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Genetic variation in *CD36* is associated with dietary intake in Korean males

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Abstract

Fat is one of the six types of taste. Perceived taste intensity could affect the preference for a food and whether or not it is consumed. Cluster of differentiation 36 (CD36) translocates fatty acids on the cellular membrane and is involved in the oral fat-sensing mechanism. Therefore, genetic variation rs1761667 in *CD36* is known to be associated with the perception of fat taste and, hence, its dietary intake. This study examined whether *CD36* rs1527479 T>C, a proxy of rs1761667, is associated with fat intake and related dietary behaviour in Koreans. Using the data of the Ansan/Ansung Study, a part of the Korean Genome Epidemiology Study, the association of rs1527479 with the intake of macronutrients, including fat and selected foods, and fat-related dietary behaviours were investigated in 3194 males and 3425 females grouped by their degree of obesity. The findings suggested that rs1527479 did not have a meaningful effect on the intake of fat or other macronutrients or on the selection of food among non-obese females and males. However, in males with obesity, the genetic variation showed a significant association with vegetable intake. Obese males with the mutant CC genotype had substantially lower cruciferous vegetable consumption (adjusted $P = 0{\cdot}0015$) than individuals with the TT and CT genotypes. Rs1527479 had no significant effect on the frequency of consuming fried foods or commonly used types of seasoning and cooking oils. In conclusion, *CD36* genetic variation was associated with the intake of cruciferous vegetables but not fat intake in obese Korean males.

Key words: **CD36: Polymorphisms: Koreans: Dietary intake**

Taste is a decisive factor in the formation of human dietary behaviour. Taste can affect the enjoyment or rejection of certain types of food, and this may lead to an individual's selective intake of nutritive compounds[1]. Therefore, the five types of tastes human can perceive – sweet, salty, sour, bitter and umami – not only result in the simple delight of eating but also have important effects on human dietary behaviour and health[1].

Fat was considered to have no taste but was rather associated with only textural characteristics. However, recent findings have suggested that fat is a sixth type of taste[2–5]. Dietary fat is critical for health since the excessive intake of fat is a major concern in the context of many degenerative and metabolic diseases, including obesity, hypertension, type 2 diabetes mellitus and colon cancer[6]. However, fat is still an important source of energy and a physiological vehicle for nonpolar compounds. Furthermore, fat in food could also modify the preference for the food due to its unique sensory traits, fattiness and creaminess[7]. Therefore, the factors related to fat perception and consumption are important in the food industry as well as in the clinical setting.

Earlier studies have suggested that proteins including cluster of differentiation 36 (CD36) and the G-protein-coupled receptor family are involved in the perception of fat. Among them, *CD36* is a commonly studied genetic component in fat perception in relation to food intake[8,9]. CD36 protein is located in the cellular membrane and has a primary role in the sensing of long-chain fatty acids by binding to various types of lipids, including cholesterol, phospholipids and lipoproteins[10,11]. For this reason, genetic variation in *CD36* is associated with the oral sensing of and preference for dietary fat and the differentiation of dietary fatty acids. A genetic variation of rs1761667 G>A in *CD36* was observed to be associated with a variation in the sensing of the taste of fat, fat consumption and differentiation of fatty acid types[12–15]. Furthermore, the variation was also associated with body composition and obesity[16]. However, findings have been inconsistent: having the A allele mutation was associated with reduced fatty food intake only in obese Brazilian children[8]. The genetic variation also showed a significant association with obesity measures in African American adults[14,17] but not in Malaysians[18]. These findings suggested that the effect of the *CD36* genetic variation could differ by ethnicity and adiposity. However, the effect of the *CD36* genetic variation has not yet been explored in the Korean population. Furthermore, fat is generally consumed in the form of food, not as a sole nutrient.

Abbreviations: CD36, cluster of differentiation 36; MAF, minor allele frequency.

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The intensity of the fat taste affects not only the simple intake of fat but also foods rich in fat, as well as other types of foods and cooking methods. Therefore, to better understand the modifying role of *CD36* in Koreans' dietary intake, it is necessary to examine how this genetic factor influences fat consumption as well as overall related dietary behaviour.

This study aimed to examine whether genetic variation in *CD36* is associated with dietary behaviour in Koreans, with a focus on fat consumption. As a genetic marker, rs1527479 T>C was used as a proxy of rs1761667 G>A. Using the data of the Ansan/Ansung Community Cohort Genome-Epidemiologic Study, analyses were performed to ascertain the effect of *CD36* genetic variation on the intake of fat, macronutrients and selected food groups, as well as the frequency of oily food consumption in Koreans stratified by adiposity level. Since sex disparities clearly exist in health and dietary behaviour[19,20], the study employed a sex-stratified approach.

