1 **The associations between bitter and fat taste sensitivity, and dietary fat intake: Are they**
2 **impacted by genetic predisposition?**
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22 **Abstract**
23   A relationship between bitter and fat taste sensitivity, *CD36* rs1761667 and *TAS2R38*
24 has been demonstrated. However, research is scarce and does not take diet into account. This
25 study aimed to explore associations between genetics, fat and bitter taste sensitivity and dietary
26 fat intake in healthy UK adults. A cross-sectional study was carried out on 88 Caucasian
27 participants (49 females and 39 males aged 35 ± 1 years; body mass index 24.9 ± 0.5 kg/m^2).
28 Bitter taste sensitivity was assessed using phenylthiocarbamide (PTC) impregnated strips and
29 the general Labelled Magnitude Scale. Fat taste sensitivity was assessed by the Ascending
30 Forced Choice Triangle Procedure and dietary intake with a semi-quantitative food frequency
31 questionnaire. Genotyping for rs713598, rs1726866, rs10246939 and rs1761667 was
32 performed. Participants with *TAS2R38* PAV/PAV diplotype perceived PTC strips as more
33 bitter than groups carrying AVI haplotypes (AVI/AVI, $p = 1 \times 10^{-6}$; AVI/AAV, $p = 0.029$).
34 *CD36* rs1761667 was associated with fat taste sensitivity ($p = 0.008$). A negative correlation
35 between bitter taste sensitivity and saturated fat intake was observed ($r_s = -0.256$, $p = 0.016$).
36 When combining the *CD36* genotypes and *TAS2R38* diplotypes into one variable, participants
37 carrying both *TAS2R38* AVI haplotype and *CD36* A allele had a higher intake of saturated fat
38 compared to carriers of *CD36* GG genotype or *TAS2R38* PAV/PAV and PAV/AAV diplotypes
39 (13.8 ± 0.3 vs 12.6 ± 0.5 %TEI, $p = 0.047$) warranting further exploration in a larger cohort.

Abbreviations:

1. Introduction:

Taste sensitivity is an important factor in dietary habit development (Karmous et al., 2018). The five defined human tastes are sweet, sour, bitter, salty and umami (Ikeda, 1909), with a potential sixth taste, fat taste ("oleogustus") recognised recently (Mattes, 2010). The consumption of large amounts of dietary fat constitutes an unhealthy dietary pattern (World Health Organisation (WHO), 2020). Differing taste sensitivity thresholds, which can impact dietary fat consumption, may influence this unhealthy dietary pattern (Duffy & Bartoshuk, 2000; Graham et al., 2021). Research has identified genetic predisposition to all six tastes (Melis et al., 2020), although these have scarcely been studied together.

A wealth of research has reported a clear disparity in the ability to detect bitter compounds such as phenylthiocarbamide (PTC) and 6-n-propylthiouracil (PROP); a disparity which may be affected by genetics. More specifically, bitter taste sensitivity follows a bimodal distribution, with distinct phenotypes being either non-taster or taster.

To date, various candidate genes have been associated with PROP taste sensitivity, such as the taste receptors from the taste receptor 2 family and the gustin gene, *carbonic anhydrase VI*, (*CA6*) (Melis et al., 2013; Roura et al., 2015). *The bitter taste receptor 2 member 38* (*TAS2R38*) is the most researched receptor to date regarding PROP or PTC taste sensitivity. It contains three coding single nucleotide polymorphisms (SNPs): rs713598 (Pro49Ala), rs1726866 (Ala262Val), and rs10246939 (Val296Ile). These may explain more than 70% of bimodal distribution in PTC taste sensitivity (Kim et al., 2003; Risso et al., 2016). They also create common taster Pro-Ala-Val (PAV) and non-taster Ala-Val-Ile (AVI) haplotypes, observed in over 90% of the Caucasian population (Kim, Wooding, Ricci, Jorde, & Drayna, 2005). In addition, rare haplotypes such as Ala-Ala-Val (AAV), Ala-Ala-Ile (AAI), Pro-Ala-Ile (PAI) and Pro-Val-Ile (PVI) have been identified and may be associated with intermediate sensitivities to PTC and PROP (Risso et al., 2016; Tepper et al., 2008).

Research on genetic determinants of PROP/PTC taste sensitivity has mostly been conducted in Caucasian populations (North Americans or Europeans) that are more likely to be carriers of the non-taster *TAS2R38* AVI haplotype compared to African or Asian populations (Risso et al., 2016). Consequently, Caucasians have also been identified as having lower PROP taste sensitivity than the two above-mentioned populations (Williams et al., 2016; Yang et al., 2020).

Regarding dietary intake, lower bitter taste sensitivity has been associated with higher acceptance and intake of foods with a bitter taste (brassica vegetables, spinach, coffee) (Akella et al., 1997; Drewnowski et al., 1998, 1999), as well as a higher preference for sweet and fatty

90 tasting foods (Duffy & Bartoshuk, 2000), however, these findings are not consistent across

91 studies (O'Brien et al., 2013; Timpson et al., 2005). Nevertheless, the association between

92 bitter taste sensitivity and intake of foods other than those containing bitter tasting compounds,

93 suggests an interaction with other taste modalities. Considering a larger proportion of bitter

94 non-taster genotypes and phenotypes in Caucasians and the fact these may be associated with

95 diets high in sugar and fat, further research is warranted in this population.

96   In addition to the above, genetic variants in fat taste sensitivity (FTS) have been

97 reported. There have been two candidate genes of focus within human research; the *cluster of*

98 *difference 36 (CD36)* and *G-protein coupled receptor 120 (GPR120)* (Costanzo et al., 2019;

99 Daoudi et al., 2015). There is significant evidence of a link between variants within *CD36* and

100 FTS, specifically the rs1761667 (A/G) SNP. This has been associated with FTS (Daoudi et al.,

101 2015; Pepino et al., 2012; Sayed et al., 2015) and dietary fat intake (Fujii et al., 2019; Pepino

102 et al., 2012; Pioltine et al., 2016; Ramos-Lopez et al., 2016). The *CD36* receptor, a membrane

103 protein belonging to the class B scavenger receptor family located in taste bud cells, has been

104 shown to bind to varying concentrations of saturated and unsaturated long-chain fatty acids

105 (LCFA) (Besnard et al., 2016). To date, it is the only defined fat receptor with a high affinity

106 to LCFA (Khan et al., 2020). Individuals with the A-allele have demonstrated reduced protein

107 levels (Ghosh et al., 2011; Love-Gregory & Abumrad, 2011), and therefore have a higher fat

108 detection threshold (hyposensitive) and consequently cannot taste fat as successfully (Melis et

109 al., 2015; A Sayed et al., 2015). These individuals are likely to consume higher quantities of

110 foods containing fatty acids, potentially leading to weight gain (Besnard et al., 2016), although

111 there is paucity in research and what is available is largely heterogeneous (Tucker et al., 2017).

112   A relationship between bitter and fat taste may be apparent. Prior to the discovery of

113 fat taste and associated receptors, Tepper and Nurse, (1997) described PROP tasters to have a

114 greater ability for oral texture perception through a greater density of trigeminal fibres, thus, a

115 better ability to detect fat. Since this, a relationship between PROP tasters and preference for

116 fat has been demonstrated (Hayes & Duffy, 2007; Tepper & Nurse, 2006). More recently, and

117 in light of this, the *CD36* rs1761667 SNP has been investigated together with PROP taster

118 status and *TAS2R38* haplotypes (Sollai et al., 2019). Although results are consistent regarding

119 the association between fat and bitter taste by both *CD36* rs1761667 and bitter taste *TAS2R38*

120 haplotypes, research is scarce and is yet to be undertaken in a healthy UK cohort

121 comprehensively assessing whether genetic disparities impact dietary intake, alongside taste

122 sensitivity. Therefore, the aim of the current study was to explore the associations between

123 genetics, fat and bitter taste sensitivity and dietary fat intake in healthy UK adults.

2. Methods

2.1 Study design and participants

The participants were healthy Caucasian adults aged 18-65 years and living in the UK. Participants were recruited via word of mouth and internet postings. Exclusion criteria were pregnancy, breastfeeding, chronic medical conditions, food allergies, smoking, lactose intolerance and intake of any medication that may affect taste perception.

At baseline visit, anthropometric measurements including weight (kg), height (m) and waist circumference (cm) were recorded by the research team. Participants provided a 2 mL saliva sample for genotyping and took part in bitter and FTS tests. Participants were asked to refrain from consumption of any food or drink for one hour prior to testing. All participants provided demographic information and completed a food frequency questionnaire (FFQ) administered online (Google Forms).

All procedures involving human participants were approved by the St Mary's and Oxford Brookes University Ethics Committees. Written informed consent was obtained from each participant before the baseline data collection, stating they can withdraw from the study at any point. This study is registered as Genetics of Bitter and Fat Taste at ClinicalTrials.gov NCT04038281.

2.2 Demographic information

Self-reported demographic data (age, sex, ethnicity, income, occupation, and education level) were collected using an online questionnaire (Google Forms).

2.3 Anthropometric measurements

Height (m) [Free Standing Height Measure, SECA GmbH & Co., Hamburg, Germany] and weight (kg) [Portable Scale MS-4203, Marsden Weighing Group, Oxfordshire, UK] were recorded by the research team to the second decimal place. Body mass index (BMI) was calculated using the equation: weight (kg)/ height (m^2) (World Health Organization, 2018).

