ISSN 2308-2097 (print)
ISSN 2518-7880 (online)

ДУ «Інститут гастроентерології НАМН України»

ГАСТРОЕНТЕРОЛОГІЯ
GASTROENTEROLOGY

Том 59, № 3, 2025

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Заснований у 1969 році

Періодичність виходу: 4 рази на рік

Том 59, № 3, 2025

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GASTROENTEROLOGY

Патологія печінки і жовчовивідної системи / Pathology of Liver and Biliary Excretion System

UDC 616.312-008.1-074-053.2:613.26:575.2 *DOI: https://doi.org/10.22141/2308-2097.59.3.2025.692*

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Taste impairment in obese children: genetic aspects of reception

Abstract. ***Background.*** *Numerous single nucleotide variants (SNV) of the taste 2 receptor member 38 (TAS2R38) gene determine the formation of individual characteristics of bitter taste perception. The aim: to study the association of SNV rs10246939, rs1726866, rs713598 of the TAS2R38 gene with the risk of metabolically unhealthy obesity (MUO) in children.* ***Materials and methods.*** *Four hundred children aged 6–18 years were examined, of which 350 with obesity were treated. The control group was represented by 50 children without obesity. Among obese children, two observation subgroups were formed: MUO (n = 204) and metabolically healthy obesity (MHO) (n = 146). The level of taste preferences was determined by the FBPQ. The level of basal glycemia, insulinemia was studied by immunochemical method with electro chemiluminescent detection, high-density lipoproteins and triglycerides — by enzymatic-colorimetric method in the Synevo (Ukraine). SNVs of the TAS2R38 gene were identified by whole-genome next-generation sequencing in 52 patients at the CeGat laboratory (Germany).* ***Results.*** *The mean levels (M ± m) of taste preferences in the comparison groups according to the FBPQ were significantly different for sweet (in obese children — (3.36 ± 0.08) points, while in the control group (3.74 ± 0.07) points, p < 0.002) and bitter tastes (in obese children it was (2.77 ± 0.15) points, while in the control group (3.37 ± 0.15) points, p < 0.00013). The mean levels of taste preferences in children with MUO compared to those with MHO were significantly different for bitter tastes — (2.75 ± 0.12) points versus (3.24 ± 0.05) points, respectively, p < 0.02. We identified four SNVs in the TAS2R38 gene: rs713598, rs1726866, rs10246939, rs145970530.* ***Conclusions.*** *CG genotype of rs713598 in the TAS2R38 gene is associated with an increased risk of developing MUO and cardiometabolic disorders.*
Keywords: *children; obesity; single nucleotide variants; taste 2 receptor member 38*

Introduction

The recognition of the five basic tastes (salty, sour, sweet, umami, and bitter) is carried out by special taste receptors (taste receptors — TASR) located on the cytoplasmic membranes of the taste papilla cells of the tongue. The reception of sweet, umami, and bitter tastes is mediated by G protein-coupled receptors (GPCRs), while the recognition of salty and sour tastes is mediated by specialized ion channels [1, 2]. Taste buds contain three types of taste epithelial cells. Type I is represented by glial-like cells, type II by receptor cells, and type III by presynaptic epithelial cells. Type II and III taste epithelial cells mediate the transmission of specific tastes. Type II cells express receptors related to GPCRs, while type III cells contain specialized ion channels [3].

TASR receptor genes, which are related to GPCRs, form two families: taste receptor family 1 (TAS1R) and taste receptor family 2 (TAS2R). The TAS1R family consists of three genetic representatives TAS1R1, TAS1R2 and TAS1R3 [4, 5]. The interaction of TAS1R family proteins determines the recognition of L-amino acids. Thus, the TAS1R1/TAS1R3 receptor complex recognizes the taste of umami; and the TAS1R2/TAS1R3 complex recognizes the taste of sweet. TAS2R receptors are responsible for the perception of bitter taste. In humans, 25 genes and 8 pseudogenes of TAS2R have been identified [5–7].

Bitter taste perception plays an extremely important role in the eating behavior of humans and animals. It is believed that bitter taste is a marker of food toxins, and its recognition allows you to avoid the consumption of harmful foods. It has been established that the perception of bitter taste is involved in the formation of food preferences, affects metabolic processes and the development of adipose tissue. Numerous variants of the TAS2R genes determine the formation of individual characteristics of the perception of bitter taste, which can lead to the development of both obesity and its various phenotypes, especially in children [6–11].

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Obesity is highly associated with the development of low-level inflammation and metabolic disorders, such as insulin resistance, diabetes, dyslipidemia, atherosclerosis, arterial hypertension, vitamin D deficiency. Currently, two phenotypes are distinguished among cases of polygenic obesity with an increase in total body weight: the first is characterized by the absence of metabolic disorders and is called metabolically healthy obesity (MHO), and the second, associated with metabolic complications of obesity, is known as metabolically unhealthy obesity (MUO). In contrast to the MHO phenotype, which is mainly caused by changes in the activity of genes expressed in the brain ("central" genes), the MUO phenotype is caused by changes in genes, most of which are expressed in peripheral tissues ("peripheral" genes) [12–14].