Materials and methods

Study population

This study was conducted with data from the Ansan/Ansung Community Cohort Study, a part of the Korean Genome and Epidemiology Study. The characteristics of the Ansan/Ansung Community Cohort study and the Korean Genome and Epidemiology Study are described elsewhere[21,22]. The materials used in this study were baseline data obtained from 2001 to 2002. Among a total of 8840 subjects (aged 40–69 years) whose genetic characteristics were analysed, subjects with no dietary data (n 290) or implausible total energetic intake (<2092 kJ/d (<500 kcal/d) or >20 920 kJ/d (>5000 kcal/d), n 77) were excluded. Additionally, subjects without anthropometric information, body composition (n 1679) or *CD36* rs1527479 genotype data (n 175) were also removed from the data set. Finally, the remaining 3194 males and 3425 females were analysed for the study (Fig. 1). The Korean Genome and Epidemiology Study was conducted following a protocol approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention. All participants provided written informed consent prior to study commencement. This study was also approved by the Institutional Review Board (40525-201802-HR-121-01).

Collection of general characteristics and anthropometric data

General characteristics, including sociodemographic and lifestyle factors (i.e. age, sex, alcohol consumption, tobacco smoking, marital status, education level and physical activity level), of the study population were obtained by trained interviewers using a questionnaire. The use of tobacco or consumption of alcoholic beverages was classified into two levels: never and ever. Subjects' physical activity levels were defined in the form of metabolic equivalents computed as the sum of metabolic equivalents for five levels of action (1 for sedentary, 1·5 for very light, 2·4 for light, 5·0 for moderate and 7·5 for intense activities)[23,24]. The education level was classified into four levels: elementary school or less (≤6 years), middle school (7–9 years), high school (10–12 years) and college or higher (≥13 years). Marital status (cohabitation) was grouped according

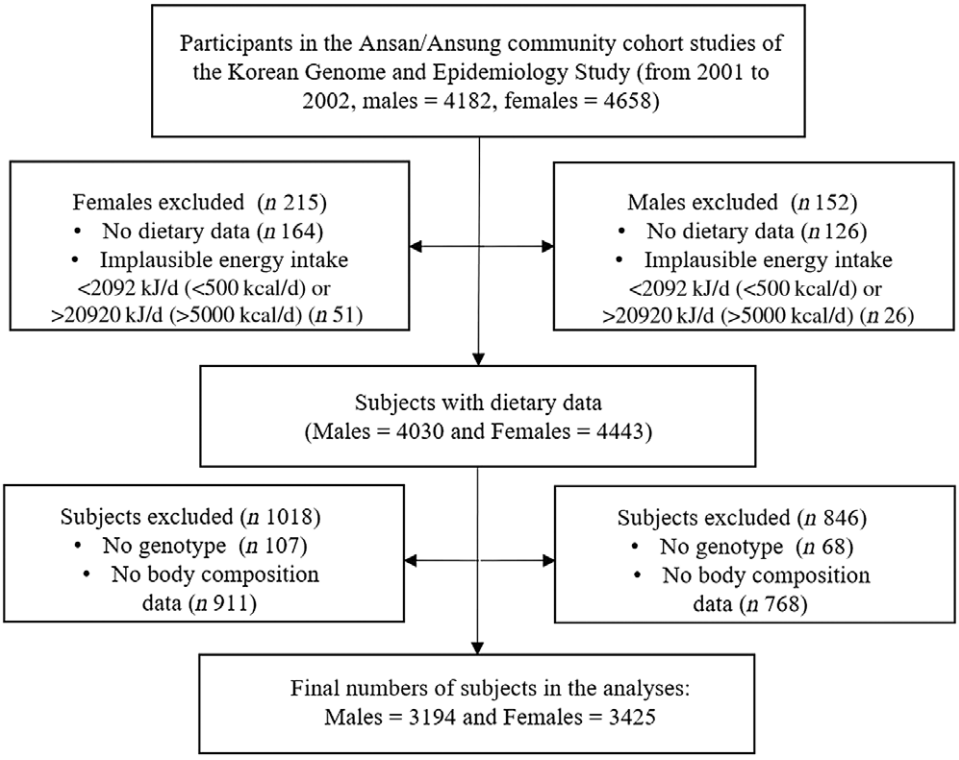

Fig. 1. Procedure for the selection of study subjects.

to the presence or absence of a partner. Body size (weight and height) was estimated to the nearest 0·1 kg and 0·1 cm, respectively, using a stadiometer. BMI was computed as weight (kg) divided by the squared height (m^2).

Collection and assessment of dietary intake and behaviour data

To collect the dietary intake data, a validated FFQ with 103 food items was employed[25]. Study participants marked the frequency of their consumption of each food based on nine response options (never or barely, 1 time/month, 2–3 times/week, 1–2 times/week, 3–4 times/week, 5–6 times/week, 1 time/d, 2 times/d or ≥3 times/d) and three differential serving sizes (small, medium or large). To estimate the intake of seasonal foods (i.e. fruits), participants were also asked to record the period of consumption (3, 6 or 9 months or a year). Nutritional intake was estimated using the Food Composition Table, Korea (7th edition). To investigate the influence of *CD36* rs1527479 on Korean males' dietary intake, the 103 food items were grouped by taking into account Koreans' dietary culture: carbohydrate foods, carbohydrate- and fat-rich foods, sweets, protein-rich foods, dairy products, meats, seafood, fatty foods, all vegetables, green vegetables, cruciferous vegetables, seaweeds, all fruits and citrus fruits. Additionally, participants recorded the frequency of consumption of fried food based on five levels (rarely, 1–2 times/month, 1–3 times/week, 4–6 times/week or every day). To investigate the preferred type of oil for seasoning and cooking, the commonly used oils in Korean cuisine (for seasoning, sesame oil and perilla oil; for cooking, soyabean oil, maize oil, olive oil and butter) were presented; however, participants were still freely able to write in a response if the preferred or commonly used oil was not listed in the questionnaire.