2.4 Bitter taste sensitivity

The participants rated the intensity of PTC impregnated strip (EISCO labs, Product FSC1031) using the general Labeled Magnitude Scale (gLMS). The gLMS weighted scale labels were: "no sensation" (0), "barely detectable" (1.4), "weak" (6), "moderate" (17), "strong" (35), "very strong" (53), and "the strongest imaginable sensation of any kind" (100)

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157 (Roura et al., 2015). Before rating the intensity of the PTC strip, participants were instructed
158 to remember the strongest sensation of any kind they had experienced or the strongest sensation
159 they could imagine happening to them. They were explained these would be deemed as the
160 strongest sensations of any kind on the gLMS scale (Hayes et al., 2013). This was used to guide
161 participants when rating the PTC intensity.
162

163 **2.5 Fat taste sensitivity**
164   The Oral Fatty Acid Threshold Assessment and Ascending Forced Choice Triangle
165 Procedure was carried out to determine each participant's oleic acid (C18:1) detection
166 threshold (FTS). The method used, and standard operating procedure followed, is described in
167 full in Haryono, Sprajcer and Keast, (2014). Briefly, each participant was presented with three
168 cups (30 mL UTH-milk based vehicles) in a random order, two controls (oleic-) and one
169 containing oleic acid (oleic+; 0.02, 0.06, 1, 1.4, 2, 2.8, 3.8, 5, 6.4, 8, 9.8, 12, 20 mM). A
170 participant was required to select the oleic+ solution correctly three times at the same
171 concentration to define their threshold. If they were incorrect at any point, a further three cups
172 were presented, one containing the higher oleic+ concentration and two oleic- solutions.
173 Participants were categorised by their FTS result: hypersensitive tasters have a FTS below 3.8
174 mM, hyposensitive tasters have a FTS above or equal to 3.8 mM and participants who fail to
175 identify the oleic+ sample at the maximum concentration (20 mM) are defined as non-tasters
176 (excluded from analysis) (Haryono et al., 2014; Stewart, Newman, & Keast, 2011).
177   Testing was conducted on one occasion for each participant. Samples were served at room
178 temperature and presented to participants in individual sections within either the St Mary's
179 University Nutrition laboratory or Oxford Brookes University sensory laboratory. Red lighting
180 was used to mask visual differences between the samples, nose clips were worn to inhibit
181 olfactory input, textural differences were avoided with the addition of textural agents (gum
182 Arabic and liquid paraffin), and post-ingestive regulation was followed by the sip-and-spit
183 procedure.
184

185 **2.6 Dietary intake**
186   Habitual dietary intake was assessed with a validated semi-quantitative FFQ (EPIC
187 Norflok). The questionnaires were analysed using the open source, cross-platform tool FFQ
188 EPIC tool for analysis (FETA) (Mulligan et al., 2014) and information on energy and dietary
189 macronutrient intake obtained. More specifically, total carbohydrate, total fat,
190 monounsaturated fatty acid (MUFA), polyunsaturated fatty acid (PUFA), saturated fatty acid

191 (SFA) and total protein were quantified. Intakes of macronutrients were converted into
192 percentage of total energy intake (%TEI) for analyses.

193

194 **2.7 Single nucleotide polymorphism genotyping**

195   From each participant, a 2 mL saliva sample was collected (SalivaGene Collection Module
196 II; Stratec Molecular GmbH). A stabiliser provided by the manufacturer was added to the saliva
197 sample which was then kept at −20°C until DNA was isolated. Genomic DNA was isolated
198 using a PSP® Saliva-Gene 17 DNA Kit 1011 (Stratec Molecular GmbH) in agreement with
199 the manufacturer procedures. Quality and quantity of the DNA were measured using
200 spectroscopy (Nanodrop, Thermo Fisher, Waltham, MA, USA). Genotyping was then
201 performed using predesigned TaqMan® SNP genotyping assays for the SNPs: rs1761667,
202 rs713598, rs1726866 and rs10246939 and the StepOnePlus thermocycler (Applied Biosystems,
203 CA, USA) with two technical replicates for each sample. The PCR amplification was then
204 completed under the conditions stated by the manufacturer. *TAS2R38* haplotypes, defined by
205 rs713598, rs1726866 and rs10246939, were determined using Haploview software (Barrett et
206 al., 2005).

207

208 **2.8 Statistical analyses**

209   Hardy Weinberg equilibrium was assessed for all SNPs using Chi-square goodness of fit
210 test. Continuous variables are presented as mean ± standard error of the mean (SEM) or median
211 (interquartile range) and were tested for normality with Shapiro-Wilk test. Categorical
212 variables are presented as absolute (relative) frequencies. Differences in anthropometry,
213 genotype frequencies, bitter and fat taste sensitivity and dietary intake between males and
214 females were tested with an independent samples t-test (with Levene's test for equality of
215 variance), Mann Whitney U or Fisher's Exact test, where appropriate. Individuals who failed
216 to identify the oleic+ solution at 20 mM were defined as non-tasters, therefore have no
217 measurable threshold and were excluded from further analyses on FTS and measurements of
218 dietary intake by *CD36* genotypes, in line with others (Burgess et al., 2018).
219   Spearman's correlation was used to explore the associations between bitter and fat taste
220 sensitivity as continuous variables. Kruskal-Wallis H tests were used to test the difference in
221 bitter taste sensitivity between *TAS2R38* diplotype groups and *CD36* genotypes. Bonferroni
222 adjustment were considered for pairwise comparisons. Mann-Whitney U test was used to
223 analyse the differences in bitter taste sensitivity according to the *TAS2R38* rs713598,
224 rs1726866 and rs10246939. Genotypes were dichotomised into carriers of non-taster (Ala, Val,

Ile) and homozygous taster alleles (Pro, Ala, Val). Chi-square or Fisher's Exact test, where appropriate, were used to assess the associations between *CD36* genotypes (AA, AG and GG, and AA/AG and GG), *TAS2R38* diplotypes and FTS categories, and to assess the associations between *CD36* genotypes (AA, AG and GG, and AA/AG and GG) and *TAS2R38* diplotypes. Kruskal-Wallis H test was used to explore the difference in fat taste threshold (mM) between *TAS2R38* diplotypes and *CD36* genotypes with Bonferroni adjustment for multiple comparisons.

Spearman's correlation was used to assess the associations between dietary fat intake (total, MUFA, PUFA and SFA) and bitter taste sensitivity, and FTS. One-way analysis of variance (ANOVA) or Kruskal Wallis H, were appropriate, were used to test for differences in dietary intake between *TAS2R38* diplotype groups, and between rs1761667 genotypes (AA, AG and GG). Independent samples t-test (with Levene's test for equality of variance) or Mann Whitney U test, where appropriate, were used to test for differences in dietary intake between rs713598, rs1726866, rs10246939 (carriers of the non-taster and homozygous taster allele), and rs1761667 genotypes (AA/AG and GG) as well as a variable combined of *CD36* genotypes and *TAS2R38* diplotypes (Non-tasters: participants carrying both *TAS2R38* AVI haplotype and *CD36* A allele vs Tasters: carriers of *CD36* GG genotype or *TAS2R38* PAV/PAV and PAV/ AAV diplotypes). Participants with AVI/PAV diplotype were grouped with non-tasters considering that larger proportion of our study population carrying this diplotype was deemed a non-taster using the classification by Roura *et al*. (2015) explained below. Finally, two-way ANOVA was conducted to explore the interaction between fat and bitter taster categories on dietary fat intake (total fat, MUFA, PUFA and SFA). For this purpose, PTC ratings were used to categorise the participants into three distinct taster groups. The cut-off criteria were: hyposensitive taster (non-taster) ≤15.5, normal taster >15.5, and hypersensitive taster ≥51 (Roura et al., 2015). Considering a low number of hypersensitive tasters, these were excluded from the analysis. Bonferroni adjustment was used for multiple comparisons.

SPSS was used throughout (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.). All tests were two-tailed, with $p < 0.05$ considered statistically significant.

3. Results

3.1 Participant characteristics

Participant characteristics are shown in Table 1. Participants were healthy Caucasians (49 females (56%) and 39 males (44%)) with mean age 35 ± 1 years and BMI 24.9 ± 0.5 kg/ m^2.

There were no differences in any of the presented variables or genotype frequencies according to sex, therefore males and females were combined in all analyses (data not shown). No differences in BMI were found between genotypes/diplotypes or bitter and fat taster categories (data not shown). Genotype/diplotype frequency of fat non-tasters can be found in Supplementary Table 1.

The *TAS2R38* and *CD36* SNPs were in Hardy Weinberg equilibrium (p = 0.825, p = 0.573, p = 0.573 and p = 0.217 for the rs713598, rs1726866, rs10246939 and rs1761667 respectively). Haplotype frequencies of *TAS2R38* in the study population were: AVI (53%), PAV (42%) and AAV (5%) and allele frequencies of *CD36* rs1761667 were A (61%) and G (39%).

3.2 Taste sensitivity and genetics

There was no correlation between fat and bitter taste sensitivity (r_s = 0.038, p = 0.758, data not shown, n = 69).

As shown in Figure 1, participants carrying PAV/PAV diplotype had higher median ratings of PTC intensity (median (IQR) 31 (30)) compared to participants with AVI haplotype (AVI/AVI, median (IQR) 2 (6) p = 1×10^{-6}; AVI/AAV, median (IQR) 4 (14), p = 0.029, n = 88)). Similarly, those classified as AVI/PAV had higher PTC ratings (median (IQR) 9 (24)) than those homozygous for AVI haplotype (p = 0.002, n = 88). Carriers of non-taster alleles for rs713598 (Ala), rs1726866 (Val) and rs10246939 (Ile) had lower ratings of bitterness compared to those homozygous for the taster alleles (Pro, Ala and Val, data not shown).

