Abnormal Taste Perception in Mice Lacking the Type 3 Inositol 1, 4, 5-Trisphosphate Receptor

Chihiro Hisatsune 1, 2, Keiko Yasumatsu 3, Hiromi Takahashi-Iwanaga 4, Naoko Ogawa 1, Yukiko Kuroda 1, Ryusuke Yoshida 3, Yuzo Ninomiya 3, and Katsuhiko Mikoshiba 1, 2, 5.

1 Laboratory for Developmental Neurobiology, RIKEN Brain Science Institute (BSI) 2-1 Hirosawa, Wako city, Saitama 351-0198, Japan.
2 Division of Molecular Neurobiology, Institute of Medical Science, University of Tokyo, 3-4-1, Shirokane-dai, Minato-ku, Tokyo 108-8639, Japan.
3 Section of Oral Neuroscience, Graduate School of Dental Science, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan.
4 Department of Anatomy, School of Medicine, Hokkaido University, Sapporo 060-8638, Japan.
5 Calcium Oscillation Project, ICORP, Japan Science and Technology Agency, 3 Nibancho, Chiyoda-ku, Tokyo 102-0084, Japan.

Corresponding author
Chihiro Hisatsune and Katsuhiko Mikoshiba
Laboratory for Developmental Neurobiology, RIKEN Brain Science Institute (BSI) 2-1 Hirosawa, Wako city, Saitama 351-0198, Japan.
E-mail: chihiro@brain.riken.go.jp
E-mail: mikosiba@brain.riken.go.jp
Tel: 81-03-5449-5316, Fax: 81-03-5449-5420

Running title: The role of IP3R3 in taste signaling.

Inositol 1, 4, 5-trisphosphate receptor (IP3R) is one of the important calcium channels expressed in the endoplasmic reticulum and has been shown to play crucial roles in various physiological phenomena. Type 3 IP3R is expressed in taste cells, but the physiological relevance of this receptor in taste perception in vivo is still unknown. Here, we show that mice lacking IP3R3 show abnormal behavioral and electrophysiological responses to sweet, umami, and bitter substances that trigger G-protein coupled receptor activation. In contrast, responses to salty and acid tastes are largely normal in the mutant mice. We conclude that IP3R3 is a principal mediator of sweet, bitter, and umami taste perception and would be a missing molecule linking phospholipase C beta 2 (PLCβ2) to TRPM5 activation.

Taste perception is a pivotal and primitive sensory system for survival in animals. By sensing taste, animals are provided with valuable information about foods (e.g., qualities and nature) and can choose the nutrient-rich foods necessary for living or avoid harmful and toxic substances. There are five taste categories (sweet, bitter, umami, sour, and salty), and recent studies have furthered our understanding of the molecular mechanisms of taste perception, especially for sweet, bitter, and umami tastes (1, 2).

For perception of sweet, bitter, and umami taste, phospholipase C beta 2 (PLCβ2) activation through G-protein coupled receptor (for sweet: T1R2+T1R3; for umami: T1R1+T1R3; for bitter: T2Rs) (1, 3-8) and the subsequent activation of PLCβ2 and transient-receptor potential receptor M5 (TRPM5) are necessary (8, 9), but the molecular mechanism by which PLCβ2 activation leads to TRPM5 activation is still unclear (2). Several reports have suggested the possible involvement of Ca2+, probably released from the intracellular stores, in the activation of TRPM5 in heterologously expressed cells (10-14) and in taste cells (15); however this remains controversial (9). Since PLCβ2 activation actually leads to
production of both IP$_3$ and diacylglycerol (DAG), it is an important issue to definitely determine which is a major player for gustatory systems. To clarify whether IP$_3$R is necessary for taste perception in vivo, we analyzed the taste signaling of IP$_3$R-deficient mice in this study (16). We found that mice lacking IP$_3$R3 showed altered taste recognition for sweet, bitter, and umami, whereas they were indistinguishable from wild-type (WT) mice in their recognition for salty and sour stimuli. However, they showed residual responses to high concentrations of sweets and bitter. Our data presented the direct validation that IP$_3$R3 is a key molecule in taste perception for sweet, bitter, and umami, but also suggested the existence of IP$_3$R3-independent taste signal transduction for recognition of high dose of these tastants.

**Experimental procedures**

**Mice**- IP$_3$R3 and IP$_3$R2 deficient mice were generated as described previously (16), and the mice intercrossed with C57BL/6 mice at least twelve times were used. WT C57BL/6 mice were littermates or purchased from SLC (Shizuoka, Japan). All experiments were performed in accordance with the Animal Experiment Committee of RIKEN Brain Science Institute.