Genotype assessment and selection of proxy marker

Genomic DNA specimens were obtained from participants' peripheral blood. The genotype was determined using the Affymetrix genome-wide human SNP array 5.0 (Affymetrix Inc.). The quality control of the genetic data obtained was performed following Bayesian robust linear modelling with the Mahalanobis distance algorithm. Samples were excluded if they presented low quality, including genotyping call rate <96 %, excessive heterozygosity, sex and ethnic mismatch, or cryptic relatedness. Genetic loci were excluded if they possessed a call rate <95 %, a low minor allele frequency (MAF) of <0·01 or deviated from Hardy–Weinberg equilibrium ($P < 1 \times 10^{-6}$)[26,27]. As genotype result for rs1761607 was not included in the data, the analyses were performed using a proxy marker. The LDlink analyses suggested that rs1527479 is located near and highly associated with the target rs1761667 (r^2 1, $D' = 1$, about 27·6 Kb downstream). This was confirmed in Japanese population data because no Korean data have been reported yet. Therefore, rs1527479 was selected as a genetic proxy marker[28].

Statistical analyses

The differences in general information among individuals with the *CD36* rs1527479 genotypes were determined using generalised linear models and χ^2 tests accounting for the type of variables. Food and nutritional intake data were adjusted for total energetic intake using Willett's residual method and were then included in the analyses[29]. The comparisons of dietary and nutritional intake and *CD36* rs1527479 genotypes were performed using generalised linear models, either with or without covariates. The *post hoc* comparisons between those three genotypes were performed with Tukey's technique. All continuous variables, including dietary and anthropometric data, were log-transformed prior to inclusion in the statistical models for better normality. The frequency of consuming oily foods was also transformed to determine the yearly frequency (e.g. rarely = 0, 1–2 times/month = 18, 1–3 times/week = 104, 4–6 times/week = 260, everyday = 365, etc.) and was then log-transformed prior to the analyses. The association between the *CD36* genotype and the mainly used type of seasoning and cooking oil was investigated using χ^2 tests. All statistical studies were performed with SAS version 9.4 (SAS Institute Inc.). Two-tailed *P* values <0·002 were recognised as statistically significant to correct for multiple test issues following Bonferroni's rule (0·002 = 0·05/24 dietary-related variables examined).

Results

Table 1 presents the descriptive information of the study population, taking into account the BMI and *CD36* rs1527479. Approximately 41·8 and 44·1 % of males and females, respectively, were defined as having obesity. In males with or without obesity, the MAF for the C allele was 0·29 and 0·30, respectively. In females with or without obesity, the MAF was 0·31 and 0·29, respectively. The MAF of rs1527479 in Koreans has not yet been reported. However, the MAF values in Han Chinese and Japanese individuals were 0·34 and 0·22, respectively, which did not deviate much from that of Koreans according to the current study[30]. The statistical analyses suggested that *CD36* rs1527479 genetic variation had no meaningful association with the subjects' age, living area, alcohol consumption status, tobacco smoking status, marital status, education level or physical activity in all subgroups, taking into account sex and obesity level.

To examine whether *CD36* genetic variation may influence the intake of total energy and macronutrients, statistical analyses were performed. The findings suggested that *CD36* rs1527479 genetic variation was not associated with total energy, fat, cholesterol, protein or carbohydrate intake or the percentage of energy content obtained from those three macronutrients (Table 2). However, the analyses regarding the association between *CD36* genotype and food intake revealed interesting findings (Table 3). In the group of males with obesity, *CD36* rs1527479 showed an association with the intake of vegetables. In the subjects with obesity, cruciferous vegetable intake was lower in individuals with the CC genotype: for the TT, CT and CC genotypes, the levels were 218·9 (SD 132·3), 226·5 (SD 125·5) and 192·1 (SD 116·2) g/d, respectively ($P = 0·0004$). This cruciferous vegetable intake and genotype association were still significant when the covariates were adjusted in the statistical models (adjusted $P = 0·0015$). However, the association was not observed in the non-obese subjects or females. In females

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Table 1. Descriptive data of the study population by *CD36* rs1527479 genotype and level of obesity in males and females (Mean values and standard deviations; numbers and percentages)

