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1 **CD36 gene polymorphism -31118 G>A (rs1761667) is associated with overweight and obesity**
2 **but not with fat preferences in Mexican children**

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14 **Running title:** CD36 SNP, fat preferences and obesity in Mexican children

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23 **Abstract**

24 CD36 glycoprotein is a candidate receptor involved in the gustatory detection of lipids and
25 emerging evidence has suggested that genetic variations in *CD36* may modulate the oral
26 perception threshold to fatty acids. Here, we analyzed the association of -31118 G>A
27 polymorphism in *CD36* gene with nutritional status and preferences for fatty foods in Mexican
28 children. Genotyping of SNP rs1761667 was performed in school-age children (n= 63) in addition
29 to sensory tests evaluating the preference and satisfaction score assigned to oil-based sauces of
30 different fatty acid composition. The G allele was associated with high BMI z-score in children
31 (OR = 2.43, 95% (CI 1.02-5.99); p = 0.02) but *CD36* genotypes (AA, GA, and GG) did not show
32 significant association with the preference and satisfaction scores assigned to oil-based sauces.
33 The BMI z-score showed no association with the preference to oil-based sauces; however,
34 children with normal weight gave higher satisfaction scores to sauces with a high content of
35 unsaturated fatty acids than to sauces rich in saturated fatty acids (0.56 ± 1.26 vs. 0.06 ± 1.22 ; p
36 = 0.02). Therefore, the G allele of -31118 G>A SNP in *CD36* gene is associated with overweight
37 and obesity in Mexican children but do not appear to modulate the preferences and satisfaction
38 scores to fat.

39 **Keywords:** childhood obesity, CD36 polymorphism, olive oil, avocado oil, fat food preferences.

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46 **Introduction**

47 Childhood obesity has reached an alarming prevalence worldwide to the point of becoming an
48 epidemic [1]. Mexico is ranked among the leading countries with the highest prevalence of
49 overweight and obesity in children with an estimated prevalence of 33% [2]. This condition
50 often has a harmful effect on health in adulthood as epidemiological studies have shown an
51 association of early obesity with an excess mortality rate in adults (from 50 to 80%). In obese
52 children, several short-term pathologies appear, such as hyperinsulinemia, increased blood
53 pressure and abnormalities of blood lipids, including hypertriglyceridemia, decreased high-
54 density lipoprotein cholesterol (HDL-cho), respiratory difficulties as well as psychological
55 problems [3]. The etiology of obesity is multifactorial, and includes a complex interaction of
56 environmental, behavioral and genetic factors [4], all of which, may also influence food
57 preferences and favor the development of obesity.

58 Fat is the most energy-dense macronutrient and contributes significantly to the taste and aroma
59 of food. High-fat and high energy-dense foods are highly preferred by the population [5].
60 Furthermore, the western diet, which is characterized by a high consumption of processed
61 foods rich in sugars and saturated fats, has been linked to the alarming rise in the prevalence of
62 obesity [6]. There is evidence showing that people with a high body mass index (BMI) prefer
63 foods high in fat and sugar content and have a lower oral detection threshold for fatty acids
64 than individuals with normal BMI [7–10].

65 Recently, both the CD36 glycoprotein and the G protein-coupled receptor GPR120 have
66 emerged as candidate receptors involved in the gustatory detection of lipids. CD36 participates

67 in several physiological process such as inflammation, innate immune responses,
68 atherosclerosis, angiogenesis, lipid metabolism among others [11], but has been implicated in
69 the orosensory detection of fat foods as it exhibits a strong affinity to long-chain fatty acids [12]
70 and is expressed in circumvallate taste buds and to a lesser extent in fungiform taste buds [13].
71 In addition, a single nucleotide polymorphism (SNP) in *CD36* gene (rs1761667) at position -
72 31118 G>A is suggested to modulate the oral perception threshold to fatty acids. In particular,
73 the G allele was related to lower oral detection thresholds to some fatty acids [9], whereas the
74 A allele was associated with lower CD36 expression and decreased lipid taste perception in
75 people with obesity [14,15]. It has been hypothesized that the low perception of oral lipids may
76 lead to high consumption and preference for rich fat foods [16,17], and in turn, oral fatty acid
77 hypersensitivity is associated with lower energy and fat intakes and lower body weight [18,19].
78 The AA genotype of rs1761667 in *CD36* was significantly associated with lower BMI as compared
79 to carriers of AG and GG genotypes in adult population from Finland [20], while some other
80 studies have identified an association of this polymorphism with obesity [13,17,21–23]. In
81 Mexican population, rs1761667 in *CD36* was studied in relationship to cardiovascular and liver
82 diseases in adult population [24,25], however, there is no data on its relationship with
83 childhood obesity and fat preferences.

