

# Recent Advances in Fatty Acid Perception and Genetics<sup>1–3</sup>

Danielle R Reed\* and Mary B Xia

Monell Chemical Senses Center, Philadelphia, PA

## ABSTRACT

This article summarizes new knowledge about the contribution of genetic variation to person-to-person differences underlying some sensory aspects of dietary fatty acids. Receptors on the taste cells of the human tongue arise from genes that have marked variation in DNA sequence, which, in some cases, is associated with differences in how these lipids in foods are perceived. These perceptual differences may affect food selection. *Adv Nutr* 2015;6:353S–360S.

**Keywords:** fatty acids, obesity, taste, lipids, genetics, polymorphism, chemosensory

## Introduction

Food is essential to our survival, and although eating is pleasant, it can also be dangerous (1). Our sense of taste developed to identify the pleasure of sweet, the tang of sour, and the brinlike quality of salt. Both the quality (e.g., sweet vs. bitter) and the perceived strength (e.g., strong vs. weak) of sensory experiences help determine whether it is best to swallow or to reject food. Other stimuli contribute to our sense of pleasure or danger from foods, such as carbonation, burn, calcium, and fats (2, 3). *Pinguis* is a Latin word that translates to “fat taste” (4), and although this is an old concept, only recently has the underlying biology of one of its components, FA perception, been discovered.

## Current Status of Knowledge

### Anatomy of the taste system

A few general principles about the taste system are useful to understand how and whether the sensations produced by lipids are part of this system (see **Figure 1**). Taste arises when chemicals stimulate special sensory cells on the

human tongue. These cells are contained in a taste bud, a structure that contains dozens of sensory cells arranged like the segments of an orange. The taste buds are contained within taste papillae. These taste papillae, which are visible on the tongue as small pink bumps, comprise 3 types, with names inspired by Latin words that describe their structure. The fungiform papillae are concentrated on the front of the tongue and owe their name to their mushroom-like appearance (from the Latin word *fungus*). Foliate papillae are concentrated on the sides of the tongue and are similar to the pages or leaves of a book (i.e., *folia*). Circumvallate papillae are located at the back of the tongue and look like they are encircled with a rampart or entrenchment, hence their name. Early anatomists called circumvallate papillae “calyciform,” which reflects their calyx or podlike appearance.

Taste receptor cells, which are contained within taste buds within papillae, convey signals via 3 sensory nerves: the chorda tympani (cranial nerve VII, one of the facial nerves), the glossopharyngeal nerve (cranial nerve IX), and the vagus nerve (cranial nerve X). These nerves relay sensory input to the nucleus of the solitary tract in the brain stem and from there to the thalamus and forebrain structures.