Males (*n* 3194)	BMI < 25 kg/m² (*n* 1859, 58·2 %)							BMI ≥ 25 kg/m² (*n* 1335, 41·8 %)						
	TT (*n* 950, 51·1 %)		TC (*n* 758, 40·8 %)		CC (*n* 151, 8·1 %)			TT (*n* 672, 50·3 %)		TC (*n* 531, 39·8 %)		CC (*n* 132, 9·9 %)		
	n	%	*n*	%	*n*	%	*P**	*n*	%	*n*	%	*n*	%	*P**
Age (years)														
Mean	51·5		51·8		51·8		0·888	49·9		49·3		50·5		0·262
SD	8·93		8·89		9·06			7·7		7·82		8·51		
Area														
Rural (Ansung)	320	33·7	249	32·9	57	37·8	0·508	167	24·9	117	22·1	35	26·5	0·397
Urban (Ansan)	630	66·3	509	67·2	94	62·3		505	75·2	414	77·9	97	73·5	
Alcohol consumption														
Never	175	18·4	150	19·79	34	22·5	0·451	111	16·5	81	15·3	26	19·7	0·457
Ever	775	81·6	608	90·21	117	77·5		561	83·5	450	84·8	106	80·3	
Smoking status														
Never	175	18·4	159	20·9	29	19·2	0·414	141	20·9	109	20·5	25	18·9	0·867
Ever	775	81·6	599	79·0	122	80·8		531	79·1	422	79·5	107	81·1	
Cohabitation (marital status)														
With partner	908	95·6	720	94·9	140	92·7	0·564	647	96·3	516	97·2	130	98·5	0·497
Alone	40	4·21	37	4·88	9	5·96		22	3·3	14	2·64	2	1·52	
Missing	2	0·21	1	0·13	2	1·32		3	0·5	1	0·19	–		
Education														
Elementary school or lower	197	20·7	135	17·8	31	20·5	0·717	86	12·8	62	11·7	19	14·4	0·353
Middle school	194	20·4	167	22·0	32	21·2		147	21·9	89	16·8	26	19·7	
High school	349	36·7	296	39·1	59	39·1		259	38·5	223	42·0	49	37·1	
College or higher	210	22·1	160	21·1	29	19·2		180	26·8	157	29·6	38	28·8	
MET-h													20·6	
Mean	23·7		23·4		23·9		0·971	20·6		20·9		20·9		0·578
SD	14·9		14·9		14·8			13·1		12·2		12·9		

Females (*n* 3425)	BMI < 25 kg/m² (*n* 1914, 55·9 %)							BMI ≥ 25 kg/m² (*n* 1511, 44·1 %)						
	TT (*n* 919, 48·0 %)		TC (*n* 813, 42·5 %)		CC (*n* 182, 9·5 %)			TT (*n* 764, 50·6 %)		TC (*n* 611, 40·4 %)		CC (*n* 136, 9·0 %)		
	n	%	*n*	%	*n*	%	*P**	*n*	%	*n*	%	*n*	%	*P**
Age (years)														
Mean	50·4		51·5		51·4		0·033	53·3		53·2		52·7		0·748
SD	8·9		9·0		9·1			8·8		8·7		8·8		
Area														
Rural (Ansung)	323	35·2	315	38·8	61	33·62	0·203	323	42·3	239	39·1	52	38·2	0·414
Urban (Ansan)	596	64·8	498	61·2	121	66·5		441	57·7	372	60·9	84	61·8	
Alcohol consumption														
Never	641	69·8	587	72·2	133	73·1	0·440	549	71·9	423	69·2	94	69·1	0·528
Ever	278	30·0	226	27·8	49	26·9		215	28·1	188	30·8	42	30·9	
Smoking status														
Never	859	93·5	769	94·6	172	94·5	0·595	718	93·9	579	94·8	128	94·1	0·819
Ever	60	6·5	44	5·4	10	5·5		46	6·1	32	5·2	8	5·9	
Cohabitation (marital status)														
With partner	803	87·4	693	85·2	153	84·1	0·231	639	83·6	514	84·1	118	86·8	0·715
Alone	110	11·9	115	14·2	29	15·9		121	15·8	92	15·1	18	13·2	
Missing	6	0·7	5	0·6	–			4	0·5	5	0·8	–		
Education														
Elementary school or lower	297	32·3	314	38·6	65	35·7	0·104	359	46·9	297	48·6	65	47·8	0·828
Middle school	224	24·4	170	20·9	35	19·2		178	23·3	144	23·6	29	21·3	
High school	31	34·2	263	32·4	61	33·5		177	23·2	139	22·8	36	26·5	
College or higher	84	9·1	66	8·1	21	11·5		50	6·5	31	5·1	6	4·4	
MET-h														
Mean	20·8		21·7		21·3		0·427	21·7		22·1		20·0		0·273
SD	13·1		13·5		13·2			13·6		14·5		12·1		

MET-h, metabolic equivalents.

* *P* values for age and metabolic equivalents were from generalised linear models, otherwise from χ^2 tests among three genotypes.

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Table 2. Total energy and macronutrient intakes for each *CD36* rs1527479 genotype group by level of obesity in males and females (Mean values and standard deviations)