**Detection of taste-related proteins in mouse taste buds**- Two mouse tongues were removed and a protease solution (140 mM NaCl, 5mM KCl, 1mM MgCl$_2$, 10 mM Hepes, 10 mM glucose, 10 mM sodium pyruvate, pH=7.4) containing 0.25 mg/ml of elastase and 2 mg/ml of collagenase type I was injected under the circumvallate papilla, and the epithelium was peeled away after 15 min. The peeled epithelium was then incubated in the enzyme solution (0.25 mg/ml elastase, 2.0 mg/ml collagenase, and 1.6 mg/ml dispase) for 5 min at room temperature and further incubated in Ca$^{2+}$ free tyrode’s solution. After 30 min, taste buds became to be loosely attached to the epithelium and we gently detached all taste buds using forceps in the buffer as possible as we could. The buffer containing all taste buds of two mice circumvallate papilla were centrifuged at 1000 g for 5 min at 4°C and the precipitated taste buds were lysed with 50 µl of sample buffer. Fifteen µl of the lysate per lane were used for western blotting analysis. Although we could not count the accurate number of taste buds, re-immunoblotting of β-actin of the same membrane helped us to confirm that lysates of WT and IP$_3$R3-deficient samples largely contained similar numbers of taste buds. Proteins were separated by 7.5% SDS-polyacrylamide gel electrophoresis and transferred to a polyvinylene difluoride membrane. The membrane was treated with the blocking solution (0.05% Tween/PBS) containing 5.0% skim milk for 1 hour, and probed with the indicated primary antibodies [monoclonal mouse antibodies, KM1112, KM1083, and KM1082 were used for detection of IP$_3$R1, IP$_3$R2, and IP$_3$R3, respectively (17). Rabbit polyclonal anti-Gustducin antibody and Rabbit polyclonal anti-PLCβ2 antibody were purchased from Santa cruz Biotechnology, Santa Cruz, CA. Monoclonal mouse anti-β-actin antibody was from Sigma, St. Louis, MO]. After incubation with horseradish peroxidase (HRP) labeled secondary antibodies (GE Healthcare, Arlington Heights, IL), the immobilized specific antigen was visualized with ECL plus detection kit (GE Healthcare).

**Immunocytochemistry**- Mouse tongue was removed and fixed with 4.0% formaldehyde/PBS for 3 hours at 4°C, then, immerged in 30% sucrose/PBS for O/N. The tissues were embedded in tissue-compound and the frozen sections at 12 µm in thickness were created using cryostat. Frozen sections of mouse lingual tissue were permeabilized with 0.2% Triton/PBS for 10 min and blocked with 1.0% goat-serum or 3.0% skim milk/PBS for 1 hour. Then, sections were incubated with primary antibodies in blocking solution for 1 hour at room temperature. The antibodies used for the experiments were: rabbit anti-IP$_3$R3 antibody (raised in rabbit using aa. 2391-2463 peptide of mIP$_3$R3 for an antigen), rabbit anti-PLCβ2...
antibody (Santa Cruz Biotechnology), rabbit anti-gustducin (Santa Cruz Biotechnology), rabbit anti-TRPM5 (kind gifts from Dr. Robert F. Margolskee), and rabbit anti-T1R3 (kind gifts from Dr. Charles S. Zuker). After washed with PBS for 15 min, sections were incubated with fluorescence conjugated secondary antibodies [Alexa 488-conjugated goat anti-mouse IgG and Alexa 594-conjugated goat anti-rabbit IgG (Invitrogen)] for 1 hour at RT. After washed with PBS for 15 min, the sections were mounted with Vectashield (Vector Laboratories, Burlingame, CA) and observed under IX-70 confocal fluorescence microscopy (Olympus, Tokyo, Japan).

