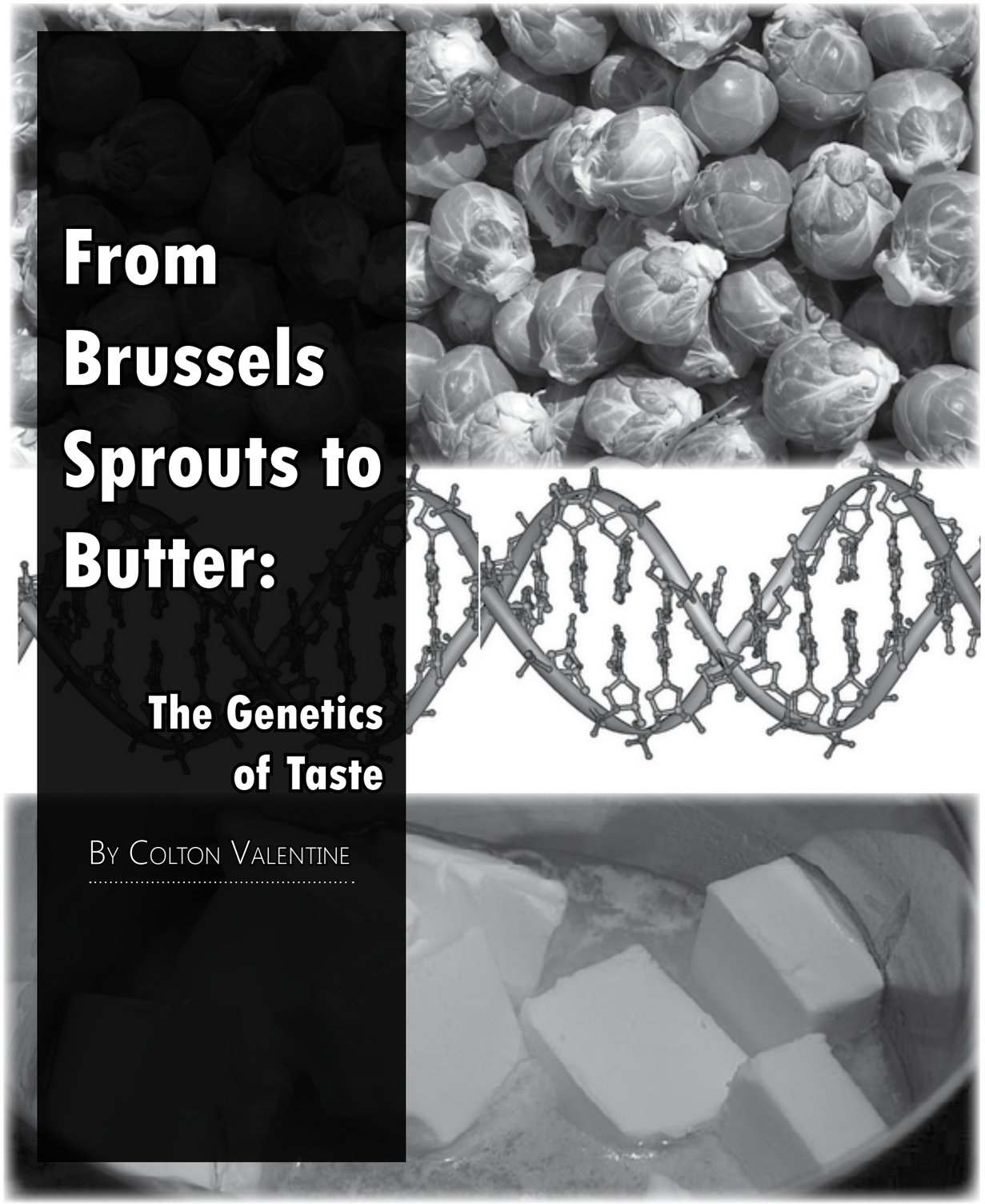

From Brussels Sprouts to Butter:

The Genetics of Taste

By Colton Valentine

She hates broccoli, he can't stand the sight of carrots, and your dad's the only one who eats radishes. It takes little scientific inquiry to identify the variability of food preferences, but what exactly makes someone have a sweet tooth? Can taste proclivities be explained solely through post-natal conditioning or is there a genetic component involved as well? Unfortunately, determining exactly why you love tartar sauce turns out to be quite a tricky process. Yet the implications for understanding these mechanisms are profound and far-reaching. After all, people eat what tastes good, and those who find that alluring flavor in spinach rather than ice cream will likely have healthier diets.