	BMI < 25 kg/m^2								BMI ≥ 25 kg/m^2							
	TT		TC		CC				TT		TC		CC			
	Mean	SD	Mean	SD	Mean	SD	*P**	*P*†	Mean	SD	Mean	SD	Mean	SD	*P**	*P*†
Males																
Total energy (kcal/d)‡	1959·6	530·9	1999·9	609·4	2031·9	554·8	0·303	0·317	2032·5	524·7	2064·4	557·8	2105·0	611·6	0·426	0·445
Fat (g/d)	35·6	11·3	34·5	10·2	35·2	10·1	0·317	0·159	35·6	10·4	36·3	10·2	35·4	9·5	0·361	0·657
Cholesterol (mg/d)	189·1	113·2	182·2	104·5	188·8	103·4	0·601	0·313	191·5	105·1	188·3	96·3	181·4	87·3	0·790	0·945
Protein (g/d)	68·8	11·3	68·8	10·7	68·9	10·3	0·973	0·775	70·4	11·1	70·9	11·0	69·8	10·4	0·446	0·891
Carbohydrates (g/d)	348·3	31·4	350·1	30·5	348·3	30·1	0·461	0·304	346·9	30·7	345·1	29·8	347·3	29·8	0·549	0·914
Percentage of energy from																
Fat	16·1	4·97	15·6	4·55	15·9	4·52	0·352	0·174	16·1	4·61	16·4	4·49	16·0	4·27	0·378	0·653
Protein	13·8	2·2	13·9	2·14	13·9	2·05	0·921	0·712	14·2	2·21	14·3	2·16	14·1	2·11	0·513	0·935
Carbohydrate	70·1	6·65	70·5	6·2	70·2	6·16	0·339	0·228	69·8	6·28	69·4	6·11	69·9	5·95	0·446	0·856
Females																
Total energy (kcal/d)‡	1853·9	619·1	1850·2	601·1	1859·5	576·8	0·907	0·622	1882·2	613·4	1823·4	577·0	1850·5	590·8	0·212	0·666
Fat (g/d)	29·8	11·0	29·2	11·1	29·0	11·5	0·278	0·585	27·5	9·7	27·8	10·6	28·6	9·6	0·382	0·525
Cholesterol (mg/d)	171·6	102·4	170·2	110·8	174·2	131·0	0·541	0·667	157·3	100·3	161·8	108·9	170·2	123·4	0·916	0·955
Protein (g/d)	63·1	10·8	62·9	10·8	63·0	11·3	0·888	0·819	62·1	10·5	62·5	10·7	62·9	9·7	0·540	0·725
Carbohydrates (g/d)	330·7	31·0	332·9	30·7	332·0	34·2	0·360	0·887	336·9	28·6	335·6	30·4	334·3	27·6	0·519	0·702
Percentage of energy from																
Fat	14·5	5·2	14·2	5·3	14·2	5·6	0·268	0·596	13·4	4·7	13·5	5·1	13·9	4·6	0·385	0·529
Protein	13·7	2·3	13·6	2·2	13·7	2·4	0·852	0·911	13·5	2·2	13·6	2·3	13·6	2·1	0·532	0·720
Carbohydrate	71·8	7·0	72·2	7·0	72·2	7·7	0·496	0·968	73·1	6·4	72·9	6·9	72·5	6·2	0·526	0·724

* *P* values were from crude generalised linear models.
† *P* values were from generalised linear models with the covariates including area, age, BMI, cohabitation, education, alcohol consumption, tobacco smoking, physical activity level and total energy intake.
‡ To convert energy values from kcal to kJ, multiply by 4·184.

Table 3. Intake of selected food groups in *CD36* rs1527479 genotype groups by level of obesity (g/d) (Mean values and standard deviations)

