# Variation in umami perception and in candidate genes for the umami receptor in mice and humans[1–4]

*Noriatsu Shigemura, Shinya Shirosaki, Tadahiro Ohkuri, Keisuke Sanematsu, AA Shahidul Islam, Yoko Ogiwara, Misako Kawai, Ryusuke Yoshida, and Yuzo Ninomiya*

**ABSTRACT**

The unique taste induced by monosodium glutamate is referred to as *umami* taste. The umami taste is also elicited by the purine nucleotides inosine 5′-monophosphate and guanosine 5′-monophosphate. There is evidence that a heterodimeric G protein–coupled receptor, which consists of the T1R1 (taste receptor type 1, member 1, *Tas1r1*) and the T1R3 (taste receptor type 1, member 3, *Tas1r3*) proteins, functions as an umami taste receptor for rodents and humans. Splice variants of metabotropic glutamate receptors, $mGluR_1$ (glutamate receptor, metabotropic 1, *Grm1*) and $mGluR_4$ (glutamate receptor, metabotropic 4, *Grm4*), also have been proposed as taste receptors for glutamate. The taste sensitivity to umami substances varies in inbred mouse strains and in individual humans. However, little is known about the relation of umami taste sensitivity to variations in candidate umami receptor genes in rodents or in humans. In this article, we summarize current knowledge of the diversity of umami perception in mice and humans. Furthermore, we combine previously published data and new information from the single nucleotide polymorphism databases regarding variation in the mouse and human candidate umami receptor genes: mouse *Tas1r1* (*TAS1R1* for human), mouse *Tas1r3* (*TAS1R3* for human), mouse *Grm1* (*GRM1* for human), and mouse *Grm4* (*GRM4* for human). Finally, we discuss prospective associations between variation of these genes and umami taste perception in both species. *Am J Clin Nutr* 2009;90(suppl):764S–9S.

## INTRODUCTION

The unique taste induced by monosodium glutamate (MSG) is referred to as the *umami* taste. It is also evoked by the purine nucleotides inosine-5′-monophosphate (IMP) and guanosine-5′-monophosphate (GMP). There is good evidence that a heterodimeric G protein–coupled receptor, which consists of the T1R1 (taste receptor type 1, member 1, *Tas1r1*) and T1R3 (taste receptor type 1, member 3, *Tas1r3*) proteins, functions as an umami taste receptor for rodents and humans. Splice variants of metabotropic glutamate receptors, $mGluR_1$ (glutamate receptor, metabotropic 1, *Grm1*) and $mGluR_4$ (glutamate receptor, metabotropic 4, *Grm4*), are also proposed as taste receptors for glutamate (6–8). A salient feature of umami taste induced by MSG in rodents and humans is its potentiation by purine nucleotides, such as IMP and GMP (9–11).

In mice and humans, there is substantial variation in umami taste sensitivity (12–17). However, little is known about the genetic basis of this variation in umami taste perception. Understanding the nature of the variation in umami taste perception, the genetic variation in its receptors, and how this variation influences diet selection may have important implications for human health.

There are several examples of sequence diversity in taste receptor genes that influences taste perception in rodents and humans. For example, sweetness preference in mice differs between inbred strains (18). The T1R2 (taste receptor type 1, member 2) and T1R3 heterodimer functions as a sweet receptor (1–5). Studies of DNA variants in genetic and cell-based assays have shown that an amino acid substitution of threonine for isoleucine at amino acid position 60 of T1R3 is the likely reason for the low saccharin preference in mice (19–26). In humans, the best-studied example of taste variation is the sensitivity to the bitter taste of propylthiouracil and phenylthiocarbamide. The taste thresholds for these 2 bitter compounds are distributed bimodally in humans and vary $\leq$1000-fold between tasters and nontasters (27, 28). Single nucleotide polymorphisms (SNPs) in a bitter taste receptor gene, *TAS2R38* (taste receptor type 2, member 38), were shown to be associated with taste sensitivity to phenylthiocarbamide and propylthiouracil in humans (29, 30). These examples raise the possibility that perceptual variation in umami taste could also be due to variation in umami taste receptor genes.