84 In recent years, the food industry has broadened the options regarding cooking oils, offering
85 some extracted from fruits and seeds such as avocado and coconut [26]. Both olive and avocado
86 oil are rich in unsaturated fatty acids such as linoleic and linolenic acid, which have been
87 associated with reduced risk of cardiovascular disease and cancer [27]. Also, Mexico is among
88 the top ten producers of coconut and the production and commercialization of coconut-oil has

89 increased in the last five years [28]. This oil is rich in lauric acid (saturated fatty acid, SFA) and
90 medium-chain fatty acids (MCFAs) and it has been suggested for the treatment of obesity
91 because these lipids oxidize easily and are not normally stored in adipose tissue, thus decreasing
92 the basal metabolic rate [29]. However, the use of coconut oil in the diet remains controversial
93 due to the possible detrimental effects of SFA and its association with dyslipidemias and
94 cardiovascular diseases [30].

95 Therefore, we performed this study with the aim of evaluate the association of rs1761667 in
96 *CD36* gene with body composition, fat preferences and the satisfaction scores to sauces
97 prepared with three oils of different fatty acids composition (avocado, olive, and coconut oil) in
98 Mexican children.

99 **Materials and methods**

100 **Study design**

101 This was a cross-sectional study. Participants attended a session at Instituto de Investigaciones
102 en Comportamiento Alimentario y Nutrición (IICAN), Universidad de Guadalajara. This session
103 included blood sample collection for DNA extraction, anthropometric evaluation, record of
104 socio-demographic data and application of sensory tests to assess children's preference to oil-
105 based sauces and degree of satisfaction to these.

106 **Participants**

107 Participants were recruited by invitation; elementary schools were visited and the project was
108 announced to principals, parents and children. Participants were eligible if they met the
109 following inclusion criteria: aged 7-12 years and being Mexican mestizos from the region of
110 Western Mexico (including the states of Jalisco and Colima) with auto-reported ancestry at least

111 three generations back. The exclusion criteria were food allergies to ingredients used in the
112 sensory test, signs of flu or cough, and withdrawal of informed consent and/or informed assent.
113 A total of sixty-three children (n = 63), including boys (n = 32) and girls (n = 41) were enrolled in
114 the study.

115 The parents of the participants gave their written informed consent prior to participation,
116 whereas children signed an informed assent. The research protocol was approved by the
117 Research Ethics Committee of the University of Guadalajara (CIEUC, Review Board registry
118 CUCPV/CEICUC/2018/002) and was conducted according to the principles of the declaration of
119 Helsinki.

120 **Anthropometrics**

121 All anthropometric measurements were taken without shoes and with light clothes, following
122 the International Society for the Advancement of Kinanthropometry guidelines [31]. To avoid
123 subjective error, all measurements were taken by the same person. Height was measured using
124 a portable stadiometer (SmartMet, Michigan, USA). Weight and the percentage of body fat
125 were measured by a bioelectrical impedance equipment (Tanita, Tokyo, Japan). The waist
126 circumference was measured in the standing position, just above the iliac crest with an
127 anthropometric tape (Hoechstmass, Sulzbach, Germany); hip circumference was measured at
128 the widest portion of the buttocks. The waist-hip ratio was calculated as waist circumference
129 divided by hip circumference. BMI z-score was calculated using the children's weight and height
130 using the BMI z-score calculation table established by the WHO for children and adolescents
131 from 5 to 19 years old. Classification of the children was as follows: adequate nutritional status
132 (from -2 to +1 SD); overweight (>+1.00 to +1.99 SD) and obesity (≥ 2.00 SD).

133 **DNA collection and genotyping**

134 Peripheral blood samples were taken in 5% EDTA-anticoagulant tubes (BD Vacutainer, Franklin
135 Lakes, NJ). The DNA extraction was performed according the manufacturer's instructions using
136 the QIAamp DNA Blood Mini Kit (QIAGEN, Hilden, Germany). The concentration and quality of
137 extracted DNA was measured using Nanodrop spectrophotometer (ThermoFisher Scientific,
138 Massachusetts, USA). Samples were stored at -20 °C for future use.

139 Genotypes rs1761667 SNP in *CD36* were obtained using the polymerase chain reaction-
140 restriction fragment length polymorphism (PCR-RFLP) using primers with the following
141 sequence: forward 5'-CAA AAT CAC AAT CTA TTC AAG ACC A - 3' and reverse 5'-TTT TGG GAG
142 AAA TTC TGA AGA G - 3' (Integrated DNA Technologies, Iowa, USA). The PCR-mixture was
143 composed of 1X buffer, MgCl₂ (2.5 mM), dNTP's (0.1 mM), primers (0.06 μM, each one), Taq
144 polymerase (1 U) and distilled water to reach a total volume of 25 μl with ~50 ng genomic DNA.
145 The PCR reaction was performed in a thermocycler (Swift MiniPro-Esco, Missouri, USA) under
146 the following conditions: initial denaturation at 95 °C for 5 min, followed by 35 cycles of
147 amplification including denaturation at 95 °C, annealing at 95 °C, and extension at 72 °C (each
148 comprising 30 s), and the final extension at 72 °C for 5 min.

149 PCR products (3μl) were digested with 5 U of *HhaI* restriction endonuclease (Promega,
150 Wisconsin, USA) at 37 °C for 4 h and fragments were separated by polyacrylamide gel
151 electrophoresis (6% polyacrylamide) and subsequently stained with silver nitrate. Afterwards,
152 the A allele was visualized as a single band (190 bp) and the G allele as two bands (138 and
153 52 bp).