	BMI < 25 kg/m^2								BMI ≥ 25 kg/m^2							
	TT		TC		CC				TT		TC		CC			
	Mean	SD	Mean	SD	Mean	SD	*P**	*P*†	Mean	SD	Mean	SD	Mean	SD	*P**	*P*†
Males																
Carbohydrate foods	842·9	136	848·5	137·2	860·4	138·3	0·325	0·495	837·7	136·3	833·5	136·2	844·6	129·4	0·602	0·866
Carbohydrate–fat rich	47·9	42·3	48·9	42·4	48·9	48·4	0·802	0·687	50·5	41·7	56·0	49·8	50·8	39·0	0·152	0·180
Sweets	51·7	58·6	50·9	61·8	58·3	60·5	0·365	0·271	52·6	62·2	56·9	56·2	51·4	60·7	0·132	0·237
Protein-rich foods	227·7	139·2	221·5	133·1	228·0	120·5	0·481	0·237	233·0	130·8	229·7	116·8	233·2	150·6	0·796	0·800
Dairy products	102·9	122·0	98·5	112·0	98·3	102·5	0·841	0·886	99·6	113·4	91·2	98·9	95·4	127·5	0·748	0·461
Meats	76·9	48·7	75·1	46·4	78·3	46·3	0·696	0·497	78·3	43·6	79·8	44·3	81·7	47·4	0·617	0·716
Seafoods	42·2	34·0	42·5	33·0	45·0	33·7	0·518	0·372	49·1	35·7	51·6	37·5	50·0	33·9	0·176	0·559
Fatty foods	5·0	5·4	5·1	5·8	4·8	5·3	0·726	0·823	5·0	5·2	5·0	4·9	4·6	5·0	0·436	0·388
All vegetables	383·7	188·9	387·6	179·9	370·0	173·3	0·282	0·296	389·7	192·8	390·4	163·9	354·6	147·2	0·052	0·081
Green	43·2	47·5	44·9	47·4	43·7	39·2	0·061	0·059	47·5	54·9	46·0	44·2	45·2	45·3	0·637	0·801
Cruciferous	221·9	137·0	221·1	138·4	210·6	124·5	0·676	0·629	218·9[a]	132·3	226·5[a]	125·5	192·1[b]	116·2	0·0004	0·0015
All fruits	195·9	187·4	202·3	204·3	180·4	153·9	0·571	0·628	205·2	199·9	208·4	188·2	225·7	200·7	0·597	0·764
Citrus	36·8	49·1	36·1	43·8	29·9	29·6	0·247	0·271	35·2	44·7	34·9	40·6	38·9	40·1	0·264	0·350
Females																
Carbohydrate foods	767·8	151·4	767·1	156·6	780·5	152·4	0·529	0·344	785·4	141·8	788·5	146·5	781·3	127·8	0·920	0·676
Carbohydrate–fat rich	30·2	38·8	28·7	37·7	28·3	31·3	0·536	0·806	26·6	32·2	26·1	33·6	26·8	31·7	0·801	0·712
Sweets	39·0	59·4	38·5	55·5	32·3	40·0	0·753	0·749	36·3	55·0	33·9	46·6	38·3	60·9	0·641	0·737
Protein-rich foods	230·1	146·1	225·4	151·2	223·1	148·6	0·730	0·469	207·8	143·6	206·3	143·5	204·8	128·1	0·766	0·817
Dairy products	127·1	130·1	126·1	133·4	121·9	119·9	0·895	0·648	112·4	124·5	110·2	124·4	104·6	105·2	0·998	0·999
Meats	57·8	42·4	55·2	39·2	56·8	43·2	0·636	0·876	53·6	40·2	53·0	42·6	56·9	39·4	0·408	0·527
Seafoods	39·8	33·8	39·4	32·0	40·9	40·1	0·670	0·302	37·3	30·6	38·2	31·1	38·2	33·9	0·862	0·718
Fatty foods	3·0	4·0	2·9	3·7	3·3	5·0	0·506	0·650	2·9	4·0	2·7	3·6	2·7	3·3	0·865	0·928
All vegetables	346·1	167·8	367·8	193·0	331·8	158·8	0·034	0·044	370·7	174·1	369·2	188·1	374·3	179·2	0·758	0·748
Green	35·9	38·3	44·2	59·2	35·3	41·9	0·039	0·012	37·1	41·0	41·0	47·2	36·1	41·4	0·453	0·412
Cruciferous	186·3	125·4	190·0	127·3	178·7	124·8	0·521	0·586	202·2	127·3	196·5	139·6	201·3	118·1	0·161	0·106
All fruits	268·3	242·9	280·5	256·5	248·2	219·7	0·203	0·177	292·2	277·7	264·4	238·6	289·3	238·8	0·248	0·303
Citrus	45·5	53·2	44·9	52·0	44·2	50·2	0·683	0·797	47·8	63·5	44·7	54·6	46·6	52·3	0·975	0·932

[a,b] Mean values within a row with unlike superscript letters were significantly different between genotypes ($P < 0·05$; determined by Tukey's method).

* *P* values were from crude generalised linear models.

† *P* values were from generalised linear models with the covariates including area, age, BMI, cohabitation, education, alcohol consumption, tobacco smoking, physical activity level and total energy intake.

Table 4. Dietary behaviour-related oil consumption in *CD36* rs1527479 genotype groups by level of obesity in males and females (Numbers and percentages)

	BMI < 25 kg/m²							BMI ≥ 25 kg/m²						
	TT		TC		CC			TT		TC		CC		
	n	%	*n*	%	*n*	%	*P**	*n*	%	*n*	%	*n*	%	*P**
Males														
Frequency of consuming fried foods														
Rarely	389	41·4	315	42·3	60	39·7	0·285	256	38·6	198	37·4	55	41·9	0·358
1–2 times/month	339	36·1	255	34·3	48	31·8		241	36·3	184	34·7	38	29·0	
1–3 times/week	199	21·2	159	21·4	39	25·8		155	23·3	128	24·2	35	26·7	
4–6 times/week	9	0·96	11	1·48	2	1·32		6	0·9	14	2·64	2	1·53	
Everyday	4	0·43	4	0·54	2	1·32		6	0·9	6	1·13	1	0·76	
Seasoning oil commonly consumed														
Sesame oil	246	25·9	223	29·4	42	27·8	0·377	192	28·6	152	28·6	35	26·5	0·735
Perilla oil	140	14·7	92	12·1	22	14·6		105	15·6	69	12·9	17	12·9	
Sesame and perilla oil	543	57·2	423	55·8	85	56·3		362	53·9	290	54·6	76	57·6	
Others	21	2·21	20	2·6	2	1·32		13	1·93	20	3·77	4	3·03	
Cooking oil commonly used														
Soyabean oil	376	47·5	322	50·8	69	54·3	0·153	293	51·3	227	50·7	54	48·7	0·839
Maize oil	403	50·9	292	46·1	56	44·1		267	46·8	210	46·9	53	47·8	
Olive oil	8	1·01	13	2·05	2	1·57		6	1·05	9	2·01	3	2·7	
Butter	2	0·25	–		–			1	0·18	1	0·22	–		
Others	3	0·38	7	1·10	–			4	0·7	1	0·22	1	0·9	
Females														
Frequency of consuming fried foods														
Rarely	444	48·8	435	54·1	94	51·9	0·466	396	52·2	340	56·0	77	57·5	0·315
1–2 times/month	277	30·4	227	28·2	48	26·5		220	29·2	175	28·8	38	28·4	
1–3 times/week	166	18·2	122	15·2	35	19·3		126	16·6	72	11·9	18	13·4	
4–6 times/week	19	2·1	13	1·6	2	1·1		12	1·6	14	2·3	1	1·8	
Everyday	4	0·4	7	0·9	2	1·1		4	0·5	6	1·0			
Seasoning oil commonly consumed														
Sesame oil	313	34·1	294	39·2	64	35·2	0·061	249	32·6	198	32·4	37	27·2	0·468
Perilla oil	84	9·1	103	12·7	21	11·5		105	13·7	97	15·9	25	18·4	
Sesame and perilla oil	520	56·6	407	50·1	95	52·2		404	52·9	311	50·9	73	53·7	
Others	2	0·2	9	1·1	2	1·1		6	0·8	5	0·8	1	0·74	
Cooking oil commonly used														
Soyabean oil	435	47·3	386	47·5	83	45·6	0·853	342	44·8	303	49·6	54	39·7	0·098
Maize oil	392	4·7	338	41·6	74	40·7		342	44·8	243	39·8	64	4·1	
Olive oil	15	1·6	19	2·3	5	2·8		11	1·4	9	1·3	5	3·7	
Butter	9	0·9	5	0·6	2	1·1		7	0·9	4	0·7	2	1·5	
Others	68	7·4	65	8·0	18	9·8		62	8·12	53	8·7	11	8·1	