### The anatomy of fat taste

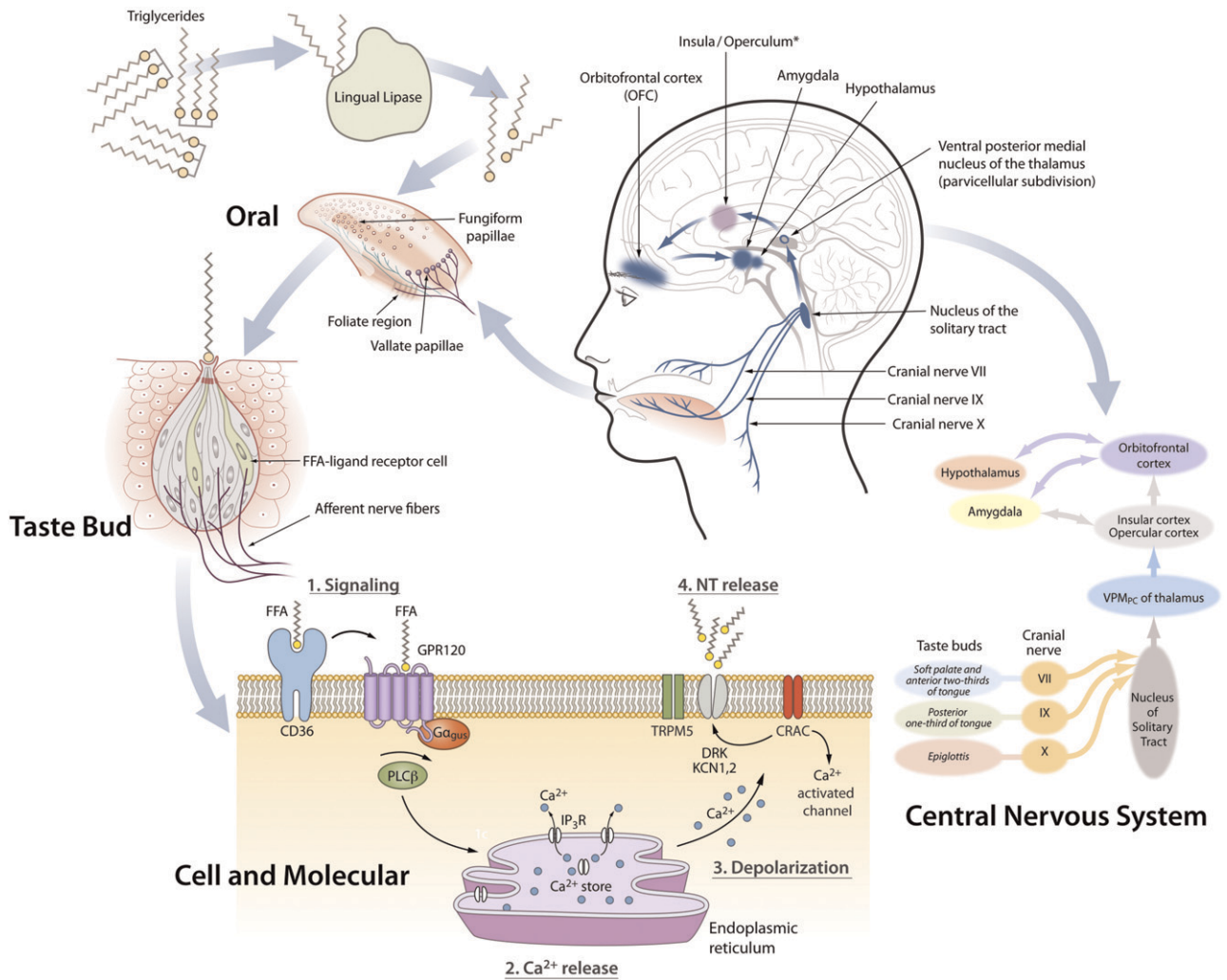
Fat has both taste and texture and only the taste part of perception is discussed here. Fat taste may arise from TGs, but more is known about how FAs elicit sensory signals. The hydrolysis of TGs produces FAs by a series of enzymatic steps that are sensed by cells in the mouth (5–7). The overall idea

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\* To whom correspondence should be addressed. E-mail: reed@monell.org.



**FIGURE 1** Process of fat taste perception. The generation of fat taste starts when TGs in the mouth are hydrolyzed into FFAs by one or more lingual lipases (upper left). FAs stimulate taste cells embedded in the fungiform, foliate, and vallate (circumvallate) papillae, which are visible as pink bumps on the human tongue. There are several types of taste cells in the taste bud, and in humans fat is likely to be detected by at least type II cells. At the surface of the cell membrane, the FFA ligand binds to 2 (and possibly more) types of proteins, a GPR120 and CD36. How these 2 molecules interact is currently unknown, and it is also hypothesized that they have nonoverlapping functions. This binding triggers a cascade of signaling events, leading to an increase in intracellular calcium and the ultimate neurotransmitter release that activates an afferent nerve fiber, which transmits the signal via the cranial nerves VII, IX, and X to the brain. \*The insula/operculum is lateral to the sagittal plane of the section shown. CRAC, calcium release-activation channel; DRK, delayed rectifying  $K^+$  channel;  $G\alpha_{gus}$ ,  $\alpha$ -gustducin; GPR120, G protein-coupled receptor 120;  $IP_3R$ , inositol triphosphate 3 receptor;  $KCN1,2$ , potassium voltage-gated channel, shaker-related subfamily, members 1 and 2; NT, neurotransmitter;  $PLC\beta$ , phospholipase C  $\beta$ ; TRPM5, transient receptor potential cation channel subfamily M, member 5;  $VPM_{pc}$ , ventral posterior medial nucleus of the thalamus, parvocellular subdivision.