In this article, we summarize current knowledge of the diversities of umami perception and its receptor candidate genes in mice and humans and discuss the prospective associations.

[1] From the Section of Oral Neuroscience, Graduate School of Dental Science, Kyushu University, Fukuoka, Japan (NS, SS, TO, KS, AASI, YO, MK, RY, and YN); the Quality Assurance and External Scientific Affairs Department, Ajinomoto Co, Inc, Tokyo, Japan (YO); and the Novel Material Research Group, Institute of Life Sciences, Ajinomoto Co, Inc, Kawasaki, Japan (MK).

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[4] Address correspondence to N Shigemura, Section of Oral Neuroscience, Graduate School of Dental Science, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan. E-mail: shigemura@dent.kyushu-u.ac.jp.

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## STRAIN DIFFERENCES IN UMAMI TASTE RESPONSES IN MICE

A comparison of the electrophysiologic responses of the chorda tympani nerve (CT), which innervates cells of the fungiform and a portion of the folliate papillae on the anterior two-thirds of the tongue, in 3 inbred mouse strains showed differences in the synergistic effect of MSG and GMP. The order of magnitude of the CT response to MSG plus GMP divided by the sum of the response to each component tested separately was as follows: the response of C3H/HeSlc strain of mice was greater than the response of C57BL/6CrSlc strain of mice, which was greater than the response of the BALB/cCrSlc strain of mice (12).

In long-term, 2-bottle preference tests, mice of the C57BL/6ByJ (B6) strain consumed more of a solution of 300 to 1000 mmol MSG/L than did mice of the 129/J (129) strain (13, 14). To assess the role of afferent gustatory inputs in the strain differences between B6 and 129 mice, Inoue et al (15) measured responses of the CT and the glossopharyngeal nerve, which innervates cells of the vallate and foliate papillae on the posterior third of the tongue, to MSG, ammonium glutamate, IMP, and GMP. The CT responses to MSG and ammonium glutamate were similar in the B6 and the 129 mice. The CT responses to IMP and GMP were lower in the B6 mice than they were in the 129 mice. Responses to umami stimuli in the glossopharyngeal nerve did not differ between the B6 and the 129 strains.

Such strain differences in umami taste perception in mice offer an opportunity to examine whether such perceptual variations are linked to variations in umami taste genes.

## VARIATION OF UMAMI TASTE RECEPTORS IN MICE

In one study, homozygous mutant mice lacking either the *Tas1r1* or *Tas1r3* gene showed an overwhelming loss of umami taste, which included all responses to IMP and behavioral attraction to MSG and L-amino acids (3). In contrast, a second study from a different laboratory reported that a disruption of the *Tas1r3* gene diminishes, but does not abolish, behavioral and neural responses to umami taste stimuli (4). The explanation for these differences is not known. Nevertheless, both studies implicate these subunits in mediating umami taste perception. Hence, sequence variants of the *Tas1r1* and *Tas1r3* may affect umami taste responses. An analysis of the $F_2$ (second filial generation) hybrids between the B6 and 129 inbred mouse strains showed that the *Tas1r3* allelic variants do not affect behavioral or neural taste responses to umami stimuli (31). Thus, although the T1R3 receptor is involved in transduction of umami taste, the B6/129 sequence variants do not affect its sensitivity to umami compounds.

