

This is the accepted manuscript version of the work. This version of the article may not completely replicate the final authoritative version published in International Journal for Vitamin and Nutrition Research at https://doi.org/10.1024/0300-9831/a000656. It is not the version of record and is therefore not suitable for citation. Please do not copy or cite without the permission of the author(s).

Document downloaded from:



- 1 CD36 gene polymorphism -31118 G>A (rs1761667) is associated with overweight and obesity
- 2 but not with fat preferences in Mexican children
- 3 Enciso-Ramírez Mayra¹, Reyes-Castillo Zyanya^{1*}, Llamas-Covarrubias Mara Anaís², Guerrero
- 4 Luis³, López-Espinoza Antonio¹, Valdés-Miramontes Elia Herminia^{1*}.
- ¹ Instituto de Investigaciones en Comportamiento Alimentario y Nutrición (IICAN), Centro
- 6 Universitario del Sur, Universidad de Guadalajara, Ciudad Guzmán, Jalisco, México.
- 7 ² Instituto de Investigación en Ciencias Biomédicas (IICB), Centro Universitario de Ciencias de la
- 8 Salud, Universidad de Guadalajara, Guadalajara, Jalisco, México.
- ³ IRTA-Monells. Institut de Recerca i Tecnologia Agroalimentàries. Granja Camps i Armet. 17121
- 10 Monells, Girona, Spain.

15

16

17

18

19

20

21

- *Correspondence authors at: Av. Enrique Arreola Silva No. 883, Colonia Centro, 49000 Ciudad
- 12 Guzmán, Jalisco, México. Phone: (+521) 575-2222 Ext. 46142. E-mail addresses:
- eliav@cusur.udg.mx (EHV), zyanya.reyes@cusur.udg.mx (ZRC).
- Running title: CD36 SNP, fat preferences and obesity in Mexican children

Abstract

23

24

25

26

27

28

29

30

31

32

33

34

35

36

37

38

39

40

41

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

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

42

43

46

47

48

49

50

51

52

53

54

55

56

57

58

59

60

61

62

63

64

65

66

Introduction

Childhood obesity has reached an alarming prevalence worldwide to the point of becoming an epidemic [1]. Mexico is ranked among the leading countries with the highest prevalence of overweight and obesity in children with an estimated prevalence of 33% [2]. This condition often has a harmful effect on health in adulthood as epidemiological studies have shown an association of early obesity with an excess mortality rate in adults (from 50 to 80%). In obese children, several short-term pathologies appear, such as hyperinsulinemia, increased blood pressure and abnormalities of blood lipids, including hypertriglyceridemia, decreased highdensity lipoprotein cholesterol (HDL-chol), respiratory difficulties as well as psychological problems [3]. The etiology of obesity is multifactorial, and includes a complex interaction of environmental, behavioral and genetic factors [4], all of which, may also influence food preferences and favor the development of obesity. Fat is the most energy-dense macronutrient and contributes significantly to the taste and aroma of food. High-fat and high energy-dense foods are highly preferred by the population [5]. Furthermore, the western diet, which is characterized by a high consumption of processed foods rich in sugars and saturated fats, has been linked to the alarming rise in the prevalence of obesity [6]. There is evidence showing that people with a high body mass index (BMI) prefer foods high in fat and sugar content and have a lower oral detection threshold for fatty acids than individuals with normal BMI [7–10]. Recently, both the CD36 glycoprotein and the G protein-coupled receptor GPR120 have emerged as candidate receptors involved in the gustatory detection of lipids. CD36 participates