The *CD36* rs1761667 was associated with FTS (p = 0.008, n = 69) when analysed as three genotype groups (AA, AG and GG). Here, a larger proportion of hyposensitive tasters had the AG genotype (55%), this remained significant after Bonferroni corrections were applied (Figure 1). For exploratory purposes only, non-tasters were included in further analysis, results were consistent (p = 0.033; Supplementary Figure 1), however this was no longer significant after Bonferroni correction applied. When genotypes were combined by variant allele (AA/AG, and GG), a larger percentage of participants carrying the A allele (67.2%) were classified as hyposensitive tasters compared to those homozygous for the G allele (p = 0.013, n = 69, data not shown). Similar was observed when fat taste threshold was treated as a continuous variable (Supplementary Table 3).

There was no association between *TAS2R38* diplotypes and *CD36* rs1761667 (p = 0.622, 0.963, respectively for AA, AG and GG, and AA/AG and GG, n = 88). There was also no difference in PTC ratings of bitterness according to *CD36* rs1761667 genotypes (p = 0.782, 1.000, respectively for AA, AG and GG, and AA/AG and GG, n = 88) or *TAS2R38* diplotypes

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and fat taste categories (p = 0.384, n = 69). There were no differences in fat taste threshold between *TAS2R38* diplotypes (Supplementary Table 3).

3.3 Associations between genetics, taste sensitivity and diet

As shown in Figure 2, the ratings of PTC intensity were negatively correlated with SFA (%TEI) (r_s = -0.256, p = 0.016, n = 88). There were no correlations between bitter taste sensitivity, total fat, MUFA and PUFA intakes. When excluding participants carrying AVI/AVI diplotype, there was no correlation between PTC bitter taste intensity and dietary fat intake (r_s = -0.229, p = 0.069; r_s = -0.199; p = 0.115; r_s = -0.184; p = 0.145; r_s = -0.166; p = 0.191 for total fat, MUFA, PUFA and SFA respectively). Similarly, there were no correlations between fat taste threshold and any of the presented variables (Figure 3, n = 69). SFA (%TEI) and total fat (%TEI) (r_s = 0.656, p = 3.9×10^{-12}) and total fat (%TEI) and energy intake (kcal) (r_s = 0.225, p = 0.035) were positively correlated in the total cohort (data not shown).

There were no differences in energy and macronutrient intakes according to *TAS2R38* diplotypes (Table 2, n = 88) or *CD36* rs1761667 (Table 3, n = 69). Similar findings were observed when rare diplotypes AVI/AAV and PAV/AAV were excluded from the analyses (data not shown, n = 78). When analysing individual *TAS2R38* SNPs, there was a significant difference in SFA between rs1726866 and rs10246939 genotypes. Those carrying the non-taster allele for both SNPs (Val and Ile) had higher intake compared to participants homozygous for the taster allele (Ala and Val), both 13.6 ± 0.3 vs 12.1 ± 0.6 %TEI, p = 0.032, n = 88. When combining the *CD36* genotypes and *TAS2R38* diplotypes into one variable, participants carrying both *TAS2R38* AVI haplotype and *CD36* A allele had a higher SFA intake compared to carriers of *CD36* GG genotype or *TAS2R38* PAV/PAV and PAV/AAV diplotypes (13.8 ± 0.3 vs 12.6 ± 0.5 %TEI, p = 0.047, Supplementary table 2, n = 88). Similar was observed when only *TAS2R38* combined diplotypes were compared (AVI/AVI, AVI/AAV, AVI/PAV vs PAV/PAV, PAV/AAV, data not shown).

Finally, results of the two-way ANOVA showed no interaction between fat (hypo and hyper) and bitter (non-taster and taster) taster categories on total fat (p = 0.111), MUFA (p = 0.474), PUFA (p = 0.220) and SFA (p = 0.218). There were also no main effects of bitter taste category on total fat (p = 0.311), MUFA (p = 0.457), PUFA (p = 0.688) and SFA (p = 0.224). Similarly, there were no main effects of fat taste category on total fat (p = 0.186), MUFA (p = 0.406), PUFA (p = 0.145) and SFA (p = 0.702, Figure 4).

4 Discussion

The aim of this study was to explore the associations between genetics, taste sensitivity (bitter and fat), and dietary fat intake in healthy UK adults. We have demonstrated a difference in bitter taste sensitivity between *TAS2R38* diplotypes and an association between *CD36* rs1761667 and FTS. We did not find an association between *TAS2R38* and FTS, and *CD36* rs1761667 and bitter taste sensitivity. When analysing dietary intake, although there was no association between either *TAS2R38* diplotypes or *CD36* rs1761667 and dietary intake, we did observe a difference in SFA according to *TAS2R38* rs1726866 and rs10246939 genotypes and a negative correlation between bitter taste sensitivity and SFA. Finally, we did not observe an interaction between bitter and fat taste phenotypes on dietary fat intake. However, when combining the *CD36* genotypes and *TAS2R38* diplotypes into one variable, participants carrying both *TAS2R38* AVI haplotype and *CD36* A allele had a higher intake of saturated fat compared to carriers of *CD36* GG genotype or *TAS2R38* PAV/PAV and PAV/AAV diplotypes.

4.1 The associations between *TAS2R38*, bitter taste and diet

We observed differences in the PTC ratings of bitterness according to *TAS238* diplotype groups. Participants with PAV/PAV diplotype had higher ratings than those carrying AVI haplotype and participants classified as AVI/PAV had higher ratings than those homozygous for AVI haplotype. This is in line with previous research where AVI haplotype was associated with bitter non-taster and PAV with a bitter taster phenotype (Bufe et al., 2005; Kim et al., 2005; Tepper, 2008).

In addition to the associations between genetics and taste perception, we also observed an inverse association between bitter taste sensitivity and SFA. Moreover, SFA was positively associated with total fat intake in our study population. This negative association between bitter taste sensitivity and dietary fat intake is in line with previous research reporting higher preference and intake of dietary fat in bitter non-tasters compared to tasters (Choi & Chan, 2015; Duffy, 2004; Tepper & Nurse, 1998). Considering that total fat intake was positively associated with energy intake, a higher intake of SFA may be an indicator of a more energy dense pattern of dietary intake. Since we did not explore dietary patterns, this warrants further research in a similar study population.

The mechanism behind the association between bitter taste sensitivity and dietary fat intake is not entirely clear. It may be that interaction between bitter and fat taste perception exists and this will be discussed later. Considering that the correlation between bitter taste sensitivity and SFA was no longer significant once participants with AVI/AVI diplotype were

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362 excluded, this association appears to be driven by genetic predisposition. In this sense,
363 *TAS2R38* is expressed in the gastrointestinal tract where it may regulate the release of satiety
364 hormones and influence the postprandial response to nutrients (Dotson et al., 2010; Rozengurt,
365 2006). We observed a higher intake of SFA in carriers of the non-taster alleles (Val and Ile) for
366 the rs1726866 and rs10246939 compared to those homozygous for the taster allele (Ala and
367 Val). Similar was observed when *TAS2R38* diplotyes were combined into carriers of the non-
368 taster AVI haplotype and compared to those carrying PAV/PAV or PAV/AAV diplotype. The
369 fact that we did not observe a similar difference in SFA when *TAS2R38* diplotypes were
370 analysed as separate groups may be due to a smaller sub-group sample size when splitting
371 participants into these; this warrants further investigation in a larger sample size study.
372 Interestingly, Dotson *et al.*, (2010) observed an increased eating disinhibition in carriers of the
373 rs1726866 Val, non-taster, allele in their population of Amish women. The authors did not
374 explore dietary intake, however the associations between saturated, total fat and energy intake
375 in our study population suggest that *TAS2R38* may be associated with both eating behaviour,
376 such as eating disinhibition, and a more energy dense dietary pattern. There are number of
377 proposed mechanisms including impaired release of satiety hormones (glucagon-like peptide
378 1 (GLP-1), insulin) and increased levels of leptin in carriers of the non-taster alleles that warrant
379 further investigation.

380   Besides the potential effects of *TAS2R38* intestinal expression on hormone signalling,
381 genetic variations in the *CA6* gene may provide an explanation for the association between
382 bitter taste sensitivity and dietary fat intake. Lower fat intake, as %TEI , was observed in UK
383 individuals carrying the AA genotype of the *CA6* rs2274333 compared to heterozygous AG
384 individuals (Shen et al., 2017). This genotype has been associated with greater bitter taste
385 sensitivity (i.e. PROP super-taster status), through greater fungiform papillae density in AA
386 genotypes compared to homozygous GG genotypes (Melis et al., 2013). Considering that
387 greater fungiform papillae density has also been associated with improved FTS (Zhou et al.,
388 2020), there may be an interaction between *TAS2R38* and *CA6* on dietary fat intake in our study
389 population. These interactions require further research in a similar study population.