By using GenBank and the Single Nucleotide Polymorphism database (dbSNP), which are available through the National Center for Biotechnology Information (NCBI) website (http://www.ncbi.nlm.nih.gov/), we found 3 SNPs with an amino acid substitution in mouse *Tas1r1* (M347T, K443N, and K626E) between C57BL/6J and 129P3/J and no SNP with an amino acid change in both mouse *Grm1* and *Grm4* in C57BL/6J, 129S1/SvImJ, 129 × 1/SvJ, and C3H/HeJ (N Shigemura and Y Ninomiya, unpublished observation, 2008). The 3 amino acid changes in T1R1 also were reported by Li et al (32). It has been speculated that MSG and IMP each bind to the T1R1, because neither has any effect on the T1R2/T1R3 sweet taste receptor (1). These results suggest that the differences in umami sensitivity between inbred strains may be related to SNPs with these amino acid mutations in *Tas1r1* but not to amino acid mutations in *Tas1r3*, *Grm1*, and *Grm4*.

## INDIVIDUAL VARIATION IN UMAMI TASTE SENSITIVITY IN HUMANS

Lugaz et al (17) reported that some humans cannot taste MSG. In this study, the sample distribution of individual MSG detection thresholds showed a bimodal distribution curve, with taste thresholds of MSG differing ≈5-fold between tasters (mean: 0.08 mmol MSG/L; range: 0.03–0.18 mmol MSG/L) and hypotasters (mean: 0.39 mmol MSG/L; range: 0.14–1.07 mmol MSG/L). They also reported that subjects could be classified into taster [81% (47/58) of subjects], hypotaster [≥10% (6/58) of subjects], and nontaster [3.5% (2/58) of subjects] categories by using 4 tests: *1*) detection threshold, *2*) isointensity (reference = 29 mmol NaCl/L), *3*) time-intensity MSG > NaCl, and *4*) discrimination test (17).

## VARIATION OF UMAMI TASTE RECEPTORS IN HUMANS

SNPs with an amino acid substitution in human *TAS1R1*, *TAS1R3*, *GRM1*, and *GRM4* coding regions available from the study reported by Kim et al (33) and from the NCBI database are listed in **Table 1**. Kim et al conducted a comprehensive evaluation of SNPs and haplotypes in human *TAS1R1*, *TAS1R2*, and *TAS1R3*. Complete DNA sequences of *TAS1R1*- and *TAS1R3*-coding regions revealed 14 and 6 nonsynonymous SNPs in *TAS1R1* and *TAS1R3*, respectively. In the dbSNP (from the NCBI) analysis, we found 7 SNPs in *TAS1R1*, 5 SNPs in *TAS1R3*, 8 SNPs in *GRM1*, and one SNP in *GRM4* for a total of 21 variant amino acid sites (N Shigemura and Y Ninomiya, unpublished observation, 2008). Of these, V110A, E347K, T372A, and C603R in *TAS1R1* and R757C in *TAS1R3* were reported by Kim et al (33).

Examination of the distribution of polymorphisms across the various domains of the protein shows that 61.1% (22/36) of the variant amino acid positions reside in the predicted N-terminal extracellular ligand-binding domain, 22.2% (8/36) in the transmembrane domain, 13.9% (5/36) in the C-terminal intracellular domain, and 2.8% (1/36) in the cysteine-rich domain, which intervenes between the N-terminal ligand-binding and transmembrane regions. One SNP, which substitutes an A for the normal G at position 2318 in the *TAS1R1* cDNA sequence, introduces a premature stop codon (33).

Population diversities of umami receptor SNPs available from the study reported by Kim et al (33) and the International HapMap Project (http://www.hapmap.org/index.html.en) are also shown in Table 1. The majority of the SNPs in *TAS1R1*, *TAS1R3*, *GRM1*, and *GRM4* were observed in 1 or 2 populations. Only 2 SNPs (A372T in *TAS1R1* and P993S in *GRM1*) were widely distributed and observed in almost all populations.