is that these FFAs bind to receptors on distinct types of taste receptor cells. The evidence for this idea comes from several types of experiments. For mice and rats, blocking the ability to convert TGs to FFAs in the mouth, either by inhibiting lingual lipase with drugs or by removing the salivary glands, reduces the animal's preference for fat. Likewise, cutting the nerves between the tongue and brain also reduces fat preference. Humans can sense FFAs emulsified in water even when other senses such as sight and trigeminal sensations (e.g., burn) are blocked. However, FFAs appear to provide a chemical signal, whereas intact TGs provide the textural signal.

Both types of information are distinct, but they both converge to the same brain areas where they contribute to the unique perception of fat. Thus, the chemical signal of fat taste appears not to act alone and instead requires textural cues for its full perceptual embodiment (8).

### Brain areas that sense fat taste

Taste cells in the mouth respond to FFAs and gustatory nerves relay information about their presence to the brain. Some brain areas respond to the texture of fat, as well as to the texture of other viscous solutions. At least one fMRI study in

individuals who tasted vegetable oil showed that the insular taste cortex is activated by fat. Sugar also activates this area (9). Dietary fat is sensed by other brain areas (10). However, these data do not address the thorny problem of what exactly is the stimulus that elicits this activation: it might be TGs or it might be the small amounts of FAs digested orally during the test. Research that parses the effects of FAs from pure TGs would be useful to help understand which signals are important for the pleasant aspects of fat taste.

### TGs vs. FAs

To understand fat taste from its chemical perspective, it would be helpful to know just how much TG is hydrolyzed to FAs by chewing food, which presumably mixes saliva and the lingual lipase it contains with TGs to incite the chemical reaction. In a recent study, people chewed high-fat foods (e.g., almonds), and the amount of FFAs liberated was measured. The results from the study allowed the investigators to conclude that chewing released sufficient FFAs to stimulate the receptors on the basis of their known receptive ranges (11). Recently, the lingual lipases most active in humans were identified, which will allow more direct study of the rates of hydrolysis (12).

FAs as pure taste stimuli (e.g., as solutions placed on the tongue) are unpleasant. Perhaps they are meant to warn against the ingestion of oxidized FAs and rancid foods (13, 14). For instance, when airborne FAs are held in the mouth, subjects describe them as “rubbery” or like plastic (15). Even from a distance, people may be able to smell taste stimuli and make judgments about their fat content (16). Thus, FAs have distinct smells as well as distinct and unpleasant tastes.

FAs are associated with rancid food odors, and people working in the food industry strive to reduce the amount of FAs in processed foods because they are off-putting. It is unclear why FAs are unpleasant in these settings, yet are pleasant when released during chewing. It may be that the concentrations of FAs released during chewing are too low to be detected retronasally (17)—that is, the odor of FAs is unpleasant but as taste stimuli in the context of eating they are pleasant. This is one of the gaps in our understanding about fat taste: why, if FAs taste and smell bad, are high-fat foods so popular?

### FA chemical transduction cascade

FAs are ligands for receptors found in the specialized taste cells. Each type of papilla—fungiform, foliate, and circumvallate—responds more or less the same to these ligands, and so there is no regional sensitivity to FAs on the tongue (18). Several lines of evidence suggest that FAs bind to at least 2 types of proteins on the cell membranes of taste cells. One type of protein is a member of the G protein–coupled receptor (GPR)<sup>4</sup> family (GPR120) and the other type is a molecule called CD36. Stimulation of these proteins generates a signal that travels through a common second-

messenger cascade similar to the one generated by bitter and sweet receptors, which couple through heterotrimeric G proteins to initiate intracellular signaling cascades involving effector enzymes, second messengers, and ion channel targets (see **Figure 2**). The steps in the pathway are thought to be 1) activation of type 3 inositol triphosphate 3 (IP3) receptors and 2) release of Ca<sup>2+</sup> from internal stores followed by 3) activation of the calcium-activated cation channel transient receptor potential cation channel subfamily M member 5 (TRPM5). TRPM5 is a key molecule in taste transduction, at least in mice, because taste cells without it fail to depolarize (19). Several other proteins that are now thought to be involved in calcium signaling also contribute to FA taste perception, such as stromal interaction molecule 1 (STIM1) (20). A recent review summarizes these studies (7).