390   Finally, due to the cross-sectional nature of the present study, it is not possible to
391 determine the direction of the association between bitter taste sensitivity and dietary fat intake.
392 Besides the possibility that lower bitter taste sensitivity leads to a higher fat intake, the opposite
393 may also be correct. Jeon *et al*. (2008) suggested that a low-cholesterol diet, likely low in
394 saturated fat, increases the sensitivity of intestinal bitter taste signalling system making the gut
395 more responsive to the presence of bitter tasting compounds. Further intervention studies are,

396 therefore, warranted to explore the cause-and-effect relationship between bitter taste and
397 dietary fat intake.
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400 **4.2 The associations between *CD36* rs1761667, fat taste and diet**
401   Furthermore, we observed that the A allele of *CD36* rs1761667 was associated with
402 FTS, specifically a larger percentage of participants carrying the A allele were classified as
403 hyposensitive tasters. This is in line with previous research (Burgess et al., 2018; Chmurzynska
404 et al., 2020; Keller et al., 2012; Melis et al., 2015; Mrizak et al., 2015; Pepino et al., 2012;
405 Amira Sayed & Khan, 2015) and supports that LCFA evoke calcium signalling in gustatory
406 cells expressing *CD36* (El-Yassimi et al., 2008), and that lower protein levels may be related
407 to the A allele hindering ability to detect fat. To date, although research is supportive towards
408 an association between rs1761667 and FTS findings are largely heterogeneous, specifically,
409 regarding ethnicity, which has been shown to modify responses to taste sensitivity (El-Sohemy
410 et al., 2007). Only Melis *et al.*, (2015); Burgess *et al.*, (2018) and Sollai *et al.*, (2019)
411 investigated a Caucasian cohort, similar to ours. Chmurzynska *et al.*, (2020) states recruitment
412 was carried out in Poland, but otherwise does not specify ethnicity of participants. Our results
413 corroborate Melis *et al.*, (2015), and Sollai *et al.*, (2019) but contrast, Burgess *et al.*, (2018)
414 who reported no association between rs1761667 genotype and FTS or perception of fat in the
415 Caucasian sub-group. Results may differ to ours due to Burgess *et al.*, (2018) having a lower
416 sample size (n = 36) than us (n = 69) and Melis *et al.*, (2015) (n = 64), and thus may have
417 resulted in a type II error. Overall, it is evident the *CD36* rs1761667 A-allele may hinder ability
418 to detect fat in Caucasian participants, although research is scarce. Here it is important to state
419 that other factors may lead to differing taste sensitivity levels alongside rs1761667 genotype.
420 This includes both mechanistic factors, for example rs1527483, another SNP on the *CD36* gene
421 that has been associated with instantaneous orosensory fat taste sensitivity (Plesnik *et*
422 *al.*, 2018), and interactions between FTS and other tastes, which will be discussed below.
423 Further, an additional factor to consider are fat non-tasters, despite constituting a
424 comparatively small percentage of the population it is unclear whether this sub-population are
425 associated with the same genetic pattern demonstrated by us and others (Burgess et al., 2018;
426 Chmurzynska et al., 2020; Keller et al., 2012; Melis et al., 2015; Mrizak et al., 2015;
427 Pepino et al., 2012; Amira Sayed & Khan, 2015). Such genotypic conclusions cannot yet be
428 drawn since many excluded non-tasters from their analysis (Bajit et al., 2020; Burgess et al.,
429 2018; Karmous et al., 2018; Melis et al., 2020) due to no measurable threshold when
undertaking the forced choice triangle 13

430　method and a small sub-sample. We have included data for the fat non-tasters in our genetic
431　analysis to aid future research comparisons.

432　　　It has been stated that a reduced ability to taste fat may lead to greater consumption
433　(Besnard *et al*., 2016). Despite the association found between *CD36* rs1761667 and FTS, we
434　did not observe a difference in dietary intake (total energy, carbohydrate, protein, fat, MUFA,
435　PUFA or SFA). Our findings may be influenced by the majority of our population carrying at
436　least one A allele (81%). To our knowledge, only Graham *et al.,* (2021) and our study assess
437　rs1761667 genotype and dietary intake on a solely Caucasian healthy cohort. Similarly, Pepino
438　*et al.*, (2012) reported no association between genotype and diet, using a mixture of Caucasian
439　and African American (n = 21) participants. Others have reported that the rs1761667 A allele
440　is associated with a higher dietary fat intake. For example, Ramos-Lopez *et al.*, (2016) reported
441　that in participants with chronic hepatitis C the AA genotype is associated with a higher total
442　fat intake (%TEI) and higher SFA (%TEI) ($p < 0.05$), using a 3-day dietary food record. No
443　differences between MUFA and PUFA were found. Similarly, Fujii *et al.*, (2019), using
444　Japanese (n = 495) participants demonstrated the AA genotype was significantly associated
445　with higher total fat, SFA, MUFA, PUFA, omega-3 and -6 intake ($p<0.05$), using a short FFQ.
446　In contrast to this, and contradicting mechanisms associated to the A allele causing a reduced
447　protein expression (Melis et al., 2017), Pioltine *et al.*, (2016) reported the A allele was
448　associated with a decreased intake of total fat (g/day), PUFA and MUFA (% kcal and g/day),
449　fatty foods (portion and g/day), and vegetable oils (mL/day) in Brazilian children and
450　adolescents with obesity, using two 24-hour dietary recalls. It is evident that research regarding
451　dietary intake and rs1761667 genotype is highly heterogeneous, preventing any clear
452　conclusion from being drawn. This warrants further research in an ethnically homogenous,
453　healthy cohort of adults or children, similar to our own, with consistent dietary collection
454　methods.

455

456　**4.3 Potential interactions between fat and bitter taste**

457　　　In our study population bitter and FTS were not correlated. Also, we found neither an
458　association between *TAS2R38* diplotypes and FTS nor *CD36* rs1761667 and bitter taste
459　sensitivity. Our findings contradict other research, reporting an association between the two
460　tastes (Melis et al., 2015; Sollai et al., 2019). Melis *et al.,* (2015), using 64 Italian participants,
461　displayed that perception of fatty acids was associated with rs1761667 *CD36* and that AVI/AVI
462　participants exhibited a 5-fold higher oleic acid threshold than their PAV/PAV counterparts.
463　Later, Sollai *et al.*, (2019), reported similar results but using electrophysiological recordings

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from the tongue in response to oleic acid in a sample of 35 Italian adults. Similar results have been reported by Karmous *et al.*, (2018), who also displayed a correlation between fat and bitter taste, however in a non-Caucasian (Tunisian) population and by Melis *et al.*, (2020) in patients with inflammatory bowel disease. The fact we did not observe similar associations may be attributed to our study population being UK based and having different allele and haplotype frequencies compared to populations such as Tunisians explored by Karmous *et al.,* (2018). Furthermore, differences in methods of taste sensitivity measurement between studies may also explain discrepancies in results.

None of the aforementioned studies explored the dietary intake of participants. In this sense, we observed an association between genetic predisposition to bitter taste, bitter taste sensitivity and dietary fat intake, where non-tasters have a higher intake of SFA than tasters. Although we did not observe an interaction between bitter and fat taste categories on dietary fat intake, we observed a higher intake of SFA in participants carrying both non-taster *CD36* allele (A) and *TAS2R38* haplotype (AVI) compared to those carrying either taster *CD36* genotype (GG) or *TAS2338* haplotype (PAV/PAV and PAV/AAV). This may suggest that genetic predisposition to hyposensitivity to both fat and bitter taste leads to an increased dietary fat intake, and supports previously observed interactions between the two tastes (Karmous et al., 2018; Melis et al., 2015, 2020; Sollai et al., 2019). It may also corroborate proposed mechanisms whereby *TAS2R38* may be involved in the textural perception of fat, whereas *CD36* may determine the chemosensory detection of fat (Keller, 2012). Considering that higher SFA intake was also observed in carriers of *TAS2R38* haplotype (AVI) compared to those carrying PAV/PAV or PAV/AAV diplotypes it may be that *TAS2R38* is driving these differences. Due to the small sample in our study, we were not able to determine exact contribution of *TAS2R38* diplotypes and *CD36* rs1761667 in explaining SFA using regression analysis. These results should therefore be considered hypothesis generating and replicated in a larger cohort.

4.4 Strengths and limitations

Besides the fact we comprehensively investigated the associations between genetics, taste and diet, a strength of this study is an ethnically homogenous population enabling a more valid interpretation of genetic association results. However, our population was not homogenous regarding sex, Barragán *et al.,* (2018) reported that sex differences exist in ability to taste. There were no differences between sexes found in any of the variables tested however future research should endeavour to recruit a sex specific cohort or have a sample large enough for

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498 sex-specific analyses. Our sample size, although in line with other published research
499 (Karmous et al., 2018; Melis et al., 2015, 2020; Sollai et al., 2019), was low regarding subgroup
500 analysis (Grimaldi *et al.*, 2017). This limits the conclusions that can be drawn and results
501 should be replicated in a larger sample size study.

502 Moreover, in future studies repeated testing of FTS should be considered. Although some
503 have demonstrated FTS is reproducible (Newman & Keast, 2013), others have demonstrated
504 improvement, specifically within the hypersensitive tasters, over time (Tucker & Mattes,
505 2013).

506 Furthermore, the use of PTC filter strips may result in misclassification of participants into
507 bitter tasters and non-tasters (Lawless, 1980). However, more recently, the use of PROP or
508 PTC paper strip has been shown as a valid method to explore genetic predisposition to PTC
509 taste sensitivity (Khataan et al., 2010) and we have used these ratings as a continuous variable
510 in the majority of our analyses. Furthermore, the gLMS may also be more reliable when
511 repeated on multiple occasions (Hayes et al., 2008) and this should be considered in future
512 research. Nevertheless, participants were instructed on the use of the scale, which has been
513 employed in similar studies exploring genetics and bitter taste sensitivity (Yang et al., 2020).