It has been established that eating behavior features, dynamic changes in total body weight and adipose tissue mass are associated with single nucleotide variants (SNV) of bitter taste receptor genes, in particular, the *TAS2R38* gene (taste 2 receptor member 38) along with other SNVs of the following genes: *5-HT2C, ACSL5, ADIPOQ, APOA-1, APOE, BDNF, CAMKK2, CAT, CD36, CD40L, CG, CLOCK, CNR1, DIO2, ESR1, FABP-2, FKBP5, FTO, GCH1, GHRL, GHSR, GLP-1R, IL-6, LEP223, LEP656, LYPAL-1, MBOAT7, MC4R, NPY, OBPIIa, PGC1a, PNPLA3, PTEN, TCF7L2, TM6SF2, TRPV1, UCP2, UCP3* [15–17].

To date, it has been demonstrated that the SNV of the "peripheral" type of the *TAS2R38* gene is associated with the level of body mass index (BMI) in obese patients. The risk of developing MUO is highly associated with the SNV rs1726866 (G>A) of the *TAS2R38* gene, and BMI is inversely related to the level of taste perception of bitter foods [18–20].

However, studies related to the study of the relationships between SNVs of the *TAS2R38* gene with taste preferences and indicators of physical development demonstrate rather contradictory results.

The aim. The aim was to study the association of SNV rs10246939, rs1726866, rs713598 of the taste 2 receptor member 38 gene with the risk of developing metabolically unhealthy obesity in children.

Materials and methods

Ethical approval. Participants provided written informed consent, and research protocols and procedures were approved according to the ethical standards of the Declaration of Helsinki 2013 and by the Human Research Ethics Committee (ethical approval DSMU/EC/19/1107). Time of data collection: January 2020 — February 2024.

Informed consent. Informed consent was obtained from all individual participants included in the study.

Study design. Observational, analytical, longitudinal, cohort study [21].

Inclusion criteria. Polygenic obesity (BMI ≥ 95 percentile), age 6–18 years.

Exclusion criteria. Monogenic and secondary forms of obesity; hereditary syndromes accompanied by obesity; diseases, the treatment of which requires the use of medications that affect the metabolism of carbohydrates and lipids; pregnancy.

Setting. To achieve the goal and solve the research tasks, we examined 400 children aged 6–18 years, of which 350 children with obesity were treated. To verify the diagnosis, the classification of obesity recommended in clinical practice was used: Order of the Ministry of Health of Ukraine No. 1732 of 24.09.2022 About the approval of Standards medical assistance "Obesity in children". The control group was represented by 50 children without obesity.

Among obese children, whose body mass index exceeded the 95 percentile according to the recommendations of the Identification and prevention of Dietary and lifestyle-induced health EFfects In Children and infantS Study (IDEFICS) consortium with a gender distribution of 47.7 % (167) boys and 52.3 % (183) girls, two observation groups with MUO (n = 204) and MHO (n = 146) were separated.

Criteria for inclusion in the MUO group. The presence of abdominal obesity [22] and two of the following criteria (hyperglycemia and/or hyperinsulinemia; dyslipidemia; systolic blood pressure (SBP) and diastolic blood pressure (DBP) above the 90 percentile for a given age, gender and height [23]. Anthropometric data were measured by a nurse in the admission department, the child was in underwear and without shoes. Height (m) was measured using Heightronic Digital Stadiometer® to the nearest 0.01 m. Weight (kg) was measured using Tefal Bodysignal body composition analyzer (France). Waist circumference (WC), hip circumference (HC) was measured using a standardized anthropometric tape, measuring the circumference at the midpoint between the top of the iliac crest and the lower part of the lateral rib cage to the nearest 0.01 m. BMI was converted to SDS by means of the current WHO growth references [24]. Systolic and diastolic blood pressure (SBP and DBP) were measured using a digital oscillometer device, Dinamap ProCare (GE Healthcare).

Immunochemical examination

The studies were carried out in a certified Synevo laboratory (Dnipro, Ukraine). The material for the study was venous blood.

To study carbohydrate metabolism disorders, the level of basal glycemia and insulinemia was determined by immunochemical testing with electro chemiluminescent detection (ECLIA). Obese children were included in the main group with a glycemic level equal to or greater than 5.6 mmol/L and/or they had an increase in insulinemia > 90 percentile according to the percentile curves recommended by the IDEFICS consortium for the European population according to age and gender of the child [25, 26].

To study lipid metabolism disorders, the level of high-density lipoproteins (HDL-C), low density lipoproteins (LDL-C) and triglycerides (TG) was determined by the enzymatic-colorimetric method using kits from Roche Diagnostics (Switzerland) on the analyzer Cobas 6000. Obese children were included in the main group with HDL-C ≤ 1.03 mmol/L or less than 10 percentile of the age norm or an increase in ≥ 1.7 mmol/L or more than the 90 percentile of the age norm [27].

Psychological research methods

To highlight the predominant taste preferences for the five most important categories (sweet, sour, umami, salty and bitter), a questionnaire was conducted using an adapted version of the IDEFICS Food and Beverage Preferences Questionnaire (FBPQ) on a 5-point scale with the calculation of the average value of the taste preference level and the

analysis of food diaries. The questionnaire consisted of 63 photographs of individual food products. Each subject rated his/her own taste preferences for the corresponding food or beverage on a 5-point Likert scale [28].