Modern taste science began, as so much science tends to do, by accident. In 1931, Arthor Fox, a DuPont chemist, accidentally released a cloud of phenylthiocarbamide ; while Fox tasted nothing, his colleague complained about the bitter taste emanating throughout the room [1]. Fox immediately recognized the importance of this differential reaction, and set to work investigating its source. Since then, no taste response has been studied more than that to PTC, but the full implications of Fox's observation are still not entirely clear. What we do know is that PTC sensitivity is largely controlled by the gene TAS2R38 and that this single bitterness response affects a wide range of taste preferences [1]. In fact, TAS2R38 has been implicated in everything from vegetable consumption to alcohol dependency [1-5]. Throw the complex idea of a "supertaster," or one who tastes certain flavors with particularly intensity, into the mix, and you can begin to see the exciting culinary and clinical applications TAS2R38 may have. But let's not get ahead of ourselves.

Introduction to TAS2R Genes

As one might expect, taste response is not mediated by a single gene, but rather by a large network of interacting mechanisms. One of the best-characterized subsets of taste genes, the TAS2R family controls the human response to bitterness. Within this group of 25 genes, perhaps the most intriguing is TAS2R38, for it controls the response that Fox discovered to PTC (and its safer equivalent PROP.) At first it was believed that this gene followed a straightforward Mendelian recessive-dominant inheritance structure. Three polymorphisms form two common versions of the gene: PAV and AVI. PAVs could taste PTC, while AVIs could not [3]. What's particularly intriguing about this gene is that these two alleles indirectly affect other taste functions, for bitterness interacts with proclivities to sweetness, saltiness, and more.

The implications for understanding the mechanisms of taste are profound and far reaching.

Yet as more research was performed, it became clear that there were actually three distinct phenotypes for the TAS2R gene. Tasters, it turned out, could be divided into two subgroups, where one had an even stronger reaction to PTC [1]. How could this be explained on the genotypic level? The key was in the difference between PAV heterozygotes and homozygotes. Anyone possessing a PAV allele was a general taster, but those with two copies, or homozygotes, had a higher sensitivity to PTC than those with a copy of each allele or heterozygotes [1]. Much of the research done in recent years has focused on these homozygotes, but occasionally all "tasters" are lumped together. These are distinctions to keep in mind when analyzing data on TAS2R38.

Supertasters

Chances are you have seen at least an article or two that involves the concept of a supertaster. Cake is more delicious for them! They make the best chefs! Test yourself easily at home! Unfortunately, the data behind these results are far less simple that the headlines purport them to be, for the word "supertaster" includes several ambiguous definitions that are often used interchangeably. The term originally emerged in 1991 in an article by Linda Bartoshuk, but it did not directly relate to PTC tolerance. Rather, she used the phrase to describe a high sensitivity to creatinine and quinine [6]. It didn't take long, however, for the phrase to take off and be applied to a variety of scientific and pseudo-scientific conditions. Often the word is used to denote PAV homozygotes who "supertaste" PTC and as a result many bitter foods; most studies investigating TAS2R38 use this terminology. In popular culture, "supertaster" is often used to describe a more general enhanced-taste phenomenon (cake being more delicious). A link exists between the two, for PAV homozygotes are more likely to have this general tasting phenotype, but many other factors influence it as well [6].

Who exactly are these generic "supertasters" then? The primary piece of evidence toward their existence is that the anterior or front regions of supertaster tongues contain more taste papillae, perhaps leading to higher flavor sensitivity [6]. However, PAV allele holders also show an increase in these papillae, though not to the same extent, making the delineation between these two groups of supertasters a tricky business [1]. For the purposes of the rest of this article, the term "PAV supertasters" will be used to denote TAS2R38 PAV homozygotes, as that is the area where specific research has been conducted. It pays to be wary of any information discussing the general phenomenon of a supertaster, as far more work needs to be done to specifically understand what the concept even means. This is a case where a scientific claim has been largely blown out of proportion in pop culture. But enough on semantics; what's far more interesting is how PAV tasters are attracted to different foods than AVI nontasters.

Food Proclivities

Since TAS2R38 controls sensitivity to bitterness, much of the food proclivity research has been done on food groups

related to this sense, especially with respect to vegetables. Several studies have shown a correlation between PROP sensitivity and perceived bitterness in vegetables, yet the exact methods and conclusions vary [1, 2]. One group demonstrated several years ago that PROP tasters and supertasters found a variety of vegetables more bitter and less sweet in a lab setting. Even more importantly, when questioned about their dietary practices, those with higher PROP sensitivities reported eating fewer vegetables [2]. It seemed that the sensitivity to bitterness was turning people off from the leafy greens, making them less likely to consume the recommended three servings a day.