154 **Food preference test**

155 Since oils are unfrequently consumed alone, but rather ingested as dressings or sauces
156 accompanying other foods, the oil preference test was applied using each oil (avocado, olive
157 and coconut, respectively) as a base for the preparation of three different sauces; these were
158 prepared with equal amounts of salt, vinegar, garlic, spices and herbs like basil. Each oil-based
159 sauce was served on top of a toasted bread, on a plate marked with a random number to
160 identify each food item. Children were blind to the order that foods were presented (olive,
161 avocado and coconut oil-based sauce); they were requested to taste each food item (without
162 eating everything) and between each sample, participants were asked to drink water to cleanse
163 the palate. Finally, they were requested to choose which sauce they preferred by marking with
164 an X the corresponding space in a food preference test format.

165 **Food satisfaction degree test**

166 In this test, participants were asked to rate the oil-based sauces using a hedonic five-point scale
167 with the following categories: "I like it very much" with a value of 2, "I like it" with a value of 1,
168 "I don't like it but don't disgust me" with value of 0, "I dislike" with a value of -1 and "I really
169 dislike" with a value of -2. Both, the food preference and food satisfaction degree tests were
170 carried out in the morning (from 8:00 am to 9:30 am) with overnight fasting of 8-12 h.

171 **Statistical analyses**

172 The distributions of all continuous variables were examined using the Shapiro–Wilk normality
173 test. For the descriptive analysis, continuous variables normally distributed were expressed as
174 mean \pm standard deviation (s.d.) and those non-normally distributed were expressed as median
175 and 25–75th centiles. Categorical variables were described with absolute and relative
176 (percentage) frequencies. Student's t-test or Mann–Whitney U-test were used to evaluate

177 differences on continuous variables between two groups, according to data normality. For the
178 genetic analyses, Hardy-Weinberg equilibrium was tested using a χ^2 test, and the strength of
179 association of *CD36* polymorphism with children obesity was assessed by Odds ratios (ORs) with
180 95% confidence intervals (CIs). Analyses were carried out using Stata 12.0 (StataCorp LLC, Texas,
181 USA) and GraphPad Prism 6.0 (GraphPad Software, California, USA). Statistical significance was
182 set as a p value ≤ 0.05 .

183 **Results**

184 **Sociodemographic and body composition characteristics of the participants**

185 Children were classified according to their BMI z-score as follows: normal-weight group (NW, n=
186 30) and group with overweight or obesity (OW/OB, n = 33). The sociodemographic,
187 anthropometric and clinical characteristics of study participants are presented in Table 1. As
188 expected, the OW/OB group had significantly higher measures for height, weight, BMI z-score
189 and body fat percent ($p = 0.0071$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$). However, with regard to
190 other sociodemographic factors, no significant differences were found between the two study
191 groups.

192 **Relationship between -31118 G>A polymorphism in *CD36* and children's BMI z-score**

193 Genotypic frequencies were in Hardy-Weinberg Equilibrium ($p = 0.58$) in the normal weight
194 group. Genotype and allele frequency distributions of rs1761667 among the study groups are
195 shown in Table 2. The AA genotype of *CD36* was the most frequent in the NW group, whereas in
196 the OW/OB group the most frequent genotype was GA, however, no significant differences
197 were observed when comparing the frequency of *CD36* genotypes according to participant's
198 BMI z-score ($p = 0.07$). The G allele was almost two-fold more frequent in the OW/OB group as

199 compared to the NW group (37.87% vs. 20.00%) and it was significantly associated with an
200 increased risk of having overweight or obesity (OR = 2.43 (CI 1.02-5.99); p = 0.02).

201 **Relationship between the preference to oil-based sauces and the BMI z-score**

202 To test the association between the BMI z-score and the preference to different oils, children
203 were asked to taste three sauces prepared with oils of different origin and fatty acids
204 composition (olive, coconut and avocado oil) and select the preferred oil-based sauce. The
205 results of food preference test showed that 50% of children in the NW group preferred the
206 avocado oil sauce, while in the OW/OB group the most preferred was the coconut oil sauce with
207 a 42.42% preference, however, there was no significant association between the preference to
208 oil-based sauces and the participant's BMI z-score (Table 3).

209 **Relationship between the preference to oil-based sauces and *CD36* -31118 G>A polymorphism**

210 Avocado oil sauce was the most preferred within carriers of the AA and GA genotypes; whereas
211 carriers of the GG genotype showed a tendency of preference towards coconut oil sauce,
212 although no significant differences were found (Table 3).

213 **Relationship between food satisfaction degree test to oil-based sauces and the BMI z-score**

214 Scores given to each oil-based sauce according to the children's BMI z-score were analyzed. The
215 NW tended to score higher the avocado oil sauce (mean score 0.73 ± 1.36) than the OW/OB
216 group (mean score 0.18 ± 1.23 , p = 0.09). No significant differences were neither observed in
217 satisfaction scores assigned to the olive and coconut oil-based sauces when analyzing by BMI z-
218 score.