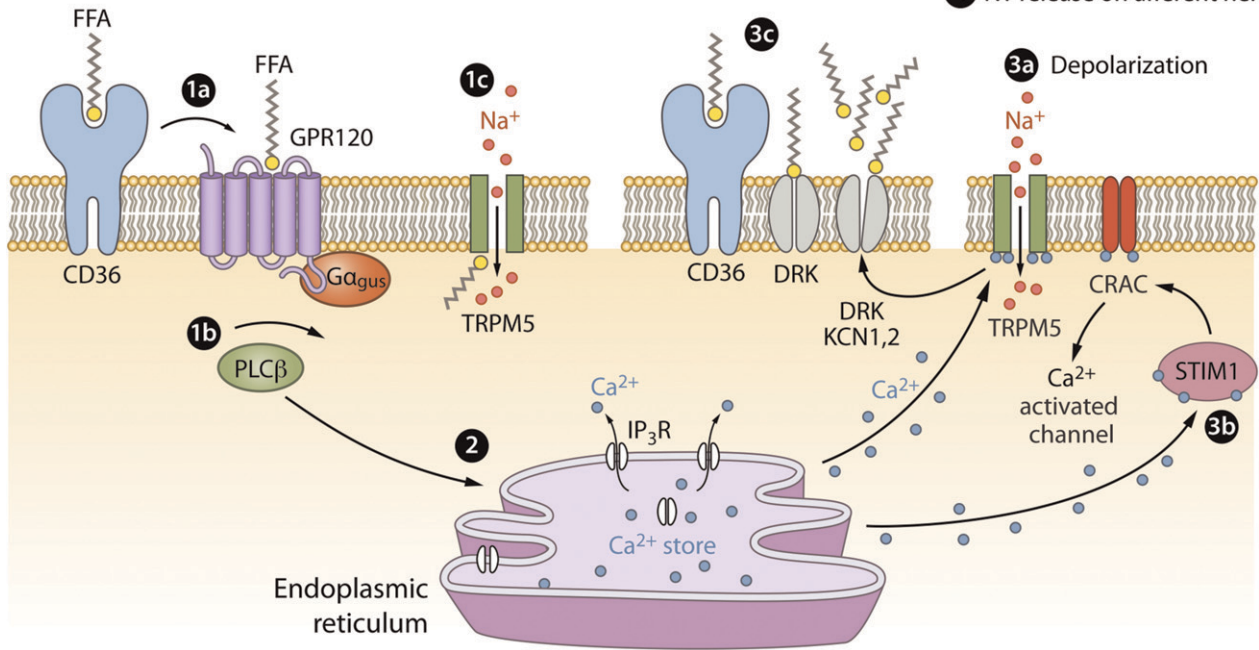
CD36 is a membrane-bound protein related to fat taste. It is found on the apical surface of taste cells in humans, a location consistent with a role in taste transduction (21). Several other lines of evidence support its role in taste. It colocalizes in taste papillae with known signaling molecules. In CD36-knockout mice, the normal increase in intracellular calcium of taste receptor cells in response to FFAs is blocked, and the activation of brain areas associated with FA stimulation is eliminated. Furthermore, CD36-knockout mice are indifferent to the same fat solutions that mice with an intact CD36 gene prefer.