514 The present study explored the associations between PTC taste sensitivity as a proxy for
515 bitter taste sensitivity and *TAS2R38* receptor as its determinant. PTC is however, only one of
516 the many bitter tasting compounds and may not be a predictor of general bitter taste sensitivity.
517 There are number of TAS2R bitter taste receptors that are activated by different bitter tasting
518 compounds such as caffeine, quinin and saccharin requiring further investigation to gain a more
519 comprehensive understanding of bitter taste variability and its effects on dietary intake (Roura
520 et al., 2015).

521 Lastly, self-reported dietary intake data, collected via validated FFQ, may be prone to
522 misreporting (Shim, Oh and Kim, 2014). However, to improve accuracy, we selected a
523 population specific FFQ (UK) and expressed macronutrients as % TEI which may improve
524 accuracy of comparisons made (Macdiarmid and Blundell, 1998). Also, although the FFQ used
525 is a validated method to collect dietary consumption over the previous 12 months and has been
526 calibrated using a 24-hour dietary recall, dietary intake may vary over time and FTS has been
527 shown to alter after only weeks of dietary modification (Costanzo et al., 2019; Newman et al.,
528 2016). Therefore, future studies should consider the use of multiple 24-hour dietary recalls to
529 collect dietary intake information.

530

531

5   Conclusion

Overall, we confirmed that *TAS2R38* haplotypes determine bitter taste sensitivity and *CD36* rs1761667 is associated with fat taste sensitivity. Lower sensitivity to bitter taste may also lead to a higher dietary intake of fat. Considering the lack of association between bitter taste sensitivity and SFA when excluding participants carrying *TAS2R38* non-taster AVI/AVI diplotype, this appears to be mainly driven by genetic predisposition. Although we did not observe an interaction between bitter and fat taste categories on dietary fat intake, we observed a higher intake of SFA in participants carrying both non-taster *CD36* allele (A) and *TAS2R38* haplotype (AVI) compared to those carrying either taster *CD36* genotype (GG) or *TAS2338* diplotype (PAV/PAV and PAV/AAV). This may suggest that genetic predisposition to hyposensitivity to both fat and bitter taste leads to an increased dietary fat intake. Nevertheless, it warrants further research in a larger cohort employing repeated measurements of bitter and FTS and a combination of dietary consumption methods such as FFQ and 24-hour recalls.

Declaration of Interest

Yiannis Mavrommatis is a shareholder for Nell Health, a lifestyle genotyping company. Leta Pilic is serving on advisory board of DNAfuel LTD.

Author Contributions

Catherine Anna-Marie Graham and Leta Pilic: Conceptualization**,** Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Visualisation **Ella Mcgrigor**: Investigation, Data Curation **Megan Brown**: Investigation, Data Curation **Isabelle Jane Easton:** Investigation, Data Curation **Jonathan Nyuma Kean**:

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551 Investigation, Data Curation **Natalie Davis**: Investigation, Data Curation **Nisrin Hares**:

552 Investigation, Data Curation **Deanna Barac** Investigation, Data Curation **Alexandra King**:

553 Writing – Review and Editing **Yiannis Mavrommatis**: Conceptualization, Methodology,

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555 All authors have approved the final article.

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References

558 Akella, G. D., Henderson, S. A., & Drewnowski, A. (1997). Sensory acceptance of Japanese

559 green tea and soy products is linked to genetic sensitivity to 6-n-Propylthiouracil.

560 *Nutrition and Cancer*, *29*(2), 146–151. https://doi.org/10.1080/01635589709514616

561 Barragán, R., Coltell, O., Portolés, O., Asensio, E. M., Sorlí, J. V., Ortega-Azorín, C.,

562 González, J. I., Sáiz, C., Fernández-Carrión, R., Ordovas, J. M., & Corella, D. (2018).

563 Bitter, sweet, salty, sour and umami taste perception decreases with age: Sex-specific

564 analysis, modulation by genetic variants and taste-preference associations in 18 to 80

565 year-old subjects. *Nutrients*, *10*(10). https://doi.org/10.3390/nu10101539

566 Barrett, J. ., Fry, B., Maller, J., & Daly, M. . (2005). Haploview: analysis and visualization of

567 LD and haplotype maps | Bioinformatics | Oxford Academic. *Bioinformatics*, *21*(2),

568 263–265. https://academic.oup.com/bioinformatics/article/21/2/263/186662

569 Besnard, P., Passilly-Degrace, P., & Khan, N. A. (2016). Taste of Fat: A Sixth Taste

570 Modality? *Physiological Reviews*, *96*(1), 151–176.

571 https://doi.org/10.1152/physrev.00002.2015

572 Bufe, B., Breslin, P. A. S., Kuhn, C., Reed, D. R., Tharp, C. D., Slack, J. P., Kim, U. K.,

573 Drayna, D., & Meyerhof, W. (2005). The molecular basis of individual differences in

574 phenylthiocarbamide and propylthiouracil bitterness perception. *Current Biology*, *15*(4),

575 322–327. https://doi.org/10.1016/j.cub.2005.01.047

576 Burgess, B., Melis, M., Scoular, K., Driver, M., Schaich, K. M., Keller, K. L., Tomassini

577 Barbarossa, I., & Tepper, B. J. (2018). Effects of CD36 Genotype on Oral Perception of

578 Oleic Acid Supplemented Safflower Oil Emulsions in Two Ethnic Groups: A

579 Preliminary Study. *Journal of Food Science*, *83*(5), 1373–1380.

580 https://doi.org/10.1111/1750-3841.14115

581 Chmurzynska, A., Mlodzik-Czyzewska, M. A., Galinski, G., Malinowska, A. M.,

582   Radziejewska, A., Mikołajczyk-Stecyna, J., Bulczak, E., & Wiebe, D. J. (2020).

583   Polymorphism of CD36 Determines Fat Discrimination but Not Intake of High-Fat Food

584   in 20- to 40-Year-Old Adults. *The Journal of Nutrition*, 1–7.

585   https://doi.org/10.1093/jn/nxaa136

586 Choi, S. E., & Chan, J. (2015). Relationship of 6-n-propylthiouracil taste intensity and chili

587   pepper use with body mass index, energy intake, and fat intake within an ethnically

588   diverse population. *Journal of the Academy of Nutrition and Dietetics*, *115*(3), 389–396.

589   https://doi.org/10.1016/j.jand.2014.09.001

590 Costanzo, A., Liu, D., Nowson, C., Duesing, K., Archer, N., Bowe, S., & Keast, R. (2019). A

591   low-fat diet up-regulates expression of fatty acid taste receptor gene FFAR4 in

592   fungiform papillae in humans: a co-twin randomised controlled trial. *BRITISH*

593   *JOURNAL OF NUTRITION*, *122*(11), 1212–1220.

594   https://doi.org/10.1017/S0007114519002368

595 Daoudi, H., Plesník, J., Sayed, A., Šerý, O., Rouabah, A., Rouabah, L., & Khan, N. A.

596   (2015). Oral Fat Sensing and CD36 Gene Polymorphism in Algerian Lean and Obese

597   Teenagers. *Nutrients*, *7*(11), 9096–9104. https://doi.org/10.3390/nu7115455

598 Dotson, C. D., Shaw, H. L., Mitchell, B. D., Munger, S. D., & Steinle, N. I. (2010). Variation

599   in the gene TAS2R38 is associated with the eating behavior disinhibition in Old Order

600   Amish women. *Appetite*, *54*(1), 93–99. https://doi.org/10.1016/j.appet.2009.09.011

601 Drewnowski, A., Henderson, S. A., Levine, A., & Hann, C. (1999). Taste and food

602   preferences as predictors of dietary practices in young women. In *Public Health*

603   *Nutrition* (Vol. 2, Issue 4). https://www.cambridge.org/core.

604 Drewnowski, A., Henderson, S. A., Shore, A. B., & Barratt-Fornell, A. (1998). Sensory

605   responses to 6-n-propylthiouracil (PROP) or sucrose solutions and food preferences in

606   young women. *Annals of the New York Academy of Sciences*, *855*, 797–801.

607   https://doi.org/10.1111/j.1749-6632.1998.tb10661.x

608 Duffy, V. B. (2004). Associations between oral sensation, dietary behaviors and risk of

609   cardiovascular disease (CVD). *Appetite*, *43*(1), 5–9.

610   https://doi.org/10.1016/j.appet.2004.02.007

611 Duffy, V. B., & Bartoshuk, L. M. (2000). Food acceptance and genetic variation in taste.

612 *Journal of the American Dietetic Association*, *100*(6), 647–655.

613 https://doi.org/10.1016/S0002-8223(00)00191-7

614 El-Sohemy, A., Stewart, L., Khataan, Ln., Fontaine-Bisson, B., Kwong, P., Ozsungur, S., &

615 Cornelis, M. C. (2007). Nutrigenomics of Taste – Impact on Food Preferences and Food

616 Production. In *Nutrigenomics - Opportunities in Asia* (Vol. 60, pp. 176–182). KARGER.

617 https://doi.org/10.1159/000107194

618 El-Yassimi, A., Hichami, A., Besnard, P., & Khan, N. A. (2008). Linoleic acid induces

619 calcium signaling, Src kinase phosphorylation, and neurotransmitter release in mouse

620 CD36-positive gustatory cells. *Journal of Biological Chemistry*, *283*(19), 12949–12959.

621 https://doi.org/10.1074/jbc.M707478200

622 Fujii, R., Hishida, A., Suzuki, K., Imaeda, N., Goto, C., Hamajima, N., Wakai, K., & Kondo,

623 T. (2019). Cluster of differentiation 36 gene polymorphism (rs1761667) is associated

624 with dietary MUFA intake and hypertension in a Japanese population. *British Journal of*

625 *Nutrition*, *121*(11), 1215–1222. https://doi.org/10.1017/S0007114519000679

626 Ghosh, A., Murugesan, G., Chen, K., Zhang, L., Wang, Q., Febbraio, M., Anselmo, R. M.,

627 Marchant, K., Barnard, J., & Silverstein, R. L. (2011). Platelet CD36 surface expression

628 levels affect functional responses to oxidized LDL and are associated with inheritance of

629 specific genetic polymorphisms. *Blood*, *117*(23), 6355–6366.