Another study took this investigation a step farther by tying vegetable intake directly to the TAS2R38 genotype. They found that PAV allele carriers perceived more bitterness in vegetables and consumed relatively fewer servings. Intriguingly, these trends were associated with all vegetables, not simply those considered bitter [1]. In this analysis, both PAV homozygotes and heterozygotes were treated as one group. Together these studies raised concerns about PAV tasters being less inclined than nontasters to eat vegetables, which raises a potential health concern.

Yet vegetable intake is not the only shifting food response PAV allele carriers have. More recently, data have circulated regarding how PROP supertasters may have altered sensitivities to salt and sugar [7, 8]. One group found those with high PROP responses are more sensitive to small increases in salt concentration of chicken broth. Yet unlike the vegetable bitterness response, this heightened perception led PROP supertasters to both prefer saltier foods more in the lab setting and consume more salt on a daily basis [8]. Although the link is still not entirely clear, one explanation is that sensing more bitterness causes PROP supertasters to desire more salt in their foods to cancel out the unpleasant acrid flavors [8]. Naturally, this affinity raises concerns for PROP supertaster's ability to regulate salt intake, a large dieting issue for many Americans.

While salt and vegetable proclivities may lead to less healthy diets for PAV allele holders, an item on the opposite end of the spectrum is sugar. One group found that PROP tasters preferred lower levels of fat and sugar in milk mixtures when compared to non-tasters [7]. Another study showed that PROP tasters consume lower levels of sweet foods [9]. Although the explanation behind this association is unclear, but it is speculated that less sugar is required to satiate an urge because a sensitivity to bitterness leads to a similar one for sugar [7, 9]. It is important to note, however, that these studies were conducted based on phenotypic PROP sensitivity and not TAS2R38 genotypes. While the two are highly linked, it's important to be wary of the distinction.

Evolutionary Explanation

As with any gene, one interesting aspect of the TAS2R family to analyze is its evolutionary development. Why would bitterness tasting be selected for or against? One study looked at TAS2R16, a gene that controls sensitivity to several different bitter compounds. Two alleles exist for this gene: N172 or higher sensitivity and K172 of lower sensitivity [10]. After examining a variety of human genomes, one group was able to determine that the N172 allele emerged and was positively selected for 78,700-791,000 years ago, before homo sapien expansion out of Africa [10]. The theory they presented behind these data was that N172 caused higher sensitivity to several cyanogenic or toxic glycosides. TAS2R16 "tasters" would be less likely to eat these toxins in plants, for the bitterness would be stronger and thus less appealing [10]. A similar scenario could be envisioned for TAS2R38 selection and possibly the entire TAS2R family.

Another intriguing study on chimpanzee TAS2R genes showed a correlation between certain alleles and vegetation environments [11]. Different ethnogeographic populations had different genotypic patterns, indicating that environment pressure through vegetation is linked to selection of these bitter-

Figure 1: Different genetic profiles, like those including PAV alleles, may make achieving this nutritional balance more difficult for some. ***Photo by Chooseemyplate.gov.***

ness genes [11]. A question that arises when following the plant toxicity line of thinking for positive selection is: why are nontaster alleles are still widespread throughout the population. Wouldn't it make sense for all individuals to be responsive to potential toxins? One theory is that a lower sensitivity to bitterness may allow for a more diverse food intake, so natural selection might favor those with nontaster alleles because they have access to more food [10]. Perhaps the reason both alleles are still quite common is that a balance between these two selective pressures exists.

The Alcohol Effect

An often-surprising component of TAS2R38 research focuses on the link between PROP sensitivity and alcohol consumption. The principle behind this connection is that ethanol will taste bitterer to TAS2R PAV allele carriers, so they will be less like to drink [3]. Considering the prevalence of alcoholism, investigating taste as a factor in why certain people consume more alcohol is an exciting field. Unfortunately, although many studies have been conducted on this topic, the results aren't entirely clear. One key paper found that PAV tasters did not have increased alcohol sensitivity, but that they did drink less alcohol on average [3]. Naturally, these results were confusing, for they demonstrated the result of theory while negating its premises. Two other papers, however, corroborated the involvement of TAS2R38 in levels of alcohol consumption [4, 5].

TAS2R38 isn't the only bitter taste gene that has been implicated in alcohol consumption. The N172 allele for TAS2R16 that confers higher bitterness sensitivity has been linked to lower levels of drinking [5, 12]. Some evidence has been put forward to support a connection to dependency, but the association isn't entirely clear [12]. Yet the fundamental issue remains in both cases: why would taste genes affect consumption but not, well, taste? One common theory is that the PAV and N172 alleles cause interactions with other bitter ligands in alcohol that aren't ethanol [3-5]. While the precise links remain uncharacterized, there's no doubt that the potential uses of identifying a gene involved in alcohol consumption and particularly dependency are vast.