physiological process such as inflammation, innate immune responses, atherosclerosis, angiogenesis, lipid metabolism among others [11], but has been implicated in the orosensory detection of fat foods as it exhibits a strong affinity to long-chain fatty acids [12] and is expressed in circumvallate taste buds and to a lesser extent in fungiform taste buds [13]. In addition, a single nucleotide polymorphism (SNP) in CD36 gene (rs1761667) at position -31118 G>A is suggested to modulate the oral perception threshold to fatty acids. In particular, the G allele was related to lower oral detection thresholds to some fatty acids [9], whereas the A allele was associated with lower CD36 expression and decreased lipid taste perception in people with obesity [14,15]. It has been hypothesized that the low perception of oral lipids may lead to high consumption and preference for rich fat foods [16,17], and in turn, oral fatty acid hypersensitivity is associated with lower energy and fat intakes and lower body weight [18,19]. The AA genotype of rs1761667 in CD36 was significantly associated with lower BMI as compared to carriers of AG and GG genotypes in adult population from Finland [20], while some other studies have identified an association of this polymorphism with obesity [13,17,21-23]. In Mexican population, rs1761667 in CD36 was studied in relationship to cardiovascular and liver diseases in adult population [24,25], however, there is no data on its relationship with childhood obesity and fat preferences. In recent years, the food industry has broadened the options regarding cooking oils, offering some extracted from fruits and seeds such as avocado and coconut [26]. Both olive and avocado oil are rich in unsaturated fatty acids such as linoleic and linolenic acid, which have been associated with reduced risk of cardiovascular disease and cancer [27]. Also, Mexico is among the top ten producers of coconut and the production and commercialization of coconut-oil has

67

68

69

70

71

72

73

74

75

76

77

78

79

80

81

82

83

84

85

86

87

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

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

Materials and methods

Study design

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

Participants

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

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

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

Anthropometrics

Helsinki.

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

DNA collection and genotyping

133

134

135

136

137

138

139

140

141

142

143

144

145

146

147

148

149

150

151

152

153

154

Peripheral blood samples were taken in 5% EDTA-anticoagulant tubes (BD Vacutainer, Franklin Lakes, NJ). The DNA extraction was performed according the manufacturer's instructions using the QIAamp DNA Blood Mini Kit (QIAGEN, Hilden, Germany). The concentration and quality of extracted DNA was measured using Nanodrop spectrophotometer (ThermoFisher Scientific, Massachusetts, USA). Samples were stored at −20 °C for future use. Genotypes rs1761667 SNP in CD36 were obtained using the polymerase chain reactionrestriction fragment length polymorphism (PCR-RFLP) using primers with the following sequence: forward 5' - CAA AAT CAC AAT CTA TTC AAG ACC A - 3' and reverse 5' - TTT TGG GAG AAA TTC TGA AGA G - 3' (Integrated DNA Technologies, Iowa, USA). The PCR-mixture was composed of 1X buffer, MgCl2 (2.5 mM), dNTP's (0.1 mM), primers (0.06 µM, each one), Tag polymerase (1 U) and distilled water to reach a total volume of 25 μl with ~50 ng genomic DNA. The PCR reaction was performed in a thermocycler (Swift MiniPro-Esco, Missouri, USA) under the following conditions: initial denaturation at 95 °C for 5 min, followed by 35 cycles of amplification including denaturation at 95 °C, annealing at 95 °C, and extension at 72 °C (each comprising 30 s), and the final extension at 72 °C for 5 min. PCR products (3µl) were digested with 5 U of Hhal restriction endonuclease (Promega, Wisconsin, USA) at 37 °C for 4 h and fragments were separated by polyacrylamide gel electrophoresis (6% polyacrylamide) and subsequently stained with silver nitrate. Afterwards, the A allele was visualized as a single band (190 bp) and the G allele as two bands (138 and 52 bp).

Food preference test

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

Food satisfaction degree test

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

Statistical analyses

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

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

Results

Sociodemographic and body composition characteristics of the participants

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

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

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

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

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

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

Relationship between the preference to oil-based sauces and *CD36* -31118 G>A polymorphism Avocado oil sauce was the most preferred within carriers of the AA and GA genotypes; whereas carriers of the GG genotype showed a tendency of preference towards coconut oil sauce, although no significant differences were found (Table 3).