630 https://doi.org/10.1182/blood-2011-02-338582

631 Graham, C. A.-M., Pilic, L., King, A., Nixon, J. E., Pipe, J., Holton, J., Tamba, K., Hearne,

632 G., Pedlar, C. R., Lorente-Cebrián, S., González Muniesa, P., & Mavrommatis, Y.

633 (2021). Genetic differences in fat taste sensitivity and dietary intake in a UK female

634 cohort. *Food Quality and Preference*, 104202.

635 https://doi.org/10.1016/j.foodqual.2021.104202

636 Grimaldi, K. A., van Ommen, B., Ordovas, J. M., Parnell, L. D., Mathers, J. C., Bendik, I.,

637 Brennan, L., Celis-Morales, C., Cirillo, E., Daniel, H., de Kok, B., El-Sohemy, A.,

638 Fairweather-Tait, S. J., Fallaize, R., Fenech, M., Ferguson, L. R., Gibney, E. R., Gibney,

639 M., Gjelstad, I. M. F., … Bouwman, J. (2017). Proposed guidelines to evaluate scientific

640 validity and evidence for genotype-based dietary advice. *Genes and Nutrition*, *12*(1), 1–

641 12. https://doi.org/10.1186/s12263-017-0584-0

642 Haryono, R. Y., Sprajcer, M. A., & Keast, R. S. J. (2014). Measuring oral fatty acid

643 thresholds, fat perception, fatty food liking, and papillae density in humans. *Journal of*

Visualized Experiments : JoVE, 88. https://doi.org/10.3791/51236

Hayes, J. E., Allen, A. L., & Bennett, S. M. (2013). Direct comparison of the generalized visual analog scale (gVAS) and general labeled magnitude scale (gLMS). *Food Quality and Preference*, *28*(1), 36–44. https://doi.org/10.1016/j.foodqual.2012.07.012

Hayes, J. E., Bartoshuk, L. M., Kidd, J. R., & Duffy, V. B. (2008). *Supertasting and PROP bitterness depends on more than the TAS2R38 gene*. CHEMICAL SENSES. https://pubmed.ncbi.nlm.nih.gov/18209019/

Hayes, J. E., & Duffy, V. B. (2007). Revisiting Sugar-Fat Mixtures: Sweetness and Creaminess Vary with Phenotypic Markers of Oral Sensation. *Chem. Senses*. https://doi.org/10.1093/chemse/bjl050

Ikeda, K. (1909). New Seasonings. *Journal of the Chemical Society of Tokyo*, *30*, 820–836.

Jeon, T. Il, Zhu, B., Larson, J. L., & Osborne, T. F. (2008). SREBP-2 regulates gut peptide secretion through intestinal bitter taste receptor signaling in mice. *Journal of Clinical Investigation*, *118*(11), 3693–3700. https://doi.org/10.1172/JCI36461

Karmous, I., Plesník, J., Khan, A. S., Šerý, O., Abid, A., Mankai, A., Aouidet, A., & Khan, N. A. (2018). Orosensory detection of bitter in fat-taster healthy and obese participants: Genetic polymorphism of CD36 and TAS2R38. *Clinical Nutrition*, *37*(1), 313–320. https://doi.org/10.1016/j.clnu.2017.06.004

Keller, K. L. (2012). Genetic influences on oral fat perception and preference: Presented at the symposium "The Taste for Fat: New Discoveries on the Role of Fat in Sensory Perception, Metabolism, Sensory Pleasure and Beyond" held at the Institute of Food Technologists 2011 Annual Meeting, New Orleans, LA, June 12, 2011. *Journal of Food Science*, *77*(3), S143-7. https://doi.org/10.1111/j.1750-3841.2011.02585.x

Keller, K. L., Liang, L. C. H., Sakimura, J., May, D., van Belle, C., Breen, C., Driggin, E., Tepper, B. J., Lanzano, P. C., Deng, L., & Chung, W. K. (2012). Common variants in the CD36 gene are associated with oral fat perception, fat preferences, and obesity in African Americans. *Obesity (Silver Spring, Md.)*, *20*(5), 1066–1073. https://doi.org/10.1038/oby.2011.374

Khan, A. S., Keast, R., & Khan, N. A. (2020). Progress in Lipid Research Preference for dietary fat : From detection to disease. *Progress in Lipid Research*, *78*(March), 101032. https://doi.org/10.1016/j.plipres.2020.101032

675 Khataan, N. H., Stewart, L., Brenner, D. M., Cornelis, M. C., & El-Sohemy, A. (2010).

676   TAS2R38 genotypes and phenylthiocarbamide bitter taste perception in a population of

677   young adults. *Journal of Nutrigenetics and Nutrigenomics*, *2*(4–5), 251–256.

678   https://doi.org/10.1159/000297217

679 Kim, Un kyung, Jorgenson, E., Coon, H., Leppert, M., Risch, N., & Drayna, D. (2003).

680   Positional cloning of the human quantitative trait locus underlying taste sensitivity to

681   phenylthiocarbamide. *Science*, *299*(5610), 1221–1225.

682   https://doi.org/10.1126/science.1080190

683 Kim, Unkyung, Wooding, S., Ricci, D., Jorde, L. B., & Drayna, D. (2005). Worldwide

684   haplotype diversity and coding sequence variation at human bitter taste receptor loci.

685   *Human Mutation*, *26*(3), 199–204. https://doi.org/10.1002/humu.20203

686 Lawless, H. (1980). A comparison of different methods used to assess sensitivity to the taste

687   of phenylthiocarbamide (PTC). *Chemical Senses*, *5*(3), 247–256.

688   https://doi.org/10.1093/chemse/5.3.247

689 Love-Gregory, L., & Abumrad, N. A. (2011). CD36 genetics and the metabolic

690   complications of obesity. *CURRENT OPINION IN CLINICAL NUTRITION AND*

691   *METABOLIC CARE*, *14*(6), 527–534. https://doi.org/10.1097/MCO.0b013e32834bbac9

692 Mattes, R. D. (2010). Fat Taste in Humans: Is it a Primary? In *Fat Detection: Taste, Texture,*

693   *and Post Ingestive Effects* (pp. 167–193). CRC Press.

694   https://books.google.co.uk/books?hl=en&lr=&id=jSb7aQxm9UEC&oi=fnd&pg=PA167

695   &dq=mattes+fat+taste+is+it+a+primary&ots=JhFBAO1mjf&sig=L5t_RFCy36IKWRG

696   k_bYEKLo1xEc&redir_esc=y#v=onepage&q=mattes fat taste is it a primary&f=false

697 Melis, M., Atzori, E., Cabras, S., Zonza, A., Calò, C., Muroni, P., Nieddu, M., Padiglia, A.,

698   Sogos, V., Tepper, B. J., & Tomassini Barbarossa, I. (2013). The Gustin (CA6) Gene

699   Polymorphism, rs2274333 (A/G), as a Mechanistic Link between PROP Tasting and

700   Fungiform Taste Papilla Density and Maintenance. *PLoS ONE*, *8*(9), e74151.

701   https://doi.org/10.1371/journal.pone.0074151

702 Melis, M., Carta, G., Pintus, S., Pintus, P., Piras, C. A., Murru, E., Manca, C., Di Marzo, V.,

703   Banni, S., & Tomassini Barbarossa, I. (2017). Polymorphism rs1761667 in the CD36

704   Gene Is Associated to Changes in Fatty Acid Metabolism and Circulating

705   Endocannabinoid Levels Distinctively in Normal Weight and Obese Subjects. *Frontiers*

706   *in Physiology*, *8*, 1006. https://doi.org/10.3389/fphys.2017.01006

707 Melis, M., Mastinu, M., Sollai, G., Paduano, D., Chicco, F., Magrì, S., Usai, P., Crnjar, R.,
708   Tepper, B. J., & Barbarossa, I. T. (2020). Taste changes in patients with inflammatory
709   bowel disease: Associations with PROP phenotypes and polymorphisms in the salivary
710   protein, gustin and CD36 receptor genes. *Nutrients*, *12*(2), 1–17.
711   https://doi.org/10.3390/nu12020409

712 Melis, M., Sollai, G., Muroni, P., Crnjar, R., & Barbarossa, I. T. (2015). Associations
713   between orosensory perception of oleic acid, the common single nucleotide
714   polymorphisms (rs1761667 and rs1527483) in the CD36 gene, and 6-n-propylthiouracil
715   (PROP) tasting. *Nutrients*, *7*(3), 2068–2084. https://doi.org/10.3390/nu7032068

716 Mozaffarian, D., Micha, R., & Wallace, S. (2010). Effects on coronary heart disease of
717   increasing polyunsaturated fat in place of saturated fat: A systematic review and meta-
718   analysis of randomized controlled trials. *PLoS Medicine*, *7*(3).
719   https://doi.org/10.1371/journal.pmed.1000252