Molecular genetic testing

To study the contribution of SNV of the *TAS2R38* gene to the formation of MUO, a molecular genetic study was carried out using next generation whole genome sequencing (NGS) according to the recommendations of the American College of Medical Genetics and Genomics (ACMG) [29] in 52 patients (31 children from the main group and 21 controls) with venous blood sampling in a certified CeGat laboratory (Tubingen, Germany) using the Illumina CSPro® certified service provider platform.

Average amount of DNA (μg) in samples was 0.875. Library preparation: quantity used 50 ng. Library preparation kit: Twist Human Core Exome plus Kit (Twist Bioscience). Sequencing parameters: NovaSeq 6000; 2 × 100bp. QC values of sequencing, Q30 value: 96.07 %.

Bioinformatics analysis

Bioinformatic analysis — demultiplexing of the sequencing reads was performed with Illumina bcl2fastq (version 2.20). Adapters were trimmed with Skewer, version 0.2.2 [30]; DNA-Seq: trimmed raw reads were aligned to the human reference genome (hg19-cegat) using the Burrows-Wheeler Aligner, BWA-mem version 0.7.17-cegat [31–34].

ABRA, version 2.18 and Genotype Harmonizer v.1.4.20 were used for local restructuring of readings in target regions to improve more accurate detection of indels in the genome during mutagenesis [35, 36].

Reference sequence obtained from the National Center for Biotechnology Information RefSeq database [37].

Statistical analysis

Statistical analysis of the obtained results was carried out using a package of application programs Statistica 6.1 (No. AGAR909E415822FA) with help a personal computer based on an Intel processor Pentium 4 and using the Python v3.11.5 programming language (https://www.python.org/downloads). The statistical hypothesis testing method was performed in the Python software package version 3.8.10 in the Visual Studio Code integrated development environment version 1.81.1. The assessment of the significance of the difference in means in multiple comparisons for quantitative traits with a normal distribution was carried out using one-way analysis of variance (ANOVA) with posterior pairwise comparisons using the Tukey test. Only essential ones were taken into account connections ($p < 0.05$).

Results

The age distribution of patients with polygenic obesity who participated in the survey was characterized by the following features: the proportion of children 6–10 years old (prepubertal period) was 5.6 %, 11–14 years old (early puberty) — 50 %, 15–18 years old (late puberty) — 44.4 %. The MUO phenotype was recorded in 58.3 % of the obese children we examined. In the MUO group, the average age of children was (12.06 ± 0.24) years, and the gender distribution was 50.9 % boys and 49.1 % girls ($p \geq 0.05$). In the MHO group, the average age of the children presented was (10.71 ± 0.28) years, and the gender distribution was 45 % boys and 55 % girls ($p \leq 0.05$).

Clinical and paraclinical characteristics of children with different obesity phenotypes are presented in Table 1.

When studying the levels of taste preferences in the comparison groups according to the FBPQ questionnaire, the average level (M ± m) of taste preferences for sweet in obese children was (3.36 ± 0.08) points, while in the control group — (3.74 ± 0.07) points, $p < 0.002$. The average level of taste preferences for salty taste in the main observation group was (2.95 ± 0.03) points, and in the control group — (3.28 ± 0.04) points, $p < 0.029$. The average level of taste preferences for bitter in obese children was (2.77 ± 0.15) points, while in the control group — (3.37 ± 0.15) points, $p < 0.00013$. The average level of taste preferences for sour and umami among obese and normal weight children did not have a significant difference (Fig. 1).

When studying the levels of taste preferences in different obesity phenotypes according to the five main taste modalities, significant differences were noted for salty and bitter taste. The average level of taste preferences for sweet in children with MUO was (3.40 ± 0.07) points, while in the MHO

Table 1 — Clinical characteristics of patients with obesity phenotypes, M ± m

Indicator	MUO (n = 204)	MHO (n = 146)	Probability, p
BMI, percentile	99.54 ± 0.21	98.74 ± 0.29	0.12
Presence of extreme obesity stage 2 (120–139 % above the 95 percentile), %	19.00 ± 3.92	16.10 ± 3.68	0.06
Presence of extreme obesity stage 3 (140 % above the 95 percentile), %	32.30 ± 4.66	0	**0.00001**
Waist circumference, percentile	96.65 ± 0.42	93.38 ± 0.82	**0.0004**
Systolic blood pressure, percentile	83.77 ± 3.05	71.38 ± 3.96	**0.014**
Diastolic blood pressure, percentile	87.48 ± 2.75	66.33 ± 4.09	**0.0006**
High-density lipoprotein cholesterol, percentile	30.83 ± 4.04	32.81 ± 2.79	0.68
Triglycerides, percentile	87.70 ± 2.28	80.33 ± 3.63	**0.04**
Fasting blood glucose, mmol/L	4.15 ± 0.37	3.36 ± 0.48	0.2
Basal insulin, μU/mL	29.47 ± 1.14	12.53 ± 1.44	**0.00001**