Clearly the impact TAS2R38 has on the mechanisms of taste extends far beyond the simple PTC reaction Arthur Fox observed 80 years ago. In being more sensitive to bitterness, PAV allele holders seem to have altered proclivities to a variety of foods and flavors, from vegetables to salt, sugar to alcohol. Aside from more confirmation studies to verify these findings and establish the links more clearly, the next step in TAS2R research is likely to look at the feasibility of specific applications. Is there a way that we can harness the positive aspects of PAV supertasting, such as reaction to sugar and alcohol, without the negative components like attraction to salt and dislike of vegetables? Can we genetically incentivize at-risk populations to eat healthier diets?

Right now, of course, the research has a long way to go to get to that point. Indeed, studies comparing BMI to PROP sensitivity have had mixed results [13, 14]. Yet even if we had the capacities to alter how someone experiences food, changing that would be an ethically dubious action. Currently, adjusting an individual's senses in modern science is a strictly positive endeavor, since it only involves improving hearing or vision. To change PROP sensitivity would be more akin to making someone see in a different, rather than better, way: perhaps in new colors or with a different conception of space.

While such explicit meddling may never be and perhaps should not be accomplished, TAS2R38 genotypes could be useful at the very least in understanding one's own food proclivities. A supertaster, for example, might be more aware of limiting salty foods and ensuring sufficient vegetable intake. This sort of application shifts research implementation from the lab to the individual in an intriguing and somewhat empowering way. Rather than depend on faraway technologies to improve our health, we can and must take personal steps toward making smarter nutritional and lifestyle choices. In a way, this is where the system of personalized genetics is headed, toward self-knowledge and individual choices rather than external, miracle aid. Not so far from now, research may fully elucidate the complex taste pathways, but it will still be our job and our privilege to make decisions enabled by this knowledge. For better or worse, the taster will remain the agent of his own fate.

Figure 2: PAV allele holders may consume less alcohol and have a lower chance of alcohol dependency. ***Photo credit to Wikimedia Commons.***

Colton Valentine is a senior in Winthrop House majoring in MCB

1. **Duffy, V.B., et al., Vegetable Intake in College-Aged Adults Is Explained by Oral Sensory Phenotypes and TAS2R38 Genotype. Chemosens Percept, 2010. 3(3-4): p. 137-148.**
2. **Dinehart, M.E., et al., Bitter taste markers explain variability in vegetable sweetness, bitterness, and intake. Physiol Behav, 2006. 87(2): p. 304-13.**
3. **Duffy, V.B., et al., Bitter receptor gene (TAS2R38), 6-n-propylthiouracil (PROP) bitterness and alcohol intake. Alcohol Clin Exp Res, 2004. 28(11): p. 1629-37.**
4. **Hayes, J.E., et al., 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): p. 311-9.**
5. **Wang, J.C., et al., Functional variants in TAS2R38 and TAS2R16 influence alcohol consumption in high-risk families of African-American origin. Alcohol Clin Exp Res, 2007. 31(2): p. 209-15.**
6. **Hayes, J.E. and R.S. Keast, Two decades of supertasting: where do we stand? Physiol Behav, 2011. 104(5): p. 1072-4.**
7. **Hayes, J.E. and V.B. Duffy, Oral sensory phenotype identifies level of sugar and fat required for maximal liking. Physiol Behav, 2008. 95(1-2): p. 77-87.**
8. **Hayes, J.E., B.S. Sullivan, and V.B. Duffy, Explaining variability in sodium intake through oral sensory phenotype, salt sensation and liking. Physiol Behav, 2010. 100(4): p. 369-80.**
9. **Duffy, V.B., et al., Genetic and environmental variation in taste: Associations with sweet intensity, preference and intake. Top Clin Nurt., 2003. 18: p. 209-220.**
10. **Soranzo, N., et al., Positive selection on a high-sensitivity allele of the human bitter-taste receptor TAS2R16. Curr Biol, 2005. 15(14): p. 1257-65.**
11. **Hayakawa, T., et al., Eco-Geographical Diversification of Bitter Taste Receptor Genes (TAS2Rs) among Subspecies of Chimpanzees (Pan troglodytes). PLoS One, 2012. 7(8): p. e43277.**
12. **Hinrichs, A.L., et al., Functional variant in a bitter-taste receptor (hTAS2R16) influences risk of alcohol dependence. Am J Hum Genet, 2006. 78(1): p. 103-11.**
13. **Duffy, V.B., et al., Genetic taste status associates with fat food acceptance and body mass index in adults. Chem Senses, 1999(24): p. 545-546.**
14. **Tepper, B.J. and N.V. Ullrich, 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): p. 305-12.**