720 Mrizak, I., Šerý, O., Plesnik, J., Arfa, A., Fekih, M., Bouslema, A., Zaouali, M., Tabka, Z., &
721   Khan, N. A. (2015). The A allele of cluster of differentiation 36 (CD36) SNP 1761667
722   associates with decreased lipid taste perception in obese Tunisian women. *The British*
723   *Journal of Nutrition*, *113*(8), 1330–1337. https://doi.org/10.1017/S0007114515000343

724 Mulligan, A. A., Luben, R. N., Bhaniani, A., Parry-Smith, D. J., O'Connor, L., Khawaja, A.
725   P., Forouhi, N. G., & Khaw, K. T. (2014). A new tool for converting food frequency
726   questionnaire data into nutrient and food group values: FETA research methods and
727   availability. *BMJ Open*, *4*(3). https://doi.org/10.1136/bmjopen-2013-004503

728 Newman, L. P., Bolhuis, D. P., Torres, S. J., & Keast, R. S. J. (2016). Dietary fat restriction
729   increases fat taste sensitivity in people with obesity. *Obesity*, *24*(2), 328–334.
730   https://doi.org/10.1002/oby.21357

731 Newman, L. P., & Keast, R. S. J. (2013). The test-retest reliability of fatty acid taste
732   thresholds. *Chemosensory Perception*, *6*(2), 70–77. https://doi.org/10.1007/s12078-013-
733   9143-2

734 O'Brien, S. A., Feeney, E. L., Scannell, A. G. M., Markey, A., & Gibney, E. R. (2013). Bitter
735   taste perception and dietary intake patterns in Irish children. *Journal of Nutrigenetics*
736   *and Nutrigenomics*, *6*(1), 43–58. https://doi.org/10.1159/000348442

737 Pepino, M. Y., Love-Gregory, L., Klein, S., & Abumrad, N. A. (2012). The fatty acid

738   translocase gene CD36 and lingual lipase influence oral sensitivity to fat in obese

739   subjects. *Journal of Lipid Research*, *53*(3), 561–566.

740   https://doi.org/10.1194/jlr.M021873

741   Pioltine, M. B., de Melo, M. E., Santos, A., Machado, A. D., Fernandes, A. E., Fujiwara, C.

742   T., Cercato, C., & Mancini, M. C. (2016). Genetic Variation in CD36 Is Associated with

743   Decreased Fat and Sugar Intake in Obese Children and Adolescents. *Journal of*

744   *Nutrigenetics and Nutrigenomics*, *9*(5–6), 300–305. https://doi.org/10.1159/000455915

745   Ramos-Lopez, O., Roman, S., Martinez-Lopez, E., Fierro, N. A., Gonzalez-Aldaco, K., Jose-

746   Abrego, A., & Panduro, A. (2016). CD36 genetic variation, fat intake and liver fibrosis

747   in chronic hepatitis C virus infection. *World Journal of Hepatology*, *8*(25), 1067–1074.

748   https://doi.org/10.4254/wjh.v8.i25.1067

749   Risso, D. S., Mezzavilla, M., Pagani, L., Robino, A., Morini, G., Tofanelli, S., Carrai, M.,

750   Campa, D., Barale, R., Caradonna, F., Gasparini, P., Luiselli, D., Wooding, S., &

751   Drayna, D. (2016). Global diversity in the TAS2R38 bitter taste receptor: Revisiting a

752   classic evolutionary PROPosal. *Scientific Reports*, *6*. https://doi.org/10.1038/srep25506

753   Roura, E., Aldayyani, A., Thavaraj, P., Prakash, S., Greenway, D., Thomas, W. G.,

754   Meyerhof, W., Roudnitzky, N., & Foster, S. R. (2015). Variability in human bitter taste

755   sensitivity to chemically diverse compounds can be accounted for by differential TAS2R

756   activation. *Chemical Senses*, *40*(6), 427–435. https://doi.org/10.1093/chemse/bjv024

757   Rozengurt, E. (2006). Taste receptors in the gastrointestinal tract. I. Bitter taste receptors and

758   α-gustducin in the mammalian gut. *American Journal of Physiology - Gastrointestinal*

759   *and Liver Physiology*, *291*(2), 171–177. https://doi.org/10.1152/ajpgi.00073.2006

760   Sayed, A, Šerý, O., Plesnik, J., Daoudi, H., Rouabah, A., Rouabah, L., & Khan, N. A. (2015).

761   CD36 AA genotype is associated with decreased lipid taste perception in young obese,

762   but not lean, children. *International Journal of Obesity (2005)*, *39*(6), 920–924.

763   https://doi.org/10.1038/ijo.2015.20

764   Sayed, Amira, & Khan, N. A. (2015). Is the single nucleotide polymorphism (SNP) of CD36,

765   a lipid-receptor, a predictor of obesity in adulthood ? *M S-MEDECINE SCIENCES*,

766   *31*(12), 1072–1074. https://doi.org/10.1051/medsci/20153112008

767   Shen, Y., Kennedy, O. B., & Methven, L. (2017). The effect of genotypical and phenotypical

768   variation in taste sensitivity on liking of ice cream and dietary fat intake. *Food Quality*

769   *and Preference*, *55*, 79–90. https://doi.org/10.1016/j.foodqual.2016.08.010

770   Sollai, G., Melis, M., Mastinu, M., Pani, D., Cosseddu, P., Bonfiglio, A., Crnjar, R., Tepper,

771   B. J., & Barbarossa, I. T. (2019). Human tongue electrophysiological response to oleic

772   acid and its associations with PROP taster status and the CD36 polymorphism

773   (rs1761667). *Nutrients*, *11*(2). https://doi.org/10.3390/nu11020315

774   Tepper, B. J. (2008). Nutritional Implications of Genetic Taste Variation: The Role of PROP

775   Sensitivity and Other Taste Phenotypes. *Annual Review of Nutrition*, *28*(1), 367–388.

776   https://doi.org/10.1146/annurev.nutr.28.061807.155458

777   Tepper, B. J., Koelliker, Y., Zhao, L., Ullrich, N. V., Lanzara, C., D'Adamo, P., Ferrara, A.,

778   Ulivi, S., Esposito, L., & Gasparini, P. (2008). Variation in the bitter-taste receptor gene

779   TAS2R38, and adiposity in a genetically isolated population in southern Italy. *Obesity*,

780   *16*(10), 2289–2295. https://doi.org/10.1038/oby.2008.357

781   Tepper, B. J., & Nurse, N. J. (2006). Prop taster status is related to fat perception and

782   preference. *Annals of the New York Academy of Sciences*, 5.

783   Tepper, B. J., & Nurse, R. J. (1997). Fat perception is related to PROP taster status.

784   *Physiology and Behavior*, *61*(6), 949–954. https://doi.org/10.1016/S0031-

785   9384(96)00608-7

786   Tepper, B. J., & Nurse, R. J. (1998). PROP taster status is related to fat perception and

787   preference. *Annals of the New York Academy of Sciences*, *855*, 802–804.

788   https://doi.org/10.1111/j.1749-6632.1998.tb10662.x

789   Timpson, N. J., Christensen, M., Lawlor, D. A., Gaunt, T. R., Day, I. N., Ebrahim, S., &

790   Smith, G. D. (2005). TAS2R38 (phenylthiocarbamide) haplotypes, coronary heart

791   disease traits, and eating behavior in the British Women's Heart and Health Study.

792   *American Journal of Clinical Nutrition*, *81*(5), 1005–1011.

793   https://doi.org/10.1093/ajcn/81.5.1005

794   Tucker, R. M., Kaiser, K. A., Parman, M. A., George, B. J., Allison, D. B., & Mattes, R. D.

795   (2017). *Comparisons of Fatty Acid Taste Detection Thresholds in People Who Are Lean*

796   *vs. Overweight or Obese: A Systematic Review and Meta-Analysis*.

797   https://doi.org/10.1371/journal.pone.0169583

798   Tucker, R. M., & Mattes, R. D. (2013). Influences of Repeated Testing on Nonesterified

799   Fatty Acid Taste. *Chem. Senses*, *38*, 325–332. https://doi.org/10.1093/chemse/bjt002

800   Williams, J. A., Bartoshuk, L. M., Fillingim, R. B., & Dotson, C. D. (2016). Exploring Ethnic
801   Differences in Taste Perception. *Chemical Senses*, *41*(5), 449–456.
802   https://doi.org/10.1093/chemse/bjw021

803   World Health Organisation. (2020, April 29). *Healthy diet*. Fact Sheet.
804   https://www.who.int/news-room/fact-sheets/detail/healthy-diet

805   Yang, Q., Williamson, A. M., Hasted, A., & Hort, J. (2020). Exploring the relationships
806   between taste phenotypes, genotypes, ethnicity, gender and taste perception using Chi-
807   square and regression tree analysis. *Food Quality and Preference*, *83*, 103928.
808   https://doi.org/10.1016/j.foodqual.2020.103928

809   Zhou, X., Yeomans, M., Thomas, A., Wilde, P., Linter, B., & Methven, L. (2020). Individual
810   differences in oral tactile sensitivity and gustatory fatty acid sensitivity and their
811   relationship with fungiform papillae density, mouth behaviour and texture perception of
812   a food model varying in fat. *Food Quality and Preference*, *90*, 104116.
813   https://doi.org/10.1016/j.foodqual.2020.104116

814 **Tables**

Table 1. Participant characteristics (n = 88, n = 69). Data presented as mean ± SEM, median (IQR) or absolute (relative) frequencies