RT-PCR- Total RNA was extracted from taste cells of three WT and IP3R3KO mice using Trizol Reagent according to the manufacturer’s instructions (Invitrogen). First strand cDNA was produced from the total RNA using reverse transcriptase Superscript II (Invitrogen) and oligonucleotide (dT) primers. The cDNAs were amplified with specific primers for mT2R108: sense 5'-ggcaccaaacgaggaaagatg-3', anti-sense 5'-tcaggaccaaagaggctactaacg-3'; mT2R138: sense 5'-atgctgagtctgactcctgtcttaac-3', anti-sense 5'-gcaggagagaagaagaacaactag-3'; and GAPDH: sense 5'-atggtgaaggtcggtgtgaaccg-3' anti-sense 5'-'aaacatgggggcatcggcagaa-3'. After an initial cycle of 2 min at 95 ºC, the reaction was cycled for 30 sec at 95 ºC, 30 sec at 55 ºC, and 1 min at 72 ºC, 30 times. The PCR products were separated by electrophoresis in 2.0% agarose gel, stained with ethidium bromide.

Electrophysiological recordings- Whole nerve responses of the chorda tympani (CT) and glossopharyngeal nerves (NGs) to lingual application of tastants were recorded as described previously (19). Briefly, tastants were applied to the tongue for 30 sec (CT) and 60 sec (NG) at a regular flow rate. Integrated whole-nerve response magnitudes (time constant, 1 sec) were measured 5, 10, 15, 20, and 25 sec (for CT) and 5, 10, 20, 30, and 40 sec (for NG) after stimulus onset. These data were averaged, normalized to the responses to 0.1 M NH4Cl, and analyzed with the general linear model multiple measures of the statistics package SPSS. For nerve recordings to MSG, we performed the experiments in the presence of 10 µM amiloride.

RESULTS

Taste bud morphology and the expression of taste-related proteins in IP3R3KO mice. We first examined the expression level of several taste-related proteins and taste bud morphology in WT and IP3R3-deficient mice.
As shown in Fig. 1A, we detected all three subtypes of IP₃Rs in WT taste bud lysates by western blotting. Consistent with the previous data using in-situ hybridization and RT-PCR (20, 21), the expression of IP₃R3 is predominant among the three subtypes of IP₃R, because the pan-IP₃R antibody, which recognizes all types of IP₃Rs at a similar level (22), detected the bands for IP₃Rs in WT taste bud lysates but not in IP₃R3-deficient taste bud lysates (Fig. 1A). The expression levels of PLCβ2 and gustducin in IP₃R3-deficient taste buds were equivalent to those in WT taste buds (Fig. 1A). Immunohistochemical studies also indicated that PLCβ2, gustducin, T1R3, and TRPM5, which are crucial molecules for taste signaling, were normally expressed in IP₃R3 deficient mice at levels comparable with those in WT mice (Fig. 1B). Immuno-signals for IP₃R3 were completely abolished in IP₃R3-deficient mice, whereas IP₃R3 signal was detected in WT taste buds (Fig. 1B), confirming the specificity of the antibody. We also tried to detect the immuno-signals for IP₃R1 and 2 in taste buds, but they were under the detection level (data not shown).

At the morphological level, no apparent alterations were detected in the taste buds of IP₃R3 deficient mice as compared with WT mice by hematoxylin-eosin staining (Fig. 1C). We further examined the taste bud morphology in electron microscopy (Fig. 2). The taste buds in the IP₃R3KO mice, as well as those in the control mice, were represented by tight aggregates of spindle-shaped cells, each of which extended from the base to the taste pore (Fig. 2A and 2B). As originally described by Takeda (23), the three major types of intragemmal cells (17) were identifiable by their cytoplasmic constituents: the type I cell possessing a nucleus with deep indentations and apical granules of high electron density, the type II cell with an oval nucleus and considerable amounts of smooth endoplasmic reticulum (Fig. 2C and 2D), and the type III cell that is characterized by a round clear nucleus and synaptic specialization: elevation in the electron density of the cell membrane and accumulation of granules. In both IP₃R3KO and WT mice, the taste-sensing type II and III cells frequently contacted with nerve endings that were rich in mitochondria and dense and clear vesicles, and type II taste cells displayed subsurface cisterns and atypical mitochondria in the contacting area [Fig. 2E and 2F, (24)]. Since taste bud sectioned through the axis passing from the base to the pore exhibited at least two type II cells and a single type III cell with their typical features in IP₃R3KO mice as similar to WT mice, the number of these cells constituting each taste bud did not seem to be largely different between IP₃R3KO and WT mice, although more detailed analysis might be required for evaluation of subtle changes in ultrastructure.