219 Since avocado and olive oil share composition characteristics (a greater amount of
220 polyunsaturated fatty acids (PUFAs) than the coconut oil), we decided to group their scores for

221 further analysis. It was observed that the average satisfaction score awarded to the PUFA-rich
222 oils by the NW group was significantly higher than the score assigned by the OW/OB group (0.57
223 ± 1.26 , vs. 0.06 ± 1.22 ; $p = 0.02$) (Figure 1).

224 **Relationship between the satisfaction degree test to oil-based sauces and *CD36* -31118 G>A** 225 **polymorphism**

226 Children were grouped according to the genotypes in *CD36* (AA, GA or GG) independently of
227 their BMI z-score to assess if this genetic variant in a gustatory lipid receptor could also have an
228 effect on the satisfaction scores assigned to the oil-based sauces, however, no significant
229 relationship was found. Furthermore, since it was found that this polymorphism in *CD36* follows
230 a dominant inheritance model in this population (data not shown), meaning that carrying a
231 single copy of G allele is sufficient to modify the risk and that being a carrier of 2 copies modifies
232 it to the same extent; we decided to compare the scores obtained in the degree of satisfaction
233 test by grouping carriers of AA genotype versus carriers of GA + GG genotypes. Again, no
234 significant relationship was found between the alleles in this *CD36* SNP and the satisfaction
235 score assigned to the oil-based sauces (data not shown).

236 **Discussion**

237 *CD36* is recognized as a gustatory lipid receptor and emerging evidence suggests that genetic
238 variants in *CD36* can modulate lipid detection thresholds and preferences [14,16]. This study
239 was conducted with the aim of evaluating the relationship of polymorphism rs1761667 in *CD36*
240 gene with body composition, fat preferences and the satisfaction score to sauces prepared with
241 three types of oils (avocado, olive, and coconut) in Mexican children. No association was found
242 between preferences for oil-based sauces and BMI z-score, nor between these preferences with

243 *CD36* genotypes, however in the satisfaction degree test, it was observed that the oil-based
244 sauces with more PUFAs content (avocado and olive oil) received higher scores in the NW group
245 than the OW/OB group. Furthermore, we found that the G allele of *CD36* gene polymorphism -
246 31118 G>A, was associated with the risk of overweight or obesity in children from western
247 Mexico.

248 Regarding the genetic analysis, the A-allele was the most frequent in our participants, in a
249 similar way to what has been reported in European and American populations, whereas in other
250 populations (African, east and south Asian) this allele is the less frequent [21]. It is worth
251 mentioning that in western Mexico there is the Nahua ethnic group, which is part of the
252 Amerindian population, but in addition to Amerindian genes, the Mexican genetic pool consists
253 of a heterogeneous mixture of European, Asian and African genes [32,33]. In this study, children
254 carrying the G allele of rs1761667 in *CD36* had increased risk of being overweight or obese in
255 comparison to carriers with the A allele. Our results coincide with those obtained by Solakivi et
256 al. in adult population from Finland; they reported that participants with the GA and GG
257 genotypes have higher BMI than participants with the AA genotype [20]. Similarly, Melis et al.
258 conducted a study with adult Caucasian population, and reported that the G allele was
259 associated to increased waist/hip ratio in obese subjects, although participants with this allele
260 showed decreased BMI when compared to participants with the AA genotype [22]. In contrast
261 to these findings, Sayed et al. reported that the A allele is frequent in obese African children and
262 that carrying this allele provides increased risk for obesity in children [17]. Daoudi et al. also
263 found, in an Arab-Berber adolescents' population, higher frequencies of AA and AG genotypes in
264 obese subjects compared to controls [13]. These conflicting results, are likely explained by

265 differences in the genetic characteristics of the studied populations, a phenomenon also known
266 as ethnogenetic heterogeneity, which refers to the genetic variations for some ethnic groups
267 that together with other genetic and environmental factors, modify the risk for certain diseases
268 [34,35,36].

269 The children's preferences for oil-based sauces showed no relationship with the *CD36*
270 genotypes or the BMI z-score. This agrees with some authors that reported no association
271 between high-fat foods preference with the BMI and *CD36* genotype in Afro-American and
272 Caucasian adult population [9,21,37]. Keller et al. showed that participants carrying the AA
273 genotype had very low thresholds of oral perception for fatty acids and suggested that a
274 decrease in the expression of *CD36* could lead to lower sensitivity to fatty acids [21], however,
275 molecular confirmatory evidence to show whether the expression of *CD36* is decreased in taste
276 receptor cells of carriers of AA genotype is still needed. Another factor that possibly contributes
277 to discrepancies of our data with other studies is the density of taste buds in the tongue.
278 Children have a lower density of papillae compared to adults [38]. In addition, these papillae are
279 less developed in children; the fungiform papillae reach their full size from 8 to 10 years of age,
280 while the circumvallate papillae continue to grow until the age of 15-16 years, and these taste
281 buds express *CD36* receptor mRNA up to 9 times more than fungiform papillae [13]. Therefore,
282 it is possible that the children participating in our study had such low *CD36* expression that the
283 differences expected according to the *CD36* genotype may have been obscured and therefore
284 no differences in the preference for oil-based sauces with different lipid profile were detected.
285 It is also important to consider that food preferences and the acceptance to food, develops
286 early in childhood and depends on many environmental factors and multiple learning