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

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

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

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

polymorphism

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

Discussion

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

CD36 genotypes, however in the satisfaction degree test, it was observed that the oil-based sauces with more PUFAs content (avocado and olive oil) received higher scores in the NW group than the OW/OB group. Furthermore, we found that the G allele of CD36 gene polymorphism -31118 G>A, was associated with the risk of overweight or obesity in children from western Mexico. Regarding the genetic analysis, the A-allele was the most frequent in our participants, in a similar way to what has been reported in European and American populations, whereas in other populations (African, east and south Asian) this allele is the less frequent [21]. It is worth mentioning that in western Mexico there is the Nahua ethnic group, which is part of the Amerindian population, but in addition to Amerindian genes, the Mexican genetic pool consists of a heterogeneous mixture of European, Asian and African genes [32,33]. In this study, children carrying the G allele of rs1761667 in CD36 had increased risk of being overweight or obese in comparison to carriers with the A allele. Our results coincide with those obtained by Solakivi et al. in adult population from Finland; they reported that participants with the GA and GG genotypes have higher BMI than participants with the AA genotype [20]. Similarly, Melis et al. conducted a study with adult Caucasian population, and reported that the G allele was associated to increased waist/hip ratio in obese subjects, although participants with this allele showed decreased BMI when compared to participants with the AA genotype [22]. In contrast to these findings, Sayed et al. reported that the A allele is frequent in obese African children and that carrying this allele provides increased risk for obesity in children [17]. Daoudi et al. also found, in an Arab-Berber adolescents' population, higher frequencies of AA and AG genotypes in obese subjects compared to controls [13]. These conflicting results, are likely explained by

243

244

245

246

247

248

249

250

251

252

253

254

255

256

257

258

259

260

261

262

263

differences in the genetic characteristics of the studied populations, a phenomenon also known as ethnogenetic heterogeneity, which refers to the genetic variations for some ethnic groups that together with other genetic and environmental factors, modify the risk for certain diseases [34,35,36]. The children's preferences for oil-based sauces showed no relationship with the CD36 genotypes or the BMI z-score. This agrees with some authors that reported no association between high-fat foods preference with the BMI and CD36 genotype in Afro-American and Caucasian adult population [9,21,37]. Keller et al. showed that participants carrying the AA genotype had very low thresholds of oral perception for fatty acids and suggested that a decrease in the expression of CD36 could lead to lower sensitivity to fatty acids [21], however, molecular confirmatory evidence to show whether the expression of CD36 is decreased in taste receptor cells of carriers of AA genotype is still needed. Another factor that possibly contributes to discrepancies of our data with other studies is the density of taste buds in the tongue. Children have a lower density of papillae compared to adults [38]. In addition, these papillae are less developed in children; the fungiform papillae reach their full size from 8 to 10 years of age, while the circumvallate papillae continue to grow until the age of 15-16 years, and these taste buds express CD36 receptor mRNA up to 9 times more than fungiform papillae [13]. Therefore, it is possible that the children participating in our study had such low CD36 expression that the differences expected according to the CD36 genotype may have been obscured and therefore no differences in the preference for oil-based sauces with different lipid profile were detected. It is also important to consider that food preferences and the acceptance to food, develops early in childhood and depends on many environmental factors and multiple learning