Most information on fat taste surrounds CD36 because this protein is well studied in other cell types such as those involved in intestinal lipid transport. However, CD36 is a complex molecule that has many alternative forms—in humans, it has many single nucleotide polymorphisms (SNPs), as well as 23 known splice variants (22), 17 of which are protein-coding. However, it is still unclear which variants are expressed for the purpose of fat perception or whether humans express different variants of CD36 depending on other factors or gene interactions upstream. It is also unclear whether some variants are expressed in human taste tissues and other forms are expressed in other tissues. One possibility is that there may be one form of CD36 specific to taste cells, but this hypothesis awaits empirical study.

GPR120 is the other protein that is consistently involved with FA taste signaling. When introduced into a cell-based assay, GPR120 causes the cell to respond to FAs by increasing intracellular calcium, similar to the response seen by other GPRs specific to classic taste stimuli. Much of the evidence on FA transduction in taste cells comes from studies of mice. However, recent evidence supports a similar role for these molecules for human FA taste. Both GPR120 and CD36 are found in human taste receptor cells, and they appear to be found in the same cells (23). The reduction in these receptors in taste cells reduces changes in intracellular calcium, commonly used to measure the vigor of receptor signaling.

However, in human cells, CD36 has higher affinity for its preferred ligand than does GPR120. This observation raises several interesting questions. CD36 may be a more general lipid sensor that can respond to many different types of FAs, even at low concentrations, whereas GPR120 may respond only to specific types of FAs (e.g., grifolic acid, found in a certain type of mushroom) (23) and only at higher concentrations. Another

<sup>4</sup> Abbreviations used: CRAC, calcium release-activation channel; DRK, delayed rectifying K<sup>+</sup> channel; GPR, G protein–coupled receptor; IP3, inositol triphosphate 3; SNP, single nucleotide polymorphism; STIM1, stromal interaction molecule; TRPM5, transient receptor potential cation channel subfamily M, member 5.



**FIGURE 2** Proposed signaling pathway for fat taste. (1a) CD36 may act as a binding protein for FFAs, such as linoleic acid. It is unclear whether and how CD36, when bound to an FFA, interacts with GPR120 and other membrane proteins. However, evidence in mice indicates that GPR120 and CD36 have different roles in signaling, with CD36 being more reliant on FFAs and GPR120 being activated by a non-FFA mechanism. The presence of CD36 and GPR120 also varies on the basis of BMI, dietary intake, and fasting state. (1b) The binding of FFAs to GPR120 leads to increased signaling in  $G\alpha_{gus}$  and PLC- $\beta$ . FFAs and CD36 may interact directly with PLC- $\beta$ . (1c) FFAs (e.g., arachidonic acid) can intracellularly activate TRPM5 channels. Intracellular  $Ca^{2+}$  can also directly interact with TRPM5 channels. (2)  $Na^+$  passes through the channel into the intracellular membrane. The result of these various signaling mechanisms is an increase in intracellular  $Ca^{2+}$  (released from IP<sub>3</sub> channels on the endoplasmic reticulum). (3a) The  $Ca^{2+}$  release ultimately leads to membrane depolarization, with positive feedback. With the increase in intracellular  $Ca^{2+}$ , TRPM5 channels are activated. (3b) STIM1, which detects lowered  $Ca^{2+}$  concentrations in the endoplasmic reticulum, may aid in the activation of store-operated  $Ca^{2+}$  channels such as CRACs. This, in conjunction with other channels, such as TRPM5, directly interacting with  $Ca^{2+}$  allows for continued membrane depolarization. (3c) The membrane potential also interacts with and opens DRK channels, such as KCN5, whereas extracellular FFAs are channel blockers. (4) Depolarization is therefore prolonged with the presence of more FFAs, with CD36 possibly aiding in the interaction between DRK channels and FFAs. The depolarization ultimately causes neurotransmitter release. CRAC, calcium release-activation channel; DRK, delayed rectifying  $K^+$  channel, shaker-related subfamily, member 5; GPR120, G protein-coupled receptor 120; IP<sub>3</sub>, inositol triphosphate 3; IP<sub>3</sub>R, inositol triphosphate 3 receptor; KCN5, potassium voltage-gated channel, shaker-related subfamily, member 5; NT, neurotransmitter; PLC $\beta$ , phospholipase C  $\beta$ ; STIM1, stromal interaction molecule; TRPM5, transient receptor potential cation channel subfamily M, member 5.

candidate fat receptor was GPR40, but recent studies failed to identify it in human taste cells (24). It may be that unidentified families of FA receptors play a role in fat taste.