* *P* values for analyses of 'Frequency of consuming fried foods' were from generalised linear models. The frequency was converted to the times per year and applied for the statistical models. Covariates including area, age, BMI, cohabitation, education, alcohol consumption, tobacco smoking, physical activity level and total energy intake were adjusted in the statistical models. *P* values for analyses of 'Seasoning oil commonly consumed' and 'Cooking oil commonly used' were from χ^2 tests between types of oil and genetic groups. 'Others' were excluded from the analyses due to rarity.

without obesity, the genotype appeared to influence the intake of green vegetables, but the statistical significance was limited.

Last, Table 4 presents the results from the analyses showing that the *CD36* rs1527479 genotype influences dietary behaviour regarding oil consumption. The findings suggested that in obese or non-obese groups of males and females, the rs1527479 genetic variation was not associated with fat-related dietary behaviours, frequency of fried food consumption or commonly used types of oils for seasoning and cooking.

Discussion

This study investigated whether the genetic variation rs1527479 T>C in *CD36* is associated with fat and nutrition intake and related dietary behaviour in Koreans. Rs1527479 was selected as a proxy marker of rs1761667 G>A previously shown to represent the phenotypic changes in fat sensing. The findings suggested that *CD36* genetic variation was not associated with fat consumption or related dietary behaviour but that it showed a significant association with vegetable intake.

CD36 rs1761667 G>A is an intronic mutation close to the 5' flanking exon region[31]. Earlier studies have suggested that rs1761667 in *CD36* was associated with the perception of fat taste. In studies of Tunisian[13] and Algerian individuals[32], individuals with the AA mutant genotype showed lower intensity of fat perception and a preference for added fat and oil; hence, these individuals had higher fat intake than individuals with the genotype with the G allele[2]. Additionally, studies have clearly suggested that the genetic variant was associated with clinical outcomes, including lower rates of hypertension, coronary artery disease and liver fibrosis[33–35]. The association between the variation in *CD36* and fat sensing may be explained as follows. *CD36* mediates the relocation of selected fatty acids across the cellular membrane. Although rs1761667 is an intronic variation, experimental evidence has suggested that the variant

results in reduced mRNA transcription and protein expression[36]. This reduction could be associated with differences in the oral perception of the intensity of fat/fatty acid taste and intake[36]. However, in this study of Korean males, the effect of the variation in *CD36* was not evident in regard to fat and macronutrient intake, the preference for and frequency of fried food consumption or the commonly consumed types of oils. These conflicting findings regarding *CD36* and dietary behaviour might be associated with diverse dietary cultures and fat intake levels in different ethnicities. In animal models, varied oral expression of *CD36* was evident based on the fat content of the diets[37,38]. As alluded to above, the effect of *CD36* genetic variation on dietary intake also differed according to ethnicity and adiposity level. The Korean population generally showed relatively lower fat intake than other populations. A traditional Korean diet could be defined as being composed mainly of vegetables and grains, with limited use of oil and high-fat fried foods[39]. Animal fats are barely used for cooking and seasoning; rather, relatively small amounts of vegetable oils, including sesame, perilla and soybean oil, are generally used[39]. In this study of Koreans over 40 years old, the average intake of fat and the percentage of total energy obtained from fat were only approximately 27–36 g/d and 13–16 %, respectively. This level of fat intake is much lower than that of other populations, showing the association of *CD36* with fat intake[8]. Such differences in the type of dietary fat consumed and the intake level may be associated with the minimal effect of *CD36* genetic variation in the Korean male population.