Previous studies of T1R2/T1R3 sweet receptor chimeras and mutants showed that there are ≥3 potential binding sites in this heterodimeric receptor. Receptor activity toward the artificial sweeteners, aspartame and neotame, depends on residues in the N-terminal domain of human T1R2. In contrast, receptor

**TABLE 1**
Single nucleotide polymorphisms (SNPs) with an amino acid substitution in human *TAS1R1*, *TAS1R3*, *GRM1*, and *GRM41*[1]

| | | | | | | Population-specific allele frequency | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Reference 33 | | | | | | | | HapMap | | | AGI | | |
| Genes | Position amino acid | dbSNP rs no. | Nucleotide | Amino acid encoded | Domain | CAM | AME | NOR | JAP | RUS | HUN | CH | PAK | CEU | HCB | JPT | YRI | ASP | CEPH |
| *TAS1R1* | | | | | | | | | | | | | | | | | | | |
| NM_138697 | | | | | | | | | | | | | | | | | | | |
| Exon 1 | 4[2] | rs35375392 | A | Tyr | EC | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | | | G | Cys | | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| Exon 2 | 95[2] | | A | Asn | EC | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0.94 | — | — | — | — | — | — |
| | | | G | Ser | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.06 | — | — | — | — | — | — |
| | 110[2,3] | rs41278020 | T | Val | EC | 1 | 1 | 0.95 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | C | Ala | | 0 | 0 | 0.05 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| | 126[3] | | C | His | EC | 0.95 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | A | Asn | | 0.05 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| | 127[3] | | T | Ile | EC | 1 | 1 | 1 | 1 | 1 | 1 | 0.85 | 1 | — | — | — | — | — | — |
| | | | T | Thr | | 0 | 0 | 0 | 0 | 0 | 0 | 0.15 | 0 | — | — | — | — | — | — |
| Exon 3 | 181[3] | | C | Gln | EC | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | G | Glu | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| | 182[3] | | A | Tyr | EC | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0.94 | — | — | — | — | — | — |
| | | | G | Cys | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.06 | — | — | — | — | — | — |
| | 191[3] | | A | Asn | EC | 1 | 1 | 1 | 1 | 1 | 1 | 0.8 | 1 | — | — | — | — | — | — |
| | | | G | Ser | | 0 | 0 | 0 | 0 | 0 | 0 | 0.2 | 0 | — | — | — | — | — | — |
| | 237[3] | | A | Ile | EC | 1 | 1 | 1 | 1 | 1 | 1 | 0.85 | 1 | — | — | — | — | — | — |
| | | | C | Leu | | 0 | 0 | 0 | 0 | 0 | 0 | 0.15 | 0 | — | — | — | — | — | — |
| | 347[2–4] | rs10864628 | G | Glu | EC | 0.78 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0.71 | 0.93 | — |
| | | | A | Lys | | 0.23 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.29 | 0.07 | — |
| | 356[2] | rs41307749 | G | Cys | EC | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | | | C | Ser | | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | 372[2–4] | rs34160967 | G | Ala | EC | 0.9 | 1 | 0.75 | 0.65 | 0.95 | 0.65 | 0.6 | 0.94 | 0.88 | 0.66 | 0.64 | 0.97 | 0.93 | — |
| | | | A | Thr | | 0.1 | 0 | 0.25 | 0.35 | 0.05 | 0.35 | 0.4 | 0.06 | 0.12 | 0.34 | 0.36 | 0.03 | 0.07 | — |
| | 373[3] | | C | His | EC | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | A | Asn | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| Exon 4 | 483[3] | | T | Ile | EC | 0.95 | 1 | 1 | 1 | 1 | 1 | 0.85 | 1 | — | — | — | — | — | — |
| | | | C | Thr | | 0.05 | 0 | 0 | 0 | 0 | 0 | 0.15 | 0 | — | — | — | — | — | — |
| Exon 5 | 507[2,4] | rs35118458 | G | Arg | CD | — | — | — | — | — | — | — | — | 0.97 | 1 | 1 | 1 | 0.97 | — |
| | | | A | Gln | | — | — | — | — | — | — | — | — | 0.03 | 0 | 0 | 0 | 0.03 | — |
| Exon 6 | 603[2,3] | rs41278022 | T | Cys | TM | 0.88 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | C | Arg | | 0.12 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| | 773[3] | | G | Trp | TM | 0.94 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | A | Stop | | 0.06 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| *TAS1R3* | | | | | | | | | | | | | | | | | | | |
| NM_152228 | | | | | | | | | | | | | | | | | | | |
| Exon 1 | 5[3] | | G | Ala | EC | 1 | 1 | 0.9 | 1 | 1 | 0.95 | 1 | 1 | — | — | — | — | — | — |
| | | | A | Thr | | 0 | 0 | 0.1 | 0 | 0 | 0.05 | 0 | 0 | — | — | — | — | — | — |
| Exon 2 | 95[3] | | T | Leu | EC | 0.98 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | C | Pro | | 0.02 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| Exon 3 | 247[3] | | G | Arg | EC | 0.75 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | A | His | | 0.25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| | 367[3] | | G | Gly | EC | 0.95 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | T | Cys | | 0.05 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| Exon 6 | 735[3] | | G | Ala | TM | 0.75 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | — | — | — | — | — | — |
| | | | A | Thr | | 0.25 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | — | — | — | — | — |
| | 757[2–4] | rs307377 | T | Cys | TM | 1 | 1 | 1 | 1 | 1 | 0.95 | 1 | 0.94 | — | — | — | — | — | 0.92 |
| | | | C | Arg | | 0 | 0 | 0 | 0 | 0 | 0.05 | 0 | 0.06 | — | — | — | — | — | 0.08 |
| | 813[2] | rs34810828 | A | Lys | TM | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | | | G | Arg | | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | 816[2] | rs12030791 | G | Val | TM | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | | | C | Leu | | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | 823[2] | rs12030797 | T | Phe | IC | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | | | C | Leu | | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | 832[2] | rs35913253 | A | Arg | IC | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | | | G | Gly | | — | — | — | — | — | — | — | — | — | — | — | — | — | — |