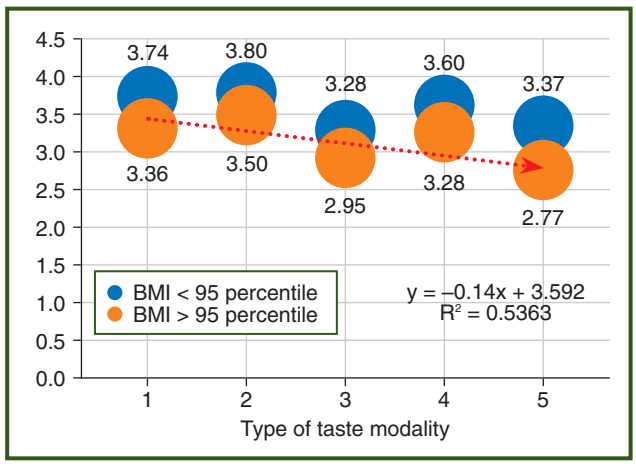


Figure 1 — Average level of taste preferences (points) in children with obesity and physiological body weight: 1 — sweet taste; 2 — sour taste; 3 — salty taste; 4 — umami taste; 5 — bitter taste

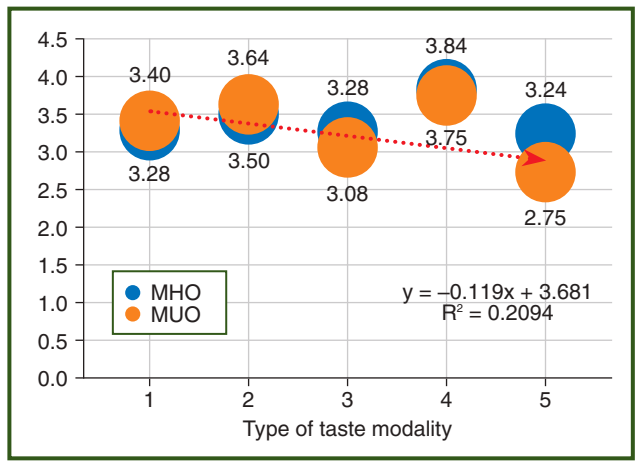
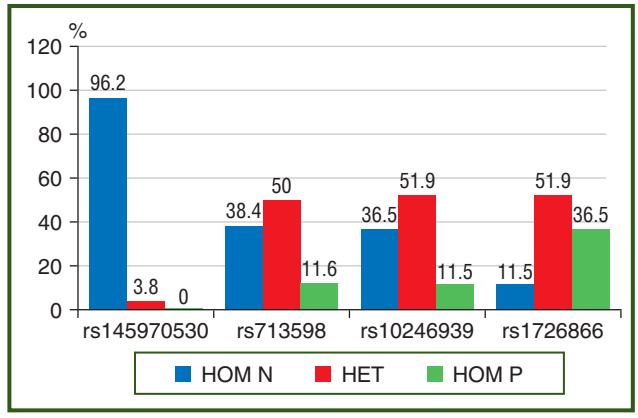


Figure 2 — Average level of taste preferences (points) in children with MUO and MHO: 1 — sweet taste; 2 — sour taste; 3 — salty taste; 4 — umami taste; 5 — bitter taste

group it was (3.28 ± 0.08) points, p > 0.05. The average level of taste preferences for sour taste in the MUO phenotype was (3.64 ± 0.06) points, and in the MHO phenotype it was (3.50 ± 0.05) points, p > 0.05. The average level of taste preferences for salty taste in the MUO group was (3.08 ± 0.06) points, and in the MHO group it was (3.28 ± 0.04) points, p = 0.05. The average level of taste preferences for umami in the MUO group was (3.75 ± 0.06) points, and in the MHO group — (3.84 ± 0.05) points, p > 0.05. The average level of taste preferences for bitter in children with MUO was (2.75 ± 0.13) points, while in the control group — (3.24 ± 0.10) points. In children with MUO, the level of taste preferences for this taste modality was lower compared to the group of children with MHO (t = 2.39; p = 0.022; critical value t = 2.023), Fig. 2.

As a result of the study, in sick children with obesity, we identified four SNVs of the *TAS2R38* gene: rs1726866, rs713598, rs145970530, rs10246939; the level of CADD (GRCh37-v1.7) in which is 16.45, 14.97, 5.55, 5.38, respectively (Fig. 3, Table 2).



Notes: HOM N — homozygous variant (absence of nucleotide substitutions); HET — heterozygous variant (single allelic single nucleotide substitution); HOM P — homozygous variant (biallelic single nucleotide substitution).