287 mechanisms, for example, the Pavlovian conditioning and the repeated exposure to foods,
288 which are well-known learning processes involved in the formation of food preferences [39, 40].
289 Results of the children's satisfaction score test to oil-based sauces showed that there was no
290 statistically significant difference according to *CD36* genotypes, however, when analyzing by
291 BMI z-score, the children of the NW group tended to assign higher satisfaction scores to PUFAs-
292 rich sauces in comparison to children of the OW/OB group. This result suggests that nutritional
293 status, in particular obesity and overweight may affect the hedonic response to fat foods.
294 Although previous studies have suggested that obesity modifies the oral transduction capacity
295 and sensitivity to medium chain fatty acids, there is still no mechanistic data to explain why
296 obese people have different sensitivity or responsiveness to fatty taste than lean people [41].
297 One biological factor to take into account is the hormonal modulation of taste, which can
298 influence daily caloric intake and possibly the food preferences and satisfaction scores [42]. For
299 example, the metabolic hormone leptin has been shown to increase *CD36* expression in cell
300 cultures of human placenta [43] and the leptin receptor (Lep-R) is expressed in type II taste
301 receptor cells [44]. Ghrelin and its receptor are also expressed in all types of taste cells [45] and
302 it has been suggested that its signaling may affect the perception of taste and the processing of
303 food-rewards and food-conditioned preferences [46]. Therefore, the interaction between these
304 hormone receptors may influence the taste transduction of fatty acids and the hedonic
305 responses (assessed by the satisfaction score test) to foods with different fatty acid
306 composition.

307 This is the first study providing information on the role of *CD36* SNP -31118 G>A on body
308 composition in children from western Mexico, as well as information on the preference and

309 satisfaction scores assigned to oils extracted from fruits highly produced in Mexico, such as
310 coconut and avocado oil. We consider that the application of sensory tests for evaluating the
311 preference and satisfaction score to foods of different fatty acid composition is more objective
312 than the application of questionnaires for self-reporting food preferences. However, the present
313 study had several limitations; the sample size is limited for a genetic association study and
314 larger confirmation studies in this population will be necessary. Also, it is worth mentioning that
315 there were differences in regards of the sensory attributes of the foods used in our preference
316 test; for example, olive oil sauce had a bitter taste whereas the coconut oil was notably sweeter.
317 It has been argued that the preference for sweet taste is innate in humans, and there is
318 evidence that people with obesity have a lower detection threshold of sweet taste [8]. In this
319 research, the coconut oil-based sauce was preferred by a higher percentage of children with
320 overweight/obesity; which coincides with the report that people with high BMI prefer fatty
321 foods rich in medium and saturated fatty acids [47].

322 In conclusion, the G allele of -31118 G>A polymorphism in *CD36* was associated to an increased
323 risk of childhood overweight and obesity, but this SNP do not appear to modulate the
324 preferences and satisfaction scores to fat in Mexican children. Although it has been reported
325 that some SNPs can modulate and/or influence the sensory variations in responses to food,
326 these genetic factors are not determining, since this complex process is mediated by the
327 interaction of multiple biological, environmental and psychological factors.

328 **Author contributions**

329 ZRC, MER and EVM were involved in the conception and design of the study, acquisition,
330 analysis, and interpretation of data as well as writing of the manuscript. MLC, LG and ALE were

331 involved in the interpretation of data and critical revision of the manuscript. All authors read
332 and approved the final version of the manuscript.

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339 **Disclosure statement**

340 The authors declare that they have no conflict of interest.

341 **References**

- 342 1. Kovesdy CP, Furth S, Zoccali C. Obesity and kidney disease: hidden consequences of the
343 epidemic. *Saudi J Kidney Dis Transpl.* 2017;28:241–52.
- 344 2. Shamah-Levy T, Cuevas-Nasu L. Encuesta Nacional de Salud y Nutrición de Medio Camino.
345 Informe final de resultados [Internet]. México: Instituto Nacional de Salud Pública; 2016
346 [updated 2016 Oct 31; cited 2019 Aug 5]. Available from:
347 <https://www.gob.mx/cms/uploads/attachment/file/209093/ENSANUT.pdf>
- 348 3. Sahoo K, Sahoo B, Choudhury AK, Sofi NY, Kumar R, Bhadoria AS. Childhood obesity: causes
349 and consequences. *J Fam Med Prim Care.* 2015;4(2):187–92.
- 350 4. Gahagan S. Development of Eating Behavior: biology and context. *J Dev Behav Pediatr.*
351 2012;33(3):261–71.