Mature taste cells may use dozens or maybe hundreds of proteins to relay FA information to downstream sensory neurons. Currently, investigators are focusing on identifying these unknown molecules. One way to achieve “genomic saturation,” meaning the identification of all relevant genes and their protein products that are crucial in this biology, is to sequence all mRNA that arises from a single taste cell, called single-cell transcriptomics. Comparing mRNA from single taste cells that respond to FFAs with RNA from taste cells that are not responsive generates a full or nearly full list of components that may be involved in fat taste. This method offers a way to identify the components of a cell type.

One hypothesis that has not received empirical testing but might be worth exploring is the idea that other taste receptors exist on taste cells that sense TGs themselves, rather

than the hydrolyzed FFAs. This idea is appealing because TGs in foods are liked but FFAs are not. It could be that FFAs and their taste receptors are there to warn about spoiled foods, whereas these hypothetical TG receptors might convey the good taste of fat. Saliva may not only produce FFAs with lipases but could contain substances that might package TGs into lipoproteins to be sensed by receptors on the tongue similar to those that respond to lipoproteins in the gut and liver. The study of saliva focuses on its catabolic properties; however, saliva may also help form complex lipid-protein mixtures that are sensed directly by cells on the tongue.

#### Cell types in fat taste

There are multiple cell types in taste buds. Type I cells are glia-like and are thought to have a role as supporting cells. Type II cells have bitter and sweet receptors but do not signal directly to the sensory nerve with a direct release of



neurotransmitter. Type III cells are mainly responsible for responding to sour and salty tastes and for the release of neurotransmitters that convey information forward through the sensory nerves to the brain. It is not clear which cell types respond to FAs on the basis of direct evidence, but from the importance of the transduction components such as TRPM5 (see Figure 2), which are components of type II cells, it would appear that this cell type is most likely involved.

Identifying cell types in human taste tissue that respond to FAs is difficult. Human taste cells in culture lose some of their characteristic morphology when they are no longer in a tight taste bud formation (25, 26). Studies that use small, interfering RNA or drugs to examine the pharmacology of FA signaling apply these compounds to the whole culture, so it is not possible to distinguish the influential cell types. There is one human taste cell line that can be grown in culture so that at least one cell type can be studied in isolation, and this cell line responds to both FAs and bitter compounds (27). However, we also know that in the fruit fly, FAs and sweet signals arise from the same cell type (28). Perhaps some type II cells coexpress FA and bitter receptors and others express FA and sweet receptors.

### FAs in other parts of the body

Another method to look for the components of fat taste is to extrapolate from cell types that respond to FAs in other parts of the body. This concept is not unique to FA receptors. Bitter and sweet taste receptors were identified by their role in taste perception in the mouth but function in other parts of the body as well (29–35). The reverse strategy may work for fat taste: FA signaling. FA detection in other tissues and organs such as the pancreas and liver is better understood than is fat signaling in taste cells and this knowledge can be a useful starting point to study taste.

### Human psychophysical studies on FFAs

Before the sensory properties of fat taste can be studied, they must be measured. The field of science devoted to these measurements is called psychophysics. Scientists trained in this field try to understand relations between physical stimuli (e.g., a tastant or odorant) and the psychological responses they elicit (e.g., taste or odor). Thus, an individual's ability to taste or smell can be determined by using psychophysical testing. For example, a common psychophysical measurement is detection threshold, which is the lowest concentration at which a compound can be detected—subjects often perceive this as only a hint of “something,” just enough to discriminate the stimulus from a blank but not necessarily enough to recognize its type or quality. In contrast, the recognition threshold is the lowest concentration at which a stimulus can be named for its quality (e.g., bitter). Detection thresholds may make more sense as a testing method than recognition thresholds for fats because there is no common word that people use to describe fat taste. To measure the intensity of stimuli, investigators offer them at readily detectible concentrations. Investigators may

ask subjects to label the type of sensations they perceive (e.g., sweet, bitter) or to rate the hedonics (e.g., the degree of pleasantness or appeal of the stimuli).