Figure 3 — The frequency of occurrence of SNV TAS2R38 gene (%) in children with obesity

Table 2 — Characteristics of SNV types of the TAS2R38 gene

SNV, ID	Position	GnomAD_ maxPOP	Ref	Alt	Consequence	Base change	CADD (GRCh37-v1.7)	Raw-Score	Clinical significance (ClinVar)
rs145970530	141673074	EAS	T	C	Missense	g.5500A>G	5.55	0.29	No data submitted for somatic clinical impact
rs713598*	141673345	EAS	C	G	Missense	c.145G>C	14.97	1.55	No data submitted for somatic clinical impact
rs10246939	141672604	EAS	T	C	Missense	c.886A>G	5.38	0.27	No data submitted for somatic clinical impact
rs1726866	141672705	SAS	G	A	Missense	c.785C>T	16.45	1.91	Benign

Notes: GnomAD_maxPOP — the frequency distribution of TAS2R38 mutations; EAS, SAS — East Asian, South Asian population groups; Ref — reference allele; Alt — alternative allele; Consequence — functional consequence of the variation in relation to the transcript. The nucleotide changes and position relative to the coding sequence of the affected transcript in HGVS nomenclature: c. CDS Position Reference Base > Alternative Base. Example: c.223A>T (c. — interpretation for DNA coding sequence). This column is empty if the variant is intergenic; CADD — combined annotation dependent depletion; * — SNV TAS2R38 are associated with MUO; GRCh37-v1.7 — Genome Reference Consortium Human Build 37.

The frequency of the CG rs713598 genotype of the *TAS2R38* gene in the MUO group (OR 1.75; 95% CI 1.1–6.35) was 1.75 times significantly higher than in the MHO group, $p < 0.05$.

Discussion

Numerous genes are involved in the perception of bitter taste in humans (Table 3), but the *TAS2R16* and *TAS2R38* receptor genes play the greatest role [38].

The human *TAS2R38* gene is located on the long arm of chromosome 7, q34. The *TAS2R38* gene is 1143 nucleotide pairs long, contains one exon and has no introns. The *TAS2R38* gene encodes a seven-membrane G-protein-coupled receptor. The TAS2R38 protein consists of 333 amino acid residues [9, 39]. The most common SNVs of the *TAS2R38* gene are rs713598 G>C (A49P), rs1726866 T>C (V262A) and rs10246939 T>C (I296V) (Fig. 4), which determine the diversity of taste sensitivity to phenylthiocarbamide (PTC), 6-n-propylthioutacyl (PROP) and chemically similar chemicals containing a thiourea fragment (N-C = S) [40].

Table 3 — Characteristics of human genes of the TAS2R family [6]

Gene	Coordinates (GRCh37-v1.7)	Transcript length	# Codons
TAS2R1	5: 9629109–9630463	1355	300
TAS2R3	7: 141463897–141464997	1101	317
TAS2R4	7: 141478242–141479235	994	300
TAS2R5	7: 141490017–141491166	1150	300
TAS2R7	12: 10954131–10955226	1096	319
TAS2R8	12: 10958650–10959892	1243	310
TAS2R9	12: 10961693–10962767	1075	313
TAS2R10	12: 10977916–10978957	1042	308
TAS2R13	12: 11060525–11062161	1637	304
TAS2R14	12: 11090005–11091862	1858	318
TAS2R16	7: 122634759–122635754	996	292
TAS2R19	12: 11174218–11175219	1002	300
TAS2R20	12: 11149094–11150474	1381	310
TAS2R30	12: 11285557–11287243	1687	320
TAS2R31	12: 11182986–11184006	1021	310
TAS2R38	7: 141672431–141673573	1143	334
TAS2R39	7: 142880512–142881528	1017	339
TAS2R40	7: 142919130–142920162	1033	324
TAS2R41	7: 143174966–143175889	924	308
TAS2R42	12: 11338599–11339543	945	315
TAS2R43	N/a	N/a	N/a
TAS2R45	N/a	N/a	N/a
TAS2R46	12: 11213964–11214893	930	310
TAS2R50	12: 11138512–11139511	1000	300
TAS2R60	7: 143140546–143141502	957	319
TAS2R2P	7: 12530721–12531630	910	~ 303
TAS2R12P	12: 11047542–11048481	940	~ 313
TAS2R15P	12: 11117024–11117951	928	~ 309
TAS2R18P	12: 11311375–11312293	919	~ 303
TAS2R62P	7: 143134127–143135066	940	~ 313
TAS2R63P	12: 11200931–11201855	925	~ 308
TAS2R64P	12: 11229915–11230841	927	~ 309
TAS2R67P	12: 11332272–11333061	790	~ 263

Note. N/a — not available.

Alleles encoding the presence of proline, alanine, and valine residues at positions 49 (Pro49), 262 (Ala262), and 295 (Val295), respectively, of the amino acid sequence of the TAS2R38 bitter taste receptor molecule, are associated with the presence of functional activity of the receptor; and alleles encoding the presence of alanine, valine, and isoleucine residues at positions 49 (Ala49), 262 (Val262), and 295 (Ile 296), respectively, of the amino acid sequence of the TAS2R38 bitter taste receptor molecule, are associated with the absence of functional activity of the receptor [41]. The molecular model of the TAS2R38 bitter taste receptor protein is shown in Fig. 5.