	All participants (n = 88)	Fat-tasters only* (n = 69)
Age (years)	35 ± 1	34.7 ± 1.7
BMI (kg/m²)	24.9 ± 0.5	25.0 ± 0.6
18.5-24.9 kg/m2 n (%)	49 (56)	41 (59)
≥25.0 kg/m2 n (%)	39 (44)	28 (41)
Sex n (%)		
Female	49 (56)	40 (58)
Male	39 (44)	29 (42)
Bitter taste intensity rating m (IQR)	6 (18.5)	8 (27.5)
Fat taste category n (%)		
Hyposensitive	42 (48)	42 (48)
Hypersensitive	27 (31)	27 (31)
Non-taster	19 (21)	-
Energy (kcal)	1656 ± 79	1709 ± 94
Carbohydrate (%TEI)	43.6 ± 0.8	44.4 ± 0.9
Protein (%TEI)	19.3 ± 0.3	19.2 ± 0.4
Total fat (%TEI)	37.5 ± 0.6	37.2 ± 0.7
MUFA (%TEI)	14.1 ± 0.3	14.1 ± 0.4
PUFA (%TEI)	6.6 ± 0.2	6.7 ± 0.3
SFA (%TEI)	13.3 ± 0.2	13.1 ± 0.3

815 *Body mass index (BMI), Interquartile range (IQR), Median (m), Monounsaturated fatty acids (MUFA),*
816 *Polyunsaturated fatty acids (PUFA), Saturated fatty acids (SFA), Total energy intake (TEI). **
817 *Participants with a defined fat taste threshold.*
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Table 2. Energy and macronutrient intakes according to *TAS2R38* diplotypes (n = 88). Data presented as mean ± SEM (One-way ANOVA)

	PAV/PAV (n = 13)	AVI/PAV (n = 41)	AVI/AVI (n = 24)	PAV/AAV (n = 3)	AVI/AAV (n = 7)	p-value
Energy (kcal)	1794 ± 224	1683 ± 137	1512 ± 89	1458 ± 100	1814 ± 289	0.666
Protein (%TEI)	20.4 ± 0.7	19.2 ± 0.6	19.0 ± 0.7	20.7 ± 2	18.9 ± 1.8	0.735
CHO (%TEI)	45. 1 ± 1.5	43.2 ± 1.3	42.3 ± 1.6	48.3 ± 4.5	44.9 ± 2.9	0.631
Total fat (%TEI)	35.2 ± 1.4	37.9 ± 1.1	38.4 ± 1.3	34.0 ± 4.2	37.4 ± 1.3	0.493
SFA (%TEI)	12.5 ± 0.7	13.5 ± 0.4	14.2 ± 0.6	10.0 ± 0.6	12.9 ± 0.6	0.082
MUFA (%TEI)	13.2 ± 0.6	14.4 ± 0.5	14.4 ± 0.6	14.0 ± 2.5	14.4 ± 0.5	0.613
PUFA (%TEI)	6.2 ± 0.3	6.8 ± 0.4	6.6. ± 0.3	6.7 ± 0.7	6.6. ± 0.5	0.928

Carbohydrate (CHO), Monounsaturated fatty acids (MUFA), Polyunsaturated fatty acids (PUFA), Saturated fatty acids (SFA), Taste 2 receptor member 38 (TAS2R38), Total energy intake (TEI).

Table 3. Energy and macronutrient intakes according to *CD36* rs1761667 (n=69). Data presented as mean ± SEM. Kruskal-Wallis, Independent T-test or Man Whitney U test where appropriate.

	AA (n = 29)	AG (n = 29)	GG (n = 11)	AA/AG (n = 58)	p-value[1]	p-value[2]
Energy (kcal)	1803 ± 152	1631 ± 156	1670 ± 150	1717 ± 109	0.416	0.611
Protein (%TEI)	19.1 ± 0.6	19.3 ± 0.7	19.1 ± 0.9	19.2 ± 2.2	0.952	0.786
CHO (%TEI)	44.7 ± 1.4	43.9 ± 1.3	45.2 ± 2.2	44.3 ± 0.9	0.846	0.703
Total fat (%TEI)	36.9 ± 1.3	37.9 ± 1.0	36.0 ± 1.7	37.4 ± 1.7	0.453	0.458
SFA (%TEI)	12.5 ± 0.5	13.8 ± 0.4	12.9 ± 1.0	13.2 ± 0.3	0.156	0.762
MUFA (%TEI)	14.2 ± 0.5	14.2 ± 0.6	13.7 ± 0.7	14.2 ± 0.3	0.869	0.811
PUFA (%TEI)	7.0 ± 0.5	6.5 ± 0.5	6.0 ± 0.3	6.8 ± 0.3	0.514	0.312

Cluster of differentiation 36 (CD36), Carbohydrate (CHO), Monounsaturated fatty acids (MUFA), Polyunsaturated fatty acids (PUFA), Saturated fatty acids (SFA), Total energy intake (TEI), p-value [1] difference in diet between three genotypes (AA, AG, GG), p-value [2] difference in diet between two genotypes (AA/AG and GG).

Supplementary Table 1. Genotype/Diplotype Frequency of Fat Non-Tasters (n = 19)

CD36 rs1761667, n (%)	
AA	6 (32)
AG	8 (42)
GG	5 (26)
TAS2R38 Diplotype, n (%)	
PAV/PAV	0 (0)
AVI/PAV	7 (37)
AVI/AVI	10 (53)
PAV/AAV	0 (0)
AVI/AAV	2 (10)

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Supplementary Table 2. Dietary fat intake and BMI according to *CD36*/*TAS2R38* combined genotypes/diplotypes (n = 88). Data presented as mean ± SEM. Independent T-test or Man Whitney U test where appropriate.

	Non-taster (n = 58)	**Taster (n = 30)**	**p-value**
BMI (kg/m^2)	24.7 ± 0.6	25.4 ± 0.9	0.747
Total fat (%TEI)	38.3 ± 0.9	35.9 ± 0.9	0.085
SFA (%TEI)	13.8 ± 0.3	12.6 ± 0.5	0.047
MUFA (%TEI)	14.5 ± 0.4	13.6 ± 0.4	0.290
PUFA (%TEI)	6.8 ± 0.3	6.3 ± 0.2	0.766

Body mass index (BMI), Cluster of differentiation 36 (CD36), Monounsaturated fatty acids (MUFA), Polyunsaturated fatty acids (PUFA), Saturated fatty acids (SFA), Taste 2 receptor member 38 (TAS2R38), Total energy intake (TEI). Non-taster: (AA/AG + AVI/AVI, AVI/PAV, AVI/AAV); Taster: (carriers of either GG or PAV/PAV, PAV/AAV).

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Supplementary Table 3. Fat taste threshold (mM) according to *CD36* genotypes and *TAS2R38* diplotypes (n = 69). Data presented as median (IQR), Kruskal-Wallis H test with Bonferroni adjustment for multiple comparisons*.

	Fat taste threshold (mM)	p-value
CD36 **genotypes**		
GG (n = 11)	2.0 (4.0)	0.019*
AG (n = 29)	5.0 (6.0)	
AA (n = 29)	5.0 (5.4)	
AA/AG (n= 58)	5.0 (6.0)	
TAS2R38 **diplotypes**		
PAV/PAV (n = 13)	5.0 (3.5)	0.732
AVI/PAV (n = 31)	3.8 (7.0)	
AVI/AVI (n = 17)	5.0 (7.4)	
PAV/AAV (n = 3)	6.4 (0.0)	
AVI/AAV (n = 5)	5.0 (11.3)	

* GG vs AG (p = 0.23), GG vs AA (p = 0.594), AA vs AG (p = 0.190). Interquartile range (IQR).

Figure legends

Figure 1. Genetics and taste sensitivity
(A) *TAS2R38 diplotypes and bitter taste sensitivity; total n = 88, PAV/PAV = 13, AVI/PAV = 41, AVI/AVI = 24, PAV/AAV = 3, AVI/AAV = 7, a: different than PAV/PAV (AVI/AVI, p = $1x10^{-6}$; AVI/AAV, p = 0.029), b: different than AVI/AVI (p = 0.002). Line represents the median and whiskers min and max values, Kruskal-Wallis H test with Bonferroni adjusted p values.*
(B) *CD36* rs1761667 and fat taste sensitivity, total n = 69, AA = 29, AG = 29, GG = 11, * p = *0.008, Fischer's Exact test.*
Cluster of differentiation 36 (CD36), Taste 2 receptor member 38 (TAS2R38).

Figure 2. The correlations between bitter taste sensitivity (PTC intensity rating) and dietary fat intake (n = 88); *Phenylthiocarbamyde (PTC), total energy intake (TEI). Spearman's correlation.*

Figure 3. The correlations between fat taste threshold and dietary fat intake (n = 69). Oleic acid concentrations/fat taste threshold was: 0.02, 0.06, 1, 1.4, 2, 2.8, 3.8, 5, 6.4, 8, 9.8, 12 and 20 mM. *Total energy intake (TEI). Spearman's correlation.*

Figure 4. Difference in dietary fat intake according to bitter taster status in A) fat hypersensitive taster (total n = 27, bitter taster = 9, bitter non-taster = 18) and B) fat hyposensitive taster group (total n = 40, bitter taster = 14, bitter non-taster = 26). *Error bars represent ± SEM.*

Supplementary Figure 1. *CD36* rs1761667 and fat taste sensitivity; *total n = 88, AA = 35, AG = 37, GG = 16, Fischer's Exact test, p = 0.033 (no longer significant after Bonferroni correction applied). Cluster of differentiation 36 (CD36).*