Most studies of FA perception in humans are conducted with precautions to guard against the subjects using sensory qualities other than pure taste. For instance, subjects might be tested with nose clips to reduce the odors arising from the fats, and they might be tested with red ambient illumination to mask the appearance of the stimuli, so they cannot tell the difference between high-fat and low-fat stimuli. Finally, investigators mask the potential sting or burn of FAs by desensitizing the tongue in advance using compounds such as capsaicin. This step helps distinguish taste from trigeminal sensory input.

Measuring the human sensory response to FFAs is not easy for technical reasons. There are dozens of forms of FFAs, which differ in chain length and degree of saturation. It is difficult to standardize stimuli from among the many types of FAs and the many methods of preparation. Investigators have typically focused on FAs found in high concentrations in common foods, but there is much to learn from conducting a broader survey of less-common FAs. SCFAs may be quite different from long-chain or very-long-chain FAs and the degree of saturation may be important, too. FFAs are typically emulsified in water, and small differences in the emulsifying agents, such as the variations that can arise from natural gums or from differences in manufacturing processes, even from the same supplier, may affect results (36). Accurate and consistent reporting about the sensory perception of FAs is also difficult because there is no simple word to describe their quality. In addition, experience and learning affect sensory testing, and subjects tested over time often improve their performance, sometimes markedly (37).

*Differences in perception of fats.* The phrase “a matter of taste” indicates that people differ in their patterns of likes and dislikes, and nowhere is this truer than in the realm of taste itself (38–40). One of the most marked human differences that arises from genetic variation is the ability to taste certain types of bitter compounds (41). Even the perception of sweet taste, which is one of the universal likes in human society, indeed in many mammals, is not immune from genetic variation. Genotype in the sweet receptor explains why some people prefer heavily sweetened foods, whereas others do not (42–44). There is diversity among humans in the perception of FAs (36, 45), and it would be logical to speculate that such differences arise from genetic differences in the receptors, as they do for bitter and sweet taste perception.

The results of 2 studies indicated that human differences in fat taste perception may relate to genetic variation in the *CD36* gene. As mentioned above, *CD36* has many forms due to alternative splicing and SNPs. One SNP in *CD36* is associated with the perception of fat (46). In a study, subjects were given samples of Italian salad dressing with varying fat content and asked to rate them for creaminess, fat, and

other variables, and their DNA was sequenced for CD36. The A/A genotype at the rs1761667 SNP was associated with all dressings tasting creamier and a higher liking for added fats and oils compared with the G/A genotype. This same SNP may also be associated with the expression of CD36, with the A/A allele being associated with lower CD36 expression and the participants with the G/G allele tasting more oleic acid and having lower oral detection thresholds for oleic acid and triolein (47). Future genetic studies could both help us learn why people differ in the liking for fats and oils and point us to essential yet undiscovered proteins in this transduction pathway.

The heritability of the perception of FAs is unclear. In the genetic studies reviewed above, the stimuli were TGs (salad oil) or an FA (oleic acid), and the presence of the genotype-phenotype relation implies that, for both stimuli, fat liking is heritable. This observation is concordant with the observation that dietary fat intake is heritable (48), but other influences in addition to liking and taste may be important determinants of how much someone eats. We do know that there are large differences between individuals in their taste thresholds (49), but estimates of heritability are needed in genetically informative populations such as twins (50). Thus, it would be possible to conduct genomewide association studies, which have identified genetic variants that influence other types of taste perception (51). Taste strips could be used for rapid testing of FA perception, i.e., with FAs embedded in a dissolvable matrix (52) rather than the use of emulsified FAs that are not easy to use in large-scale testing. Thus far, genomewide association studies have reported loci for dietary fat intake (53) but have not examined fat perception.