- 352 5. Drewnowski A. Energy Density, Palatability, and Satiety: Implications for Weight Control.
353 Nutr Rev. 2009;56(12):347–53.
- 354 6. Hurt RT, Kulisek C, Buchanan LA, McClave SA. The obesity epidemic: challenges, health
355 initiatives, and implications for gastroenterologists. Gastroenterol Hepatol (N Y).
356 2010;6(12):780–92.
- 357 7. Asano M, Hong G, Matsuyama Y, Wang W, Izumi S, Izumi M, et al. Association of oral fat
358 sensitivity with body mass index, taste preference, and eating habits in healthy Japanese
359 young adults. Tohoku J Exp Med. 2016;238(2):93-103.
- 360 8. Drewnowski A. Food perceptions and preferences of obese adults: a multidimensional
361 approach. Int J Obes. 1985;9(3):201–12.
- 362 9. Pepino MY, Love-Gregory L, Klein S, Abumrad NA. The fatty acid translocase gene CD36 and
363 lingual lipase influence oral sensitivity to fat in obese subjects. J Lipid Res. 2012;53(3):561-
364 66.
- 365 10. Salbe AD, DelParigi A, Pratley RE, Drewnowski A, Tataranni PA. Taste preferences and body
366 weight changes in an obesity-prone population. Am J Clin Nutr. 2004;79(3):372–78.
- 367 11. Glatz JFC, Luiken JJFP. From fat to FAT (CD36/SR-B2): Understanding the regulation of
368 cellular fatty acid uptake. Biochimie. 2017;136:21–26.
- 369 12. Pepino MY, Kuda O, Samovski D, Abumrad NA. Structure-function of CD36 and Importance
370 of fatty acid signal transduction in fat metabolism. Annu Rev Nutr. 2014;34:281–303.
- 371 13. Daoudi H, Plesník J, Sayed A, Šerý O, Rouabah A, Rouabah L, et al. Oral fat sensing and
372 CD36 gene polymorphism in Algerian lean and obese teenagers. Nutrients.
373 2015;7(11):9096–104.

- 374 14. Martin C, Passilly-Degrace P, Gaillard D, Merlin J-F, Chevrot M, Besnard P. The lipid-sensor
375 candidates CD36 and GPR120 are differentially regulated by dietary lipids in mouse taste
376 buds: impact on spontaneous fat preference. *PLoS One*. 2011; 6(8): e24014.
- 377 15. Mrizak I, Šerý O, Plesnik J, Arfa A, Fekih M, Bouslema A, et al. The A allele of cluster of
378 differentiation 36 (CD36) SNP 1761667 associates with decreased lipid taste perception in
379 obese Tunisian women. *Br J Nutr*. 2015;113(8):1330–37.
- 380 16. Mattes RD. Accumulating evidence supports a taste component for free fatty acids in
381 humans. *Physiol Behav*. 2011;104(4):624–31.
- 382 17. Sayed A, Šerý O, Plesnik J, Daoudi H, Rouabah A, Rouabah L, et al. CD36 AA genotype is
383 associated with decreased lipid taste perception in young obese, but not lean, children. *Int*
384 *J Obes*. 2015;39(6):920–24.
- 385 18. Stewart JE, Newman LP, Keast RSJ. Oral sensitivity to oleic acid is associated with fat intake
386 and body mass index. *Clin Nutr Edinb Scotl*. 2011;30(6):838–44.
- 387 19. Stewart JE, Feinle-Bisset C, Golding M, Delahunty C, Clifton PM, Keast RSJ. Oral sensitivity
388 to fatty acids, food consumption and BMI in human subjects. *Br J Nutr*. 2010;104(11):145-
389 52.
- 390 20. Solakivi T, Kunnas T, Nikkari ST. Contribution of fatty acid transporter (CD36) genetic
391 variant rs1761667 to body mass index, the TAMRISK study. *Scand J Clin Lab Invest*.
392 2015;75(3):254–58.
- 393 21. Keller KL, Liang LCH, Sakimura J, May D, van Belle C, Breen C, et al. Common variants in the
394 CD36 gene are associated with oral fat perception, fat preferences, and obesity in African
395 Americans. *Obesity*. 2012;20(5):1066–73.

- 396 22. Melis M, Carta G, Pintus S, Pintus P, Piras CA, Murru E, et al. Polymorphism rs1761667 in
397 the CD36 gene is associated to changes in fatty acid metabolism and circulating
398 endocannabinoid levels distinctively in normal weight and obese subjects. *Front Physiol.*
399 2017;8:01-09.
- 400 23. Pioltine MB, de Melo ME, Santos A, Machado AD, Fernandes AE, Fujiwara CT, et al. (2016)
401 Genetic variation in CD36 is associated with decreased fat and sugar intake in obese
402 children and adolescents. *J Nutrigenet Nutrigenomics.* 2016;9(5-6):300-305.
- 403 24. Ramos-Arellano LE, Salgado-Bernabé AB, Guzmán-Guzmán IP, Salgado-Goytia L, Muñoz-
404 Valle JF, Parra-Rojas I. CD36 haplotypes are associated with lipid profile in normal-weight
405 subjects. *Lipids Health Dis.* 2013;12:01-09.
- 406 25. Ramos-Lopez O, Roman S, Martinez-Lopez E, Fierro NA, Gonzalez-Aldaco K, Jose-Abrego A,
407 et al. CD36 genetic variation, fat intake and liver fibrosis in chronic hepatitis C virus
408 infection. *World J Hepatol.* 2016;8(25):1067–74.
- 409 26. Lima R da S, Block JM. Coconut oil: what do we really know about it so far? *Food Qual Saf.*
410 2019;3(12):61–72.
- 411 27. Briggs MA, Petersen KS, Kris-Etherton PM. (2017) Saturated fatty acids and cardiovascular
412 disease: replacements for saturated fat to reduce cardiovascular risk. *Healthcare (Basel).*
413 2017;5(2):E29.
- 414 28. Secretaría de Agricultura, Ganadería, Desarrollo Rural, Pesca y Alimentación [SAGARPA].
415 Planeación Agrícola Nacional 2017-2030. Palma de coco mexicana [Internet]. México:
416 SAGARPA; 2017 [updated 2017 Ene; cited 2019 Aug 5]. Available from:
417 https://www.gob.mx/cms/uploads/attachment/file/257082/Potencial-Palma_de_Coco.pdf