Abnormal taste perception of sweet, bitter, and umami in IP₃R3KO mice. We next examined the taste perception of IP₃R3 deficient mice using the 48-hour two-bottle preference tests. Mice were provided with two sipper bottles (one bottle contained distilled water and the other contained a tastant solution), and the preference ratio (intake of tastant solution to total liquid intake) was calculated for each tastant solution at various concentrations. We found an obvious abnormality in taste perception in the IP₃R3-deficient mice as shown in Fig. 3. Mice deficient for IP₃R3 showed decreased responses to sweet (sucrose and saccharin), umami (monosodium glutamate), and bitter (quinine sulfate, denatonium benzoate, and cycloheximide) tastes, whereas WT mice responded to the tastes in a dose-dependent manner. In contrast, the behavioral response of IP₃R3-deficient mice to salty taste (NaCl) was normal (Fig. 3). Likewise, IP₃R3-deficient mice avoided the sour solution (HCl) in a dose-dependent manner, similar to the WT mice. By contrast, mutant mice lacking IP₃R2 largely did not show any apparent abnormalities in taste perception, although there was a tendency that the mice showed a slightly reduced (sucrose, HCl) and stronger (denatonium, quinine sulfate, and NaCl) behavior responses compared to WT mice. Since we detected the IP₃R2 expression
in taste buds in a lower level (Fig. 1A), IP₃R2 may be partially involved in the signal transduction for these tastants. Even if, our data strongly indicated a specific role for IP₃R3 in \textit{in vivo} taste signaling. We could not perform similar experiments in IP₃R1-deficient mice because of their epilepsy and postnatal death within 21 days (25). Thus, the contribution of IP₃R1 to taste signal transduction remains unknown.

\textit{Electrical recordings of taste nerve responses in IP₃R3KO mice.} To further test the deficit of peripheral taste signaling in the IP₃R3-deficient mice, we finally took electrical recordings of the chorda tympani (CT) branch of the facial nerve and the glossopharyngeal nerve (NG), which innervate taste buds in the anterior and the posterior part of the tongue, respectively. Consistent with the behavioral data described above, the CT and NG electrical responses in IP₃R3-deficient mice to sweet (sucrose, glucose, sorbitol, sucralose, maltose, and fructose, SC45647, acesulfame K, and saccharin), bitter (denatonium, cycloheximide, and quinine), and umami tastes were greatly reduced but not abolished compared with those of the WT mice, as shown in Fig. 4. On the contrary, almost no significant differences were observed between IP₃R3-deficient mice and WT mice in the CT and NG responses to sour and salty tastes, which again was consistent with the behavioral data described in Fig 3. Taken together, these results indicate that IP₃R3 is a crucial mediator of sweet, bitter, and umami taste perception.

\textbf{Discussion}

Here, we have presented conclusive evidence from the behavioral experiments and electrical recordings that mice lacking IP₃R3 show abnormal taste perception for sweet, bitter, and umami tastes, with gustation of sour and salty compounds being well preserved. Since the taste bud morphology of IP₃R3 KO mice were apparently normal both in light and electron microscopic observation (Fig. 1C and 2) and the taste cells normally expressed several taste-related proteins other than IP₃R3 at an equivalent level to WT cells by immunoblotting, immunohistochemistry, and RT-PCR (Fig. 1A, Fig. 1B, and Supplemental Fig. 1), the abnormal development of taste buds in IP₃R3 KO mice did not explain the deficit of taste recognition. Consistent with the finding that IP₃R3 was the dominant isoform among the three types of IP₃Rs in taste buds (Fig. 1A), the abnormality of taste perception was specific for IP₃R3-deficient mice and IP₃R2-deficient mice generally showed normal taste perception (Fig. 3). Interestingly, however, IP₃R3-deficient mice showed a residual behavioral response to sweet, and bitter substances at high concentration (Fig. 3). Electrical recordings of taste nerve responses further supported the behavioral results and showed a slight difference in the degree of the reduction in responses from the two taste nerves. As for the sweet taste, CT responses were almost completely diminished, whereas NG responses were reduced but still weak with a dose-dependent increase [e.g., sucrose (> 0.3 mM), acesulfame K at 0.3M]. Electrophysiological responses of both CT and NG nerves to bitter substances (quinine sulfate and denatonium) were generally reduced but were not diminished in response to high concentrations. As for the umami taste response, CT nerve responses were significantly reduced in IP₃R3-deficient mice, whereas considerable responses were observed in IP₃R3-deficient NGs. Recently, similar residual responses to a higher dose of tastants were found in TRPM5-deficient mice (26). In addition, taste recognition of high doses of quinine and denatonium but not sucrose in PLCβ2-deficient mice was also reported by Dotson et. al (27). The reason for the residual behavioral and electrophysiological responses to sweet, bitter, and umami tastes in IP₃R3-deficient mice is unknown; however our results indicate the contribution of IP₃R-independent signal transduction, although we cannot rule out the involvement of a residual amount of expression of IP₃R1, IP₃R2, or other subtypes of PLC on taste signaling. Judging from the
evidence that IP3R3-deficient but not PLCβ2-deficient mice showed residual responses to high concentrations of sucrose, diacylglycerol produced by PLCβ2 may play an important role in taste perception for sucrose at a high concentration (Fig. 5). By contrast, taste recognition of high doses of denatonium and quinine seems to be completely independent from the PLCβ2-IP3R3 signal pathway, because both IP3R3-deficient and PLCβ2-deficient mice showed behavioral responses to the bitter compounds. Excitation of taste cells through activation of a cyclic nucleotide-gated channel (28, 29) or inactivation of K⁺ channels (30, 31) in the downstream events of taste receptor activation may explain the PLCβ2-independent residual response to high doses of bitter stimuli.