**Habitual diet, body weight, and fat taste.** In addition to genotype, other factors may affect individual differences in FA perception, with the 2 most salient being habitual diet and BMI. For instance, it could be that people who habitually consume fat are accustomed to its taste and are less sensitive to low concentrations of FAs. To test this idea directly, investigators measured FA thresholds in the same people who were fed both high-fat and low-fat diets. Consuming a low-fat diet for a 2-wk period increased individual sensitivity to fat, whereas consuming a high-fat diet decreased sensitivity—but only in the lean people, presumably because the overweight and obese subjects were already habituated to a high-fat diet (54). Likewise, those individuals whose diets were higher in fat and who were heavier for their height than those who ate less fat were less sensitive to low concentrations of FAs (55).

This insensitivity to FAs also extends beyond the mouth to the gut. Obese men were less sensitive to oral FAs and to infusions of FAs into the gut than were lean men (56). In mice, CD36 expression is reduced in obese compared with lean mice (23), but when CD36 is experimentally manipulated, lean and obese mice showed equal reductions in mRNA involved in the decreased ability to sense fat (57). Studies of rodents also showed that experience is a key

determinant of fat intake, and even short periods of access to high-fat foods increase later intake (58). Likewise, rodents fed a diet high in fat drives fat preference even higher (59).

### Fat liking and digestion

The fat sensors on the tongue do more than generate taste perception; they are also able to influence digestion even while fats are still in the mouth. Humans who swallowed tasteless capsules of safflower oil and then tasted but did not swallow a high-fat food had higher blood lipid profiles than did subjects who took the capsules but did not taste the high-fat food (14). This result suggests that there is a cephalic phase of digestion, in which the brain sends preparatory signals to the digestive organs in response to sensory cues that are especially potent for fat. Fats are calorically dense and not water soluble, so the body may need extra time to prepare for incoming TGs, for instance by helping the body titer the amount of lipases to secrete in the gastrointestinal tract.

The fat sensors on the tongue are also present in the gut and may affect an animal's avidity for dietary fat. One study in rodents found that a flavor paired with an infusion of fat directly into the stomach, bypassing the mouth, is preferred over flavors not paired with fat infusions, and that this preference is markedly attenuated in animals that lack a fat receptor gene (60). These results suggest that stimulation of this fat receptor (GPR120; discussed below) may drive fat intake and liking, but the effects may derive from the absorption of fat and its calories rather than from the stimulation of the oral receptors and the pleasure that sensation may bring.

### Fat substitutes

Public policy makers and food makers want to reduce fat in food. Noncaloric molecules that mimic the taste of fat would be one method to reduce calories but not fat flavors. Artificial sweeteners—high-potency molecules that provide a strong sweet taste with fewer calories than sugar—provide many examples of the popularity of such substitutes. Whether a similar high-potency fat substitute with the appropriate textural qualities could be developed that becomes as popular as sweeteners such as sucralose is unclear. One way to pursue this idea is to screen small molecule libraries for agonists of GPRs such as GPR120. However, in initial attempts, agonists that alter the signaling cascade through this receptor did not engender a preference in the same way that lipids do (24). Attempts to create products that have a fat texture but are not absorbed, such as olestra, have met with only limited success, in part because of the unpleasant digestive side effects. The failed attempts to find a low-calorie but high-pleasure fat substitute likely reflect our imperfect understanding of the fat taste system.

### Conclusions

The study of fat as a taste quality has lagged behind the other more obvious tastes such as sweet or bitter. It is currently unclear whether FAs are the only ligands that stimulate the sense of taste or whether other unknown receptors exist,

for instance, for TGs. One puzzle is that FAs taste and smell bad but TGs are well liked. Fat taste may depend on the brain's integration of multiple inputs, such as texture and odor, more so than do other taste qualities, and thus may be less amenable to the study of fat molecules in isolation. Regardless of the difficulties, it is important to understand why the taste of fat, defined narrowly or broadly, is appealing. High-fat diets contribute to many of the chronic health problems in developed and developing countries, so solving how they are perceived and why they are liked may suggest rational strategies for dietary change. Inborn differences in genotype explain at least some differences between individuals in the perception of FFAs.

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