In the present study, *CD36* genetic variation had a significant effect on cruciferous vegetable intake but not on fat consumption. Males with obesity and the CC genotype showed significantly lower cruciferous vegetable intake than those with the TT and CT genotypes. Cruciferous vegetables contain glucosinolate molecules with thiourea moieties, resulting in bitterness[40]. Earlier studies have reported that the bitterness genotype and phenotype defined by 6-n-propylthiouracil are associated with fat taste intensity. 6-n-propylthiouracil bitterness non-tasters were not able to distinguish the differences in the fat content of oil dressing[41] and had greater preference for high-fat oil dressing and daily discretionary fats[41,42]. Studies have attempted to explain the association between bitterness and fat taste intensity. Individual bitterness phenotypes result from multiple genetic traits, including taste receptor 2 member 38 (*TAS2R38)* and carbonic anhydrase 6. The lower taste intensity is the consequence of the structural change in the proteins due to the individuals' genetic characteristics and, hence, reduced differentiation of taste cells[17,43]. Those less-differentiated cells with functionally altered proteins therefore could modify the sensing of overall taste, including bitterness and possibly the fat taste[17,44]. A recent study also revealed a more direct relationship between *CD36* fatty acid sensing and the bitterness phenotype[45]. In this Korean study, the *CD36* genotype showed a significant association with cruciferous vegetable consumption. As alluded to above, fat has less significant meaning in Korean dietary culture than in other non-East Asian ethnicities. However, cruciferous vegetables account for a substantial amount, approximately 60 %, of the vegetables consumed by this Korean male population. Therefore, the effect of *CD36* genetic variation may be evident in bitter-tasting cruciferous vegetable intake due to the link between the fat and bitter taste phenotypes. Additionally, studies have attempted to investigate the genetic factors associated with vegetable consumption because consuming a sufficient amount of vegetables is important because they are not only a great source of dietary fibre but are also high in nutritive compounds[46]. The *TAS2R38* diplotype was known to be associated with cruciferous vegetable consumption in studies, but this association is still inconclusive in Koreans[47–49]. The present findings suggest that the potential effect of *CD36* genetic variation, not *TAS2R38*, is associated with vegetable intake in obese males. Overall, the present study could provide evidence that the putative link between bitterness and fat taste phenotypes and genotypes may play a role in Korean vegetable consumption.

Last, in the current study, the association between dietary intake and *CD36* genetic variation differed according to sex and level of obesity: the effect of *CD36* genetic variation was evident in only obese males but not in non-obese males or females. The association between *CD36* polymorphisms and the intensity of fat perception has been evident mainly in females[13,32]. However, controversies remain. The association of the *CD36* genotype with fat intensity varied between studies[2,18]. Limited numbers of studies have also adopted a sex-stratified design or were performed in male subjects. Sex is a decisive factor in health behaviour, including dietary consumption. Males and females have different levels of health knowledge and willingness to adopt healthy behaviours[20]. Males and females also experience different taste intensities from childhood[19]. These sex-specific characteristics might result in the differential effect of the *CD36* variant in dietary intake. Additionally, one experimental study verified that *CD36* rs1761667 was associated with fatty acid metabolism and the circulating endocannabinoid levels involved in energy metabolism by regulating appetite, and these effects of *CD36* varied by individual adiposity level (BMI)[16]. This may provide evidence on how the *CD36* genetic variation has a differential effect on dietary behaviour according to the level of obesity. Given all these findings, the design of the study, milieu and biological factors interactively contributed to the association identified between Korean males' dietary consumption and *CD36* genotype in the current study. Further experimental and epidemiological studies are required to explain the sex- and adiposity-specific underlying mechanisms of the potential modifying effects of *CD36* on dietary behaviour and health outcomes.

This study examined the association between *CD36* and dietary behaviour in Koreans with the rs1527479 genetic variation as a modifying factor. Limited knowledge regarding genetic factors in Korean dietary behaviour is currently available; therefore, this study may provide preliminary evidence. However, the study could have limitations. First, this study was performed with the data of approximately 6600 subjects from the Ansan/Ansung Community Cohort Study, a representative large genome-epidemiological study cohort. However, the size of the study population might be relatively small, and the subjects were over 40 years old, which may not fully represent the characteristics of all Koreans. Second, the study provided only limited information regarding fat intake. The full information regarding fat consumption, such as detailed types and intake of fatty acids, could not be

analysed in this study. Third, *CD36* is a critical genetic locus for fat sensing and metabolism. However, taste perception is a highly complicated mechanism, and the effects of other genes and environmental factors were not considered in this study. Last, the dietary information was collected using a FFQ. This may be associated with an accuracy issue in capturing a small amount of food and nutrition intake, as well as recall bias[50]. Therefore, findings must be interpreted with caution.

In conclusion, rs1527479 (a proxy of rs1761667) in *CD36* was not associated with fat, macronutrient intake or fat-related dietary behaviour in Korean males. However, this genetic variation was associated with cruciferous vegetable intake in obese males. These findings may aid in the understanding of the role of CD36 in the dietary intake and behaviour of Koreans.

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J. H. C. conducted this work and is responsible for the final content. J. H. C. conceived and designed the study, performed all analyses and wrote the manuscript.

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Supplementary material

For supplementary material referred to in this article, please visit https://doi.org/10.1017/S0007114520003748

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