- 418 29. DiNicolantonio JJ, O'Keefe JH. Good Fats versus Bad Fats: A comparison of fatty acids in the
419 promotion of insulin resistance, inflammation, and obesity. *Mo Med*. 2017;114(4):303–07.
- 420 30. Assunção ML, Ferreira HS, dos Santos AF, Cabral CR, Florêncio TMMT. Effects of dietary
421 coconut oil on the biochemical and anthropometric profiles of women presenting
422 abdominal obesity. *Lipids*. 2009;44(7):593–601.
- 423 31. Marfell-Jones MJ, Stewart AD, de Ridder JH. International standards for anthropometric
424 assessment. Wellington, New Zealand: International Society for the Advancement of
425 Kinanthropometry; 2012. 54–84.
- 426 32. Gonzalez-Aldaco K, Rebello Pinho JR, Roman S, Gleyzer K, Fierro NA, Oyakawa L, et al.
427 Association with spontaneous Hepatitis C viral clearance and genetic differentiation of
428 IL28B/IFNL4 haplotypes in populations from Mexico. *PLoS One*. 2016;11(11):e0146258.
- 429 33. Panduro A, Ramos-Lopez O, Campollo O, Zepeda-Carrillo EA, Gonzalez-Aldaco K, Torres-
430 Valadez R, et al. High frequency of the DRD2/ANKK1 A1 allele in Mexican Native
431 Amerindians and Mestizos and its association with alcohol consumption. *Drug Alcohol*
432 *Depend*. 2017;172:66-72.
- 433 34. Dickerson JE, Zhu A, Robertson DL, Hentges KE. Defining the Role of Essential Genes in
434 Human Disease. *PLoS One*. 2011;6(11): e27368.
- 435 35. Keith BP, Robertson DL, Hentges KE. Locus heterogeneity disease genes encode proteins
436 with high interconnectivity in the human protein interaction network. *Front Genet*.
437 2014;5:01-11.
- 438 36. Kochi Y, Suzuki A, Yamada R, Yamamoto K. Ethnogenetic heterogeneity of rheumatoid
439 arthritis-implications for pathogenesis. *Nat Rev Rheumatol*. 2010;6(5):290-5.

- 440 37. Ma X. A common haplotype at the CD36 locus is associated with high free fatty acid levels
441 and increased cardiovascular risk in Caucasians. *Hum Mol Genet.* 2004;13(19):2197-205.
- 442 38. Segovia C, Hutchinson I, Laing DG, Jinks AL. A quantitative study of fungiform papillae and
443 taste pore density in adults and children. *Dev Brain Res.* 2002;138(2):135-46.
- 444 39. Birch LL. Development of food preferences. *Annu Rev Nutr.* 1999;19:41–62.
- 445 40. Guidetti M, Cavazza N. Structure of the relationship between parents' and children's food
446 preferences and avoidances: An explorative study. *Appetite.* 2008;50(1):83-90.
- 447 41. Tucker RM, Kaiser KA, Parman MA, George BJ, Allison DB, Mattes RD. Comparisons of fatty
448 acid taste detection thresholds in people who are lean vs. overweight or obese: a
449 systematic review and meta-analysis. *PLoS One.* 2017;12(1):e0169583.
- 450 42. Loper HB, La Sala M, Dotson C, Steinle N. Taste perception, associated hormonal
451 modulation, and nutrient intake. *Nutr Rev.* 2015;73(2):83-91.
- 452 43. Mousiolis A. Effects of leptin on the expression of fatty acid-binding proteins in human
453 placental cell cultures. *Mol Med Rep.* 2012;5(2):497-502.
- 454 44. Calvo SS-C, Egan JM. The endocrinology of taste receptors. *Nat Rev Endocrinol.*
455 2015;11(4):213-27.
- 456 45. Shin Y-K, Martin B, Kim W, White CM, Ji S, Sun Y, et al. Ghrelin is produced in taste cells
457 and ghrelin receptor null mice show reduced taste responsivity to salty (NaCl) and sour
458 (citric acid) tastants. *PLoS One.* 2010;5(9):e12729.
- 459 46. Sclafani A, Touzani K, Ackroff K. Ghrelin signaling is not essential for sugar or fat
460 conditioned flavor preferences in mice. *Physiol Behav.* 2015;149:14–22.