The functionally active dominant haplotype, designated by the first letters of the associated amino acid residues in the bitter taste receptor protein TAS2R38, is called PAV, and the non-functional recessive haplotype is called AVI. PAV/PAV homozygotes have a high sensitivity to the bitter taste PTC/PROP and have a phenotype known as the super-taster phenotype, while AVI/AVI homozygotes are the least sensitive to bitter taste (non-taster) [43]. Interestingly, the super-taster phenotype in adults is associated with higher alcohol consumption (OR = 5.15; 95% CI [2.66, 9.98]; $p < 0.001$) and tobacco smoking (OR = 1.73; 95% CI [1.24, 2.42]; $p = 0.001$) [41].

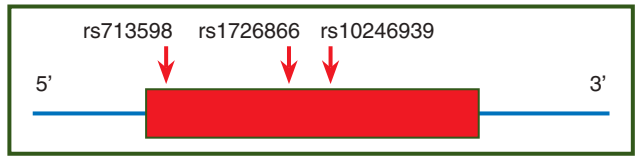


Figure 4 — Location of SNV of the TAS2R38 gene

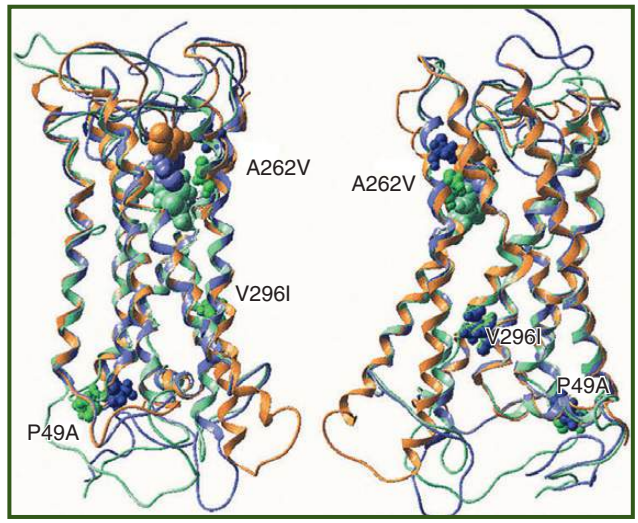
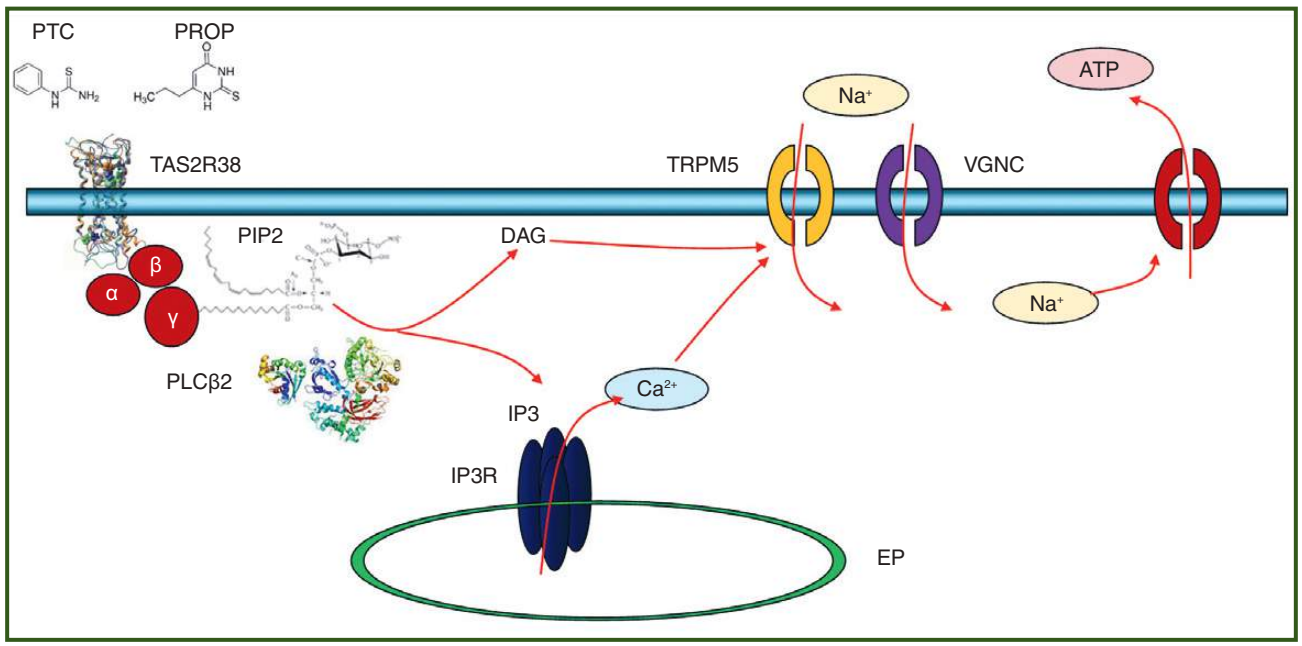


Figure 5 — Molecular structure of the bitter taste receptor protein TAS2R38 [42]