*(Continued)*

**TABLE 1** (*Continued*)

| Genes | Position amino acid | dbSNP rs no. | Nucleotide | Amino acid encoded | Domain | Population-specific allele frequency | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Reference 33 | | | | | | | | HapMap | | | AGI | | |
| | | | | | | CAM | AME | NOR | JAP | RUS | HUN | CH | PAK | CEU | HCB | JPT | YRI | ASP | CEPH |
| *GRM1* | | | | | | | | | | | | | | | | | | | |
| NM_000838 | | | | | | | | | | | | | | | | | | | |
| Exon 1 | 34[2] | rs12190109 | A | Tyr | EC | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | | | C | Ser | | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| Exon 2 | 285[2,4] | rs7760248 | G | Arg | EC | — | — | — | — | — | — | — | — | 1 | 1 | 1 | 0.98 | — | — |
| | | | A | Lys | | — | — | — | — | — | — | — | — | 0 | 0 | 0 | 0.02 | — | — |
| Exon 7 | 593[2,4] | rs1047005 | T | Ser | EC | — | — | — | — | — | — | — | — | 1 | 1 | 0.99 | 1 | — | — |
| | | | C | Pro | | — | — | — | — | — | — | — | — | 0 | 0 | 0.01 | 0 | — | — |
| | 729[2] | rs41305288 | A | Thr | TM | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | | | C | Pro | | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | 741[2] | rs3025919 | T | Asp | TM | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | | | A | Glu | | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| | 884[2,4] | rs362936 | G | Gly | IC | — | — | — | — | — | — | — | — | 0.97 | 1 | 1 | 1 | — | — |
| | | | A | Glu | | — | — | — | — | — | — | — | — | 0.03 | 0 | 0 | 0 | — | — |
| Exon 8 | 929[2,4] | rs2941 | G | Val | IC | — | — | — | — | — | — | — | — | 0.93 | 0.99 | 1 | 1 | — | — |
| | | | A | Ile | | — | — | — | — | — | — | — | — | 0.07 | 0.01 | 0 | 0 | — | — |
| | 993[2,4] | rs6923492 | C | Pro | IC | — | — | — | — | — | — | — | — | 0.56 | 0.48 | 0.52 | 0.69 | — | — |
| | | | T | Ser | | — | — | — | — | — | — | — | — | 0.44 | 0.52 | 0.48 | 0.31 | — | — |
| *GRM4* | | | | | | | | | | | | | | | | | | | |
| NM_000841 | | | | | | | | | | | | | | | | | | | |
| Exon 1 | 169[2,4] | rs452752 | C | Leu | EC | — | — | — | — | — | — | — | — | 1 | 1 | 0.99 | 1 | — | — |
| | | | T | Phe | | — | — | — | — | — | — | — | — | 0 | 0 | 0.01 | 0 | — | — |