461 47. Tashani OA, Astita R, Sharp D, Johnson MI. Body mass index and distribution of body fat
 462 can influence sensory detection and pain sensitivity. Eur J Pain. 2017;21(7):1186-1196.

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Table 1. Sociodemographic, anthropometric and clinical data of the participants.

| Variable | NW (n=30) | OW/OB ^a (n=33) | <i>p</i> |
|-------------------------------|-------------------|------------------------------|----------|
| <i>Gender</i> | | | |
| Male, % (n) | 14.2 (19) | 20.6 (13) | 0.4 |
| Female, % (n) | 33.3 (21) | 31.7 (20) | |
| Age, years | 9.4 ± 1.1 | 9.8 ± 1.3 | 0.21 |
| Height, cm | 137.4 ± 10.1 | 144.1 ± 11.5 | 0.0071 |
| Weight, kg | 31.0 (26.5- 36.8) | 52.6 (45.6- 57.5) | < 0.0001 |
| BMI ^c | 16.8 (15.3-18) | 23.5 (21.8- 26.6) | < 0.0001 |
| Waist-hip ratio, cm | 0.86 ± 0.04 | 0.89 ± 0.05 | 0.02 |
| Body fat, % | 21.9 (18-25) | 35.0 (30.7- 39.2) | < 0.0001 |
| Fat free mass, % | 78.1 (75-82) | 65.3 (61.5- 71.75) | < 0.0001 |
| <i>Family disease history</i> | | | |
| Hypertension, % (n) | 37.5 (21) | 37.5 (21) | 0.5 |
| T2D, % (n) | 46.4 (26) | 41 (23) | 0.1 |
| Heart attack, % (n) | 23.2 (13) | 19.6 (11) | 0.4 |
| Cardiovascular, % (n) | 23.2 (13) | 21.4 (12) | 0.5 |
| Diseases, % (n) | | | |
| Smoking, % (n) | 8.9 (5) | 12.5 (7) | 0.6 |
| <i>Clinical history</i> | | | |
| Infections, % (n) | 6.6 (2) | 15.15 (5) | 0.2 |
| Surgeries, % (n) | 10 (3) | 3.33 (1) | 0.2 |
| Allergies, % (n) | 16.6 (5) | 21.21 (7) | 0.6 |

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465 Nominal variables are expressed in percentages and frequencies. *p*: Chi-square test. Continuous
 466 variables with normal distribution are expressed as mean ± SD. *p*: Student's T-test. Continuous
 467 variables with non-normal distribution are expressed as median (p25-p75). *p*: Mann-Whitney
 468 Test. ^aGroups were classified according to the WHO BMI z-score.

469 Abbreviations: NW, normal weight; OW/OB, overweight and obesity; T2D, Type 2 diabetes.

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Table 2. Genotypic and allelic frequencies according to children's BMI z-score

| Genotype | NW (n=30) % (n) | OW/OB (n=33) % (n) | <i>p</i> | OR (95% CI); <i>p</i> |
|-----------------|-----------------------|--------------------------|-------------------|------------------------|
| AA ^a | 63.33 (19) | 36.36 (12) | | 1 |
| GA | 33.33 (10) | 51.51 (17) | 0.09 ^b | 2.1 (0.68-6.71); 0.14 |
| GG | 1.58 (1) | 12.12 (4) | | 4 (0.35-203.62); 0.20 |
| Allele | | | | |
| A ^a | 80 (48) | 62.12 (41) | 0.02 ^c | 1 |
| G | 20 (12) | 37.87 (25) | | 2.43 (1.02-5.99); 0.02 |

475 ^aReference category. ^bFisher's exact test. ^cChi-square test.

476 Abbreviations: NW, normal weight; OW/OB, overweight and obesity; OR, odds ratio; 95% CI,
477 95% confidence interval.

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Table 3. Oil-based sauces preference according to children’s BMI z-score and *CD36* genotype

| | NW (n=30) | OW/OB (n=33) | p^a | AA genotype (n=31) | GA genotype (n=27) | GG genotype (n=5) | p^b |
|-------------------------------|--------------|-----------------|-------|--------------------------|--------------------------|-------------------------|-------|
| | % (n) | % (n) | | % (n) | % (n) | % (n) | |
| Avocado oil-based sauce | 50 (15) | 39.39 (13) | | 51.61 (16) | 40.74 (11) | 20 (1) | |
| Olive oil- based sauce | 26.66 (8) | 18.18 (6) | 0.26 | 19.35 (6) | 25.92 (7) | 20 (1) | 0.62 |
| Coconut oil-based sauce | 23.23 (7) | 42.42 (14) | | 29.03 (9) | 33.33 (9) | 60 (3) | |

490 ^aChi squared test. ^bFisher’s exact test.

491 Abbreviations: NW, normal weight; OW/OB, overweight and obesity.

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Figure legends

506 Figure 1. Satisfaction scores assigned by children to the oil-based sauces. Scores were obtained

507 by the degree of satisfaction test. Mean and standard error of the mean (SEM, bars) are shown.

508 *p*: Student's T-test. Abbreviations: NW, normal weight group; OW/OB overweight and obesity

509 group.