Notes: ligand interaction with the bitter taste receptor TAS2R38 leads to the dissociation of heterotrimeric GTP-coupled G-proteins, such as α-gustducin, β-, γ-protein. G-proteins subsequently activate membrane-bound phospholipase Cβ2 (PLCβ2), which converts phosphatidylinositol 4,5-bisphosphate (PIP2) to diacylglyceride (DAG) and inositol-1,4,5-triphosphate (IP3). In turn, IP3 binds to its cognate receptor, which is located in the endoplasmic reticulum (ER) membrane, and induces the influx of calcium ions (Ca^{2+}) into the cytoplasm of the cell. Ca^{2+} ions and DAG activate transient receptor potential melastatin channel subtype 5 (TRPM5), causing activation of voltage-gated Na^{+} channels (VGNC) and, subsequently, due to the influx of sodium ions (Na^{+}) into the cell from the extracellular space — calcium homeostasis modulators CALHM1/CALHM3. Activation of the CALHM1/CALHM3 modulators induces the release of ATP, which excites purinergic receptors on afferent nerve fibers and causes the sensation of bitter taste [9].

Figure 6 — Intracellular signaling pathways associated with the bitter taste receptor TAS2R38 [7, modification]

Simone Perna et al. [44] demonstrated that in body-positive people, the frequency of occurrence of the CC, GG and CG genotypes of SNV rs713598 of the *TAS2R38* gene is 20.3, 29.7 and 50.0 %, respectively. At the same time, biochemical parameters and body composition markers did not differ between subjects with different genotypes. The shown distribution of SNV rs713598 genotypes of the *TAS2R38* gene practically coincides with the results of our study. Adult carriers of the minor allele C of SNV rs713598 of the *TAS2R38* gene are characterized by a higher threshold for perception of bitter taste and prefer high-energy foods, such as beer, oil and dried meat [45].

According to our study results, the heterozygous genotype of the CG pathogenic variant rs713598 of the *TAS2R38* gene was highly associated with the development of metabolically unhealthy obesity [45]. Also, Hae Young Kim and Jeong-Hwa Choi demonstrated that among the Korean population, obesity is associated with the SNV genotypes rs713598, rs1726866 and rs10246939 of the *TAS2R38* gene, which are associated with a decrease in the perception of bitter taste. In contrast, there is evidence that obesity is accompanied by a significant increase in the expression of TAS2R38 RNA in gastric mucosal epithelial cells [46]. At the same time, Mohammad K. Shushari et al. [20] showed that SNVs rs713598, rs1726866, rs10246939 of the *TAS2R38* gene are not associated with body fat mass. Currently, there is no data in the literature regarding the somatic clinical impact of the SNV rs145970530 of the *TAS2R38* gene.

It is possible that the change in the structure of the TAS2R38 protein, caused by the presence of an alanine residue at position 49, differently affects the activity of intracellular signaling pathways in different cell types. It is known that activation of the TAS2R38 receptor leads to disruption of intracellular signaling pathways that cause the sensation of bitter taste and regulate numerous metabolic processes, including lipid metabolism (Fig. 6).

It has been established that TAS2R is expressed not only by taste bud cells, but also by other extraoral cells, including adipocytes of adipose tissue, which allows us to assume that TAS2R is involved in the regulation of adipogenic processes. It has been shown that bitter substances induce adipogenesis, and mutations in bitter taste receptor genes are accompanied by inhibition of the differentiation activity of precursor cells into mature adipocytes. In obese people, increased expression of the *TAS2R38* gene in adipocytes is observed, which is associated with adipocyte hypertrophy and the development of adipocyte pathology [40, 46–50].

Raffaella Cancello et al. [51] studied the expression of the *TAS2R38* gene in subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) adipose tissue from 32 obese and 18 lean individuals, in whom the SNV rs713598 was identified. The authors demonstrated that the level of TAS2R38 mRNA concentration was significantly higher in both SAT and VAT adipocytes from obese individuals. The level of TAS2R38 mRNA expression was not associated with

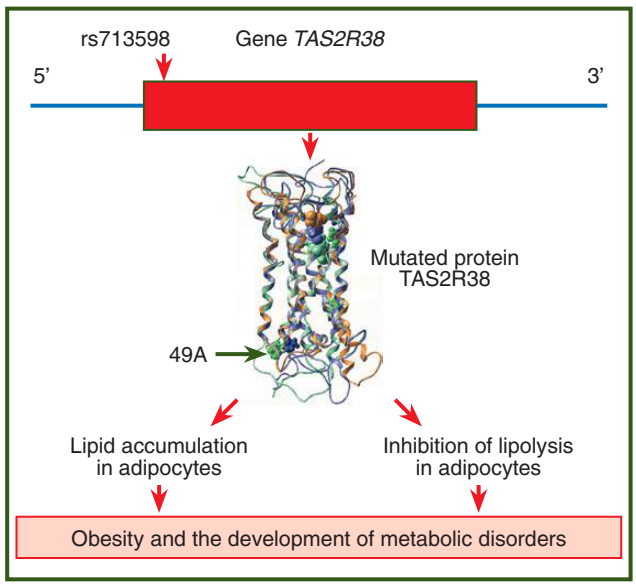


Figure 7 — The influence of the CG rs713598 genotype of the TAS2R38 gene on the development of metabolically unhealthy obesity

SNV rs713598. It was found that bitter agonists induce significant delipidating and inhibit lipid accumulation activity in differentiated adipocytes.

