephalic-phase insulin secretion in normal and pancreatic islet-transplanted rats. Am J Physiol. 1980;238(4):E336–40.
91. Kokrashvili Z, Margolskee RF. Taste cells express and secrete glucagon-like peptide 1. Chemical Senses. 2009;34(7):A77.
92. Teff K, Devine J, Engelman K. Sweet taste: effect on cephalic phase insulin release in men. Physiol Behav. 1995;57(6):1089–95.
93. Teff K. Cephalic phase pancreatic polypeptide responses to liquid and solid stimuli in humans. Physiol Behav. 2010;99(3):317–23.
94. Bartoshuk LM, Duffy VB, Hayes JE, Moskowitz HR, Snyder DJ. Psychophysics of sweet and fat perception in obesity: problems, solutions and new perspectives. Philos Trans R Soc Lond B Biol Sci. 2006;361(1471):1137–48.
95. Drewnowski A, Brunzell J, Sande K, Iverius P, Greenwood M. Sweet tooth reconsidered: taste responsiveness in human obesity. Physiol Behav. 1985;35(4):617–22.
96. Salbe A, DelParigi A, Pratley R, Drewnowski A, Tataranni P. Taste preferences and body weight changes in an obesity-prone population. Am J Clin Nutr. 2004;79(3):372–8.
97. Chen L, Caballero B, Mitchell D, Loria C, Lin P, Champagne C, et al. Reducing consumption of sugar-sweetened beverages is associated with reduced blood pressure. A prospective study among United States adults. Circulation 2010.
98. Malik VS, Popkin BM, Bray GA, Després JP, Willett WC, Hu FB. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. Diabetes Care. 2010;33(11):2477–83.
99. Bachmanov AA, Bosak NP, Floriano WB, Inoue M, Li X, Lin C, et al. Genetics of sweet taste preferences. Flavour Fragr J. 2011;26(4):286–94.
100. Felsted JA, Ren X, Chouinard-Decorte F, Small DM. Genetically determined differences in brain response to a primary food reward. J Neurosci. 2010;30(7):2428–32.