265

266

267

268

269

270

271

272

273

274

275

276

277

278

279

280

281

282

283

284

285

mechanisms, for example, the Pavlovian conditioning and the repeated exposure to foods, which are well-known learning processes involved in the formation of food preferences [39, 40]. Results of the children's satisfaction score test to oil-based sauces showed that there was no statistically significant difference according to CD36 genotypes, however, when analyzing by BMI z-score, the children of the NW group tended to assign higher satisfaction scores to PUFAsrich sauces in comparison to children of the OW/OB group. This result suggests that nutritional status, in particular obesity and overweight may affect the hedonic response to fat foods. Although previous studies have suggested that obesity modifies the oral transduction capacity and sensitivity to medium chain fatty acids, there is still no mechanistic data to explain why obese people have different sensitivity or responsiveness to fatty taste than lean people [41]. One biological factor to take into account is the hormonal modulation of taste, which can influence daily caloric intake and possibly the food preferences and satisfaction scores [42]. For example, the metabolic hormone leptin has been shown to increase CD36 expression in cell cultures of human placenta [43] and the leptin receptor (Lep-R) is expressed in type II taste receptor cells [44]. Ghrelin and its receptor are also expressed in all types of taste cells [45] and it has been suggested that its signaling may affect the perception of taste and the processing of food-rewards and food-conditioned preferences [46]. Therefore, the interaction between these hormone receptors may influence the taste transduction of fatty acids and the hedonic responses (assessed by the satisfaction score test) to foods with different fatty acid composition. This is the first study providing information on the role of CD36 SNP -31118 G>A on body

composition in children from western Mexico, as well as information on the preference and

287

288

289

290

291

292

293

294

295

296

297

298

299

300

301

302

303

304

305

306

307

satisfaction scores assigned to oils extracted from fruits highly produced in Mexico, such as coconut and avocado oil. We consider that the application of sensory tests for evaluating the preference and satisfaction score to foods of different fatty acid composition is more objective than the application of questionnaires for self-reporting food preferences. However, the present study had several limitations; the sample size is limited for a genetic association study and larger confirmation studies in this population will be necessary. Also, it is worth mentioning that there were differences in regards of the sensory attributes of the foods used in our preference test; for example, olive oil sauce had a bitter taste whereas the coconut oil was notably sweeter. It has been argued that the preference for sweet taste is innate in humans, and there is evidence that people with obesity have a lower detection threshold of sweet taste [8]. In this research, the coconut oil-based sauce was preferred by a higher percentage of children with overweight/obesity; which coincides with the report that people with high BMI prefer fatty foods rich in medium and saturated fatty acids [47]. In conclusion, the G allele of -31118 G>A polymorphism in CD36 was associated to an increased risk of childhood overweight and obesity, but this SNP do not appear to modulate the preferences and satisfaction scores to fat in Mexican children. Although it has been reported that some SNPs can modulate and/or influence the sensory variations in responses to food, these genetic factors are not determining, since this complex process is mediated by the interaction of multiple biological, environmental and psychological factors.

Author contributions

309

310

311

312

313

314

315

316

317

318

319

320

321

322

323

324

325

326

327

328

329

330

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

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

Acknowledgements

333

334

335

336

337

338

339

341

MER would like to thank to Consejo Nacional de Ciencia y Tecnología (CONACyT) for the fellowship received (No. 491139). Authors are grateful to Laboratorio de Análisis Clínicos and Laboratorio de Nutrición Animal from CUSur, UdG, for the facility support in the development of the research. Funding for this study came from the program SEP-PRODEP-CAEF granted to the academic body UDG-CA-954 from University of Guadalajara.

Disclosure statement

The authors declare that they have no conflict of interest.

References

- 1. Kovesdy CP, Furth S, Zoccali C. Obesity and kidney disease: hidden consequences of the 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.
- 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
- 3. Sahoo K, Sahoo B, Choudhury AK, Sofi NY, Kumar R, Bhadoria AS. Childhood obesity: causes
- and consequences. J Fam Med Prim Care. 2015;4(2):187–92.
- 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
- 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
- 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
- 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
- weight changes in an obesity-prone population. Am J Clin Nutr. 2004;79(3):372–78.
- 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.
- 12. Pepino MY, Kuda O, Samovski D, Abumrad NA. Structure-function of CD36 and Importance
- of fatty acid signal transduction in fat metabolism. Annu Rev Nutr. 2014;34:281–303.
- 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.