Although our behavioral data were generally consistent with the electrophysiological data, there is a dichotomy between the behavior and the neural responses in IP3R3KO mice: the mutant mice showed residual nerve response to MSG (the reduced CT nerve responses and the considerable NG responses), but abolished their preference for MSG. The similar dichotomy for MSG was also reported in α-Transducin and α-Gustducin double KO mice (32). In mice, umami taste is known to elicit both CT and NG nerve responses (33). CT nerve response is related to the preference for MSG, whereas the NG neural response is related to aversion at higher concentrations (32). Therefore, one explanation is that if the inputs from the two nerves are equal in net, the two signals may cancel each other, resulting in their behavior responses to be indifferent. Alternatively, electrophysiological signals may be not enough to elicit the behavioral response in the two-bottle preference tests.

Based on our data and the previous findings that Ca²⁺ activates TRPM5 in heterologous cells (10, 12-14) and in taste cells (15), we propose the following model: IP3 produced by PLCβ2 in response to G-protein-coupled receptor stimulation triggers Ca²⁺ release through IP3R3 from the endoplasmic reticulum, which in turn activates TRPM5 in vivo (Fig. 5). Thus, IP3R3 is a key molecule to couple PLC with TRPM5 and plays an indispensable role in taste perception for sweet, bitter, and umami tastes.

Reference


FOOTNOTES

We thank Dr. Robert F. Margolskee and Dr. Charles S. Zuker for their kind gifts of anti-TRPM5 antibody and anti-T1R3 antibody, respectively. We also thank all members of our laboratories, especially, A. Terauchi for breeding mice, and Dr. T. Inoue for experimental advice. Supported by grants from the Ministry of Education, Science, and Culture of Japan (K. M. and Y. N.), Grant-in-Aid for Young Scientists (C. H.), and the Japan Science and Technology Agency.

FIGURE LEGENDS.

FIGURE 1. Taste bud morphology and the expression of taste signaling molecules in IP3R3-deficient mice. (A) The expression of IP3R subtypes and the taste-related proteins in
taste buds from WT and IP3R3-deficient mice. (B) Immunohistochemistry of the expression of several proteins important for taste transduction in taste buds in circumvallate papillae from WT and IP3R3-deficient mice. a) gustducin, b) IP3R3, c) T1R3, d) PLCβ2, e) TRPM5. Scale bar: 20 µm. All experiments were performed at three times and the representative data were shown. (C) Morphology of taste buds of circumvallate papillae from WT and IP3R3-deficient mice stained with hematoxylin-eosin (HE). Scale bar: 50 µm.

FIGURE 2. Ultrastructure of taste buds from WT and IP3R3-deficient mice. (A and B) Taste buds of WT (A) and IP3R3KO (B) mice. Type I, II and III taste cells are labeled with corresponding numbers. Arrows indicate taste pores. Bars: 10 µm. (C and D) Basal portions of type II taste cells (II) in WT (C) and IP3R3KO (D) mice. Fig. 2C corresponds to the square area in A. In both animals, the cells are equipped with a considerable amount of smooth endoplasmic reticulum (stars), and brought into direct contact with intragemmal nerve fibers (N) with subsurface cisterns extended along the contacting area (arrowheads). Mitochondria in the IP3R3KO cell, as well as those in the wild type cell, were normal with no pathological signs of swelling or enlargement (arrows). I: type I cells. Bars, 1.0 µm. (E and F) The square areas in C and D are presented in higher magnification by E and F, respectively. Nerve fibers (N) contain clear vesicles (short arrows) and a dense-cored vesicle (long arrow). Cyttoplasm of type II cells appears spongy because of labyrinthine lumina of smooth endoplasmic reticulum. The subsurface cisterns are separated from the taste cell membrane by a 20 nm gap which contains an electron-dense material (arrowheads). M: mitochondria. Bars: 500 nm.