[1] dbSNP, Single Nucleotide Polymorphism database (http://www.ncbi.nlm.nih.gov/); EC, extracellular; TM, transmembrane; IC, intracellular; CAM, Cameroonian ($n$ = 20); AME, Amerindian ($n$ = 10); NOR, Northern European ($n$ = 10); JAP, Japanese ($n$ = 10); RUS, Russian ($n$ = 10); HUN, Hungarian ($n$ = 10); CH, Chinese ($n$ = 10); PAK, Pakistani ($n$ = 8); CEU, European [30 mother-father-child trios from the Centre d'Etude du Polymorphisme Human (CEPH) collection (Utah residents with ancestry from northern and Western Europe)]; HCB, Asian: 45 unrelated Han Chinese in Beijing, China; JPT, Asian: 44 unrelated Japanese in Tokyo; AGI, The Applera Genomics Initiative (http://www.applera.com/); YRI, sub-Saharan African: 30 Yoruba mother-father-child trios in Ibadan, Nigeria; ASP, African American: population samples from Coriell Cell Repositories Apparently Normal Collection; CEPH, genomic DNA samples were obtained for a panel of 92 unrelated individuals chosen from CEPH pedigrees [the genomic DNA comprised Utah (93%), French (4%), and Venezuelan (3%)].

[2] From dbSNP.

[3] From reference 33.

[4] From the International HapMap Project (http://www.hapmap.org/index.html.en).

activity toward the sweetener cyclamate and the sweet taste inhibitor lactisole depends on residues within the transmembrane domain of human T1R3. Furthermore, receptor activity toward the sweet protein brazzein depends on the cysteine-rich domain of human T1R3 (5, 34–36). Previous studies of T1R2/T1R3 sweet receptor suggest that there may be multibinding sites in T1R1/T1R3 heterodimer for umami substances and that all SNPs in extracellular, transmembrane, and cysteine-rich domains may affect umami taste sensitivity in humans. In particular, 2 SNPs (A372T in *TAS1R1* and P993S in *GRM1*) were widely distributed and observed in almost all populations with different minor allele frequencies (0–36% and 31–51%, respectively), which may relate not only to individual differences but also to population differences in umami sensitivities.

## CONCLUSIONS

Relations of umami taste phenotypes to variations in umami taste receptor genes remain unclear at this point, but the functional analysis with a heterologous expression system may account for such perceptual differences in umami sensitivity. Many protein (amino acid)–rich foods, including meat, milk, and seafood, taste delicious (umami) to humans and are attractive to rodents and other animals, which suggests that umami perception plays a key role in ingestion of amino acids (in particular L-glutamate), which act as biosynthetic precursors of various molecules, metabolic fuels, and neurotransmitters. Thus, elucidating the causes of the differences in umami taste perception in rodents and people as well as umami taste mechanisms and pathways has significant evolutionary implications for human health. (Other articles in this supplement to the Journal include references 37–65.)

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