- 14. Martin C, Passilly-Degrace P, Gaillard D, Merlin J-F, Chevrot M, Besnard P. The lipid-sensor candidates CD36 and GPR120 are differentially regulated by dietary lipids in mouse taste buds: impact on spontaneous fat preference. PLoS One. 2011; 6(8): e24014.
- 15. Mrizak I, Šerý O, Plesnik J, Arfa A, Fekih M, Bouslema A, et al. The A allele of cluster of differentiation 36 (CD36) SNP 1761667 associates with decreased lipid taste perception in obese Tunisian women. Br J Nutr. 2015;113(8):1330–37.
- 16. Mattes RD. Accumulating evidence supports a taste component for free fatty acids in humans. Physiol Behav. 2011;104(4):624–31.
- 17. Sayed A, Šerý O, Plesnik J, Daoudi H, Rouabah A, Rouabah L, et al. CD36 AA genotype is associated with decreased lipid taste perception in young obese, but not lean, children. Int J Obes. 2015;39(6):920–24.
- 18. Stewart JE, Newman LP, Keast RSJ. Oral sensitivity to oleic acid is associated with fat intake and body mass index. Clin Nutr Edinb Scotl. 2011;30(6):838–44.
- 19. Stewart JE, Feinle-Bisset C, Golding M, Delahunty C, Clifton PM, Keast RSJ. Oral sensitivity to fatty acids, food consumption and BMI in human subjects. Br J Nutr. 2010;104(11):145-52.
- 20. Solakivi T, Kunnas T, Nikkari ST. Contribution of fatty acid transporter (CD36) genetic variant rs1761667 to body mass index, the TAMRISK study. Scand J Clin Lab Invest. 2015;75(3):254–58.
- 21. Keller KL, Liang LCH, Sakimura J, May D, van Belle C, Breen C, et al. Common variants in the CD36 gene are associated with oral fat perception, fat preferences, and obesity in African 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
- the CD36 gene is associated to changes in fatty acid metabolism and circulating
- 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)
- 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-
- 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,
- 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
- 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].
- Planeación Agrícola Nacional 2017-2030. Palma de coco mexicana [Internet]. México:
- 416 SAGARPA; 2017 [updated 2017 Ene; cited 2019 Aug 5]. Available from:
- https://www.gob.mx/cms/uploads/attachment/file/257082/Potencial-Palma_de_Coco.pdf

- 29. DiNicolantonio JJ, O'Keefe JH. Good Fats versus Bad Fats: A comparison of fatty acids in the
- 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
- abdominal obesity. Lipids. 2009;44(7):593–601.
- 423 31. Marfell-Jones MJ, Stewart AD, de Ridder JH. International standards for anthropometric
- 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.
- 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-
- 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
- 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
- arthritis-implications for pathogenesis. Nat Rev Rheumatol. 2010;6(5):290-5.

- 37. Ma X. A common haplotype at the CD36 locus is associated with high free fatty acid levels
- and increased cardiovascular risk in Caucasians. Hum Mol Genet. 2004;13(19):2197-205.
- 38. Segovia C, Hutchinson I, Laing DG, Jinks AL. A quantitative study of fungiform papillae and
- taste pore density in adults and children. Dev Brain Res. 2002;138(2):135-46.
- 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
- 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
- acid taste detection thresholds in people who are lean vs. overweight or obese: a
- 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
- 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.

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

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

Variable	NW	OW/OB ^a	р	
	(n=30)	(n=33)		
Gender				
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	ight, cm 137.4 ± 10.1		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	
Family disease history				
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	
Clinical history				
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	

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

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

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

Genotype	NW	OW/OB	р	OR (95% CI); p	
	(n=30)	(n=33)			
	% (n)	% (n)			
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	

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

Abbreviations: NW, normal weight; OW/OB, overweight and obesity; OR, odds ratio; 95% CI,

95% confidence interval.

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	GA genotype	GG genotype	ρ^{b}
	% (n)	% (n)		(n=31) % (n)	(n=27) % (n)	(n=5) % (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)	

^aChi squared test. ^bFisher's exact test.

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

500
501
502
503
504
505
Figure legends
506
Figure 1. Satisfaction scores assigned by children to the oil-based sauces. Scores were obtained 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 group.