We believe that the disruption of the functional activity of the TAS2R38 receptor, which is caused by a change in the amino acid sequence due to the presence of SNV rs713598, is accompanied by a deviation of intracellular signaling pathways in adipocytes, which leads to increased lipid accumulation and the occurrence of metabolic disorders (Fig. 7).

Conclusions

Thus, a decrease in taste preferences for sweet, salty and bitter foods is associated with the formation of obesity in children, and de-escalation of preferences for bitter and salty foods is characteristic of children with a metabolically unhealthy phenotype.

A feature of the structure of obesity phenotypes among the children we examined is the prevalence of the MUO phenotype (58.3 %) by 1.4 times, which emphasizes the need to introduce preventive measures in this target group aimed at stratifying cardiometabolic risk.

The contribution of SNVs of the salt taste receptor gene (transient receptor potential cation channel subfamily V member 1) requires further study among children with different obesity phenotypes.

SNVs of the bitter taste receptor genes determine the trajectory of body fat development. Four SNVs (rs713598, rs1726866, rs10246939, rs145970530) of the bitter taste receptor gene *TAS2R38* have been identified in obese children. The single nucleotide variant rs713598 is associated with the development of a metabolically unhealthy obesity phenotype. The CG genotype rs713598 of the *TAS2R38* gene is associated with an increased risk of developing cardiometabolic disorders.

It is likely that the synthesis of the mutated protein of the bitter taste receptor TAS2R38 leads to impaired lipid metabolism, contributing to excessive accumulation of lipids in adipocytes.

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Received 01.08.2025
Revised 12.08.2025
Accepted 09.09.2025

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Conflicts of interests. Authors declare the absence of any conflicts of interests and own financial interest that might be construed to influence the results or interpretation of the manuscript.

Information about funding. The work is a fragment of the research work of the Department of Pediatrics 1 and Medical Genetics of the Dnipro State Medical University "Prediction of the development of childhood diseases associated with civilization" (No. 0120U101324), "Precision approaches to the diagnosis and treatment of somatic and endocrine diseases in children" (No. 0123U105100).

Authors' contribution. A. Abaturov — conceptualization, methodology, software, validation, formal analysis, investigation, resources, original draft preparation, review and editing, visualization, supervision, project administration, funding acquisition; A. Nikulina — conceptualization, validation, formal analysis, investigation, resources, data curation, original draft preparation, review and editing, visualization, supervision, funding acquisition.

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Порушення смаку в дітей з ожирінням: генетичні аспекти рецепції

Резюме. ***Актуальність.*** Численні однонуклеотидні варіанти (single nucleotide variants — SNV) гена члена 38 рецептора смаку 2 (taste 2 receptor member 38 — TAS2R38) зумовлюють формування індивідуальних особливостей сприйняття гіркого смаку. ***Мета:*** дослідити асоціації SNV rs10246939, rs1726866, rs713598 гена *TAS2R38* із ризиком розвитку метаболічно нездорового ожиріння (metabolically unhealthy obesity — MUO) у дітей. ***Матеріали та методи.*** Обстежено 400 дітей віком 6–18 років, з яких проліковано 350 пацієнтів з ожирінням. Контрольну групу становили 50 дітей без ожиріння. Серед пацієнтів з ожирінням за рекомендаціями консорціуму IDEFICS були сформовані дві підгрупи: з MUO (n = 204) та метаболічно здоровим ожирінням (metabolically healthy obesity — MHO) (n = 146). Рівень смакових уподобань визначали за опитувальником FBPQ. Базальну глікемію, інсулінемію досліджували імунохімічним методом з електрохемілюмінесцентною детекцією, уміст ліпопротеїнів високої щільності й тригліцеридів — ферментативно-колориметричним методом в лабораторії Synevo (Дніпро, Україна). SNV гена *TAS2R38* ідентифікували повногеномним секвенуванням наступного покоління в 52 пацієнтів (31 — із MUO та 21 — із MHO) в лабораторії CeGat (Тюбінген, Німеччина). ***Результати.*** Середні рівні (M ± m) смакових уподобань у групах порівняння за опитувальником FBPQ вірогідно відрізнялись до солодкого (у дітей з ожирінням — (3,36 ± 0,08) бала, у групі контролю — (3,74 ± 0,07) бала, p < 0,002) та гіркого смаків (у дітей з ожирінням становили (2,77 ± 0,15) бала, у контрольній групі — (3,37 ± 0,15) бала, p < 0,00013). Середні рівні смакових уподобань у дітей із MUO порівняно з дітьми з MHO вірогідно відрізнялись до гіркого смаку — відповідно (2,75 ± 0,12) бала проти (3,24 ± 0,05) бала, p < 0,02. Ідентифіковано чотири SNV гена *TAS2R38*: rs713598, rs1726866, rs10246939, rs145970530. ***Висновки.*** Генотип CG rs713598 гена *TAS2R38* пов'язаний із підвищеним ризиком розвитку MUO та кардіометаболічних порушень.

Ключові слова: діти; ожиріння; однонуклеотидні варіанти; член 38 рецептора смаку 2