FIGURE 3. Mean taste preference ratios of WT, IP3R2-deficient, and IP3R3-deficient mice using 48-hour two-bottle (tastant versus distilled water) preference tests. (A) Behavioral responses to saccharin (0.25, 0.5, 1.0, 4.0, 16, and 32 mM). (B) Behavioral responses to sucrose (3, 15, 30, 60, 120, 300 mM) of WT, IP3R2-deficient, and IP3R3-deficient mice. (C) Behavioral responses to monosodium glutamate (MSG) (3, 10, 30, 100, and 300 mM). (D) Behavioral responses to cycloheximide (0.1, 0.5, 1.0, and 3.0 µM). (E) Behavioral responses to quinine sulfate (0.001, 0.01, 0.1, 0.3, 0.6, and 1.0 mM). (F) Behavioral responses to denatonium benzoate (0.01, 0.05, 0.3, 0.6, 1.0, 5.0, and 10 mM). (G) Behavioral responses to HCl (0.1, 1.0, 10, and 100 mM). (H) Behavioral responses to NaCl (75, 150, 300, and 600 mM). The values were means ± SEM. (n=5) * P < 0.05 (t-test).

FIGURE 4. Whole nerve recordings from CT and NG taste nerves of WT and IP3R3-deficient mice upon lingual application of taste stimuli. (A) Dose-dependent response of the CT nerve from WT and IP3R3-deficient mice to various tastants: sweet (sucrose, SC45647, acesulfame K), bitter (denatonium, quinine sulfate, quinine-HCl), sour (HCl), salty (NaCl), and umami (MSG). (B) Whole-nerve responses from the CT nerve of WT and IP3R3-deficient mice to sweet (sorbitol, sucralose, saccharin, glucose, maltohexose, fructose), bitter (caffeine, cycloheximide), and umami (L-proline, L-alanine, glycine, D-alanine, D-tryptophan) tastes. (C) Dose-dependent response of NG nerve from WT and IP3R3-deficient mice to various taste stimuli. (D) Whole-nerve responses from the NG nerve of WT and IP3R3-deficient mice to sweet (sorbitol, sucralose, saccharin, glucose, maltohexose, fructose), bitter (caffeine, cycloheximide), and umami (L-proline, L-alanine, glycine, D-alanine, D-tryptophan) tastes. Data are mean ± SEM. The number of experiments was at least 5 times. *P < 0.05 (t-test).

FIGURE 5. A schematic model of taste signaling for bitter, sweet, and umami. Taste stimuli (sweet, bitter, and umami) trigger the activation of PLCβ2 through the taste receptors (T1Rs and T2Rs), resulting in the production of IP3 and DAG. Then, IP3 binds to IP3R3, and IP3R3 releases Ca2+ from the ER. The elevation of intracellular Ca2+ triggers TRPM5 activation, which induces the depolarization of taste cells. In addition to this main signal...
pathway, the unknown signal pathways may also contribute to depolarization of taste cells for the detection of taste stimuli at the high concentration (dotted line).
SUPPLEMENTAL FIGURE 1. **The expression level of bitter taste-related receptors.**

The mRNA expression in WT and IP$_3$R3KO taste cells was examined by RT-PCR using the specific primers for the bitter-related receptors, mT2R108 and mT2R138. The expression level of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was examined as an internal control.
Abnormal taste perception in mice lacking the type 3 inositol 1, 4, 5-trisphosphate receptor

Chihiro Hisatsune, Keiko Yasumatsu, Hiromi Takahashi-Iwanaga, Naoko Ogawa, Yukiko Kuroda, Ryusuke Yoshida, Yuzo Ninomiya and Katsuhiko Mikoshiba

J. Biol. Chem. published online October 9, 2007

Access the most updated version of this article at doi: 10.1074/jbc.M705641200

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

Supplemental material:
http://www.jbc.org/content/suppl/2007/10/10/M705641200.DC1.html

This article cites 0 references, 0 of which can be accessed free at
http://www.jbc.org/content/early/2007/10/09/jbc.M705641200.citation.full.html#ref-list-1