British Journal of Nutrition (2019), 121, 1215–1222

doi:10.1017/S0007114519000679

British Journal of Nutrition

Cluster of differentiation 36 gene polymorphism (rs1761667) is associated with dietary MUFA intake and hypertension in a Japanese population

Ryosuke Fujii[1,2]*, Asahi Hishida[3], Koji Suzuki[1], Nahomi Imaeda[4], Chiho Goto[5], Nobuyuki Hamajima[6], Kenji Wakai[3] and Takaaki Kondo[2]

[1]*Department of Preventive Medical Sciences, Fujita Health University School of Health Sciences, Kutsukake-cho, Toyoake 470-1192, Japan*
[2]*Department of Pathophysiological Laboratory Sciences, Nagoya University Graduate School of Medicine, Higashi-ku, Nagoya 461-8673, Japan*
[3]*Department of Preventive Medicine, Nagoya University Graduate School of Medicine, Showa-ku, Nagoya 466-8550, Japan*
[4]*Department of Nutrition, Faculty of Wellness, Shigakkan University, Yokonemachi, Obu 474-8651, Japan*
[5]*Department of Health and Nutrition, Nagoya Bunri University, Inazawa 492-8520, Japan*
[6]*Department of Healthcare Administration, Nagoya University Graduate School of Medicine, Showa-ku, Nagoya 466-8550, Japan*

(Submitted 11 November 2018 – Final revision received 21 February 2019 – Accepted 12 March 2019 – First published online 28 May 2019)

Abstract

Cluster of differentiation 36 (*CD36*) is a membrane receptor expressed on a wide variety of human cells. *CD36* polymorphisms are reportedly associated with oral fat perception, dietary intake and metabolic disorders. The present study examined associations of two *CD36* polymorphisms (rs1761667 and rs1527483) and dietary fat intake, and metabolic phenotypes in a Japanese population. This cross-sectional study was conducted based on clinical information collected from health check-ups in Japan (n 495). Dietary nutrient intake was estimated from a validated short FFQ and adjusted for total energy intake using the residual method. Mean blood pressure was calculated from systolic blood pressure (SBP) and diastolic blood pressure (DBP). Hypertension was defined as SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg, or use of antihypertensive drugs. Genotyping was performed using PCR with confronting two-pair primers method. Mean age was 63·4 (SD 9·9) years. Individuals with the *AA* genotype showed higher total fat and MUFA intake (standardised $\beta = 0{\cdot}110$ and 0·087, $P = 0{\cdot}01$ and 0·05, respectively) compared with the *GG* and *GA* genotypes. For metabolic phenotypes, the *AA* genotype of rs1761667 had a lower blood pressure compared with the *GG* genotype (standardised $\beta = -0{\cdot}123$, $P = 0{\cdot}02$). Our results suggested that the *AA* genotype of rs1761667 in the *CD36* gene was associated with higher intake of total fat and MUFA and lower risk of hypertension in a Japanese population.

Key words: **CD36: Blood pressure: Fatty acids: Single nucleotide polymorphisms**

Cluster of differentiation 36 (*CD36*) is a membrane-bound protein expressed on several cell types, and regulates uptake of long-chain fatty acids across the membrane as a transporter[1,2]. Recent studies in humans and animals have proposed that *CD36* is expressed in taste bud cells from circumvallate foliate and fungiform papillae[3,4], suggesting that *CD36* may play an important role in oral fat perception (OFP) and individual preferences for fatty foods. Previous studies in different ethnic subpopulations have revealed that *CD36* SNP were significantly associated with *CD36* mRNA expression level[5] and threshold values to detect fat content[6–13]. Following studies on *CD36* genetic variants and OFP, the associations between *CD36* polymorphisms and dietary intake of fatty acids have gained a great deal of attention. Although prior studies have focused on populations of Europeans[4] and Latin Americans[14–16], such associations in Asian populations remain unclear.

Along with the nutritional perspective, many *CD36* SNP have been reported to be associated with various diseases and metabolic abnormalities in European and African American populations[5,8,10,11,13–15,17–24]. Based on these previous studies, recent

Abbreviations: *CD36*, cluster of differentiation 36; DBP, diastolic blood pressure; MBP, mean blood pressure OFP, oral fat perception; SBP, systolic blood pressure.

* **Corresponding author:** Ryosuke Fujii, email rfujii@fujita-hu.ac.jp

case–control studies have investigated the associations of *CD36* polymorphisms with ischaemic stroke[25,26] and CHD in Asian populations[27–29]. Given the previous studies of *CD36* polymorphisms, we hypothesised that fat perception based on *CD36* polymorphisms could be an important factor for metabolic profile and disease onset in human. Therefore, a comprehensive analysis is needed to elucidate individual differences in nutritional intake and metabolic indices based on *CD36* polymorphisms.

In the present study, two candidate SNP in the *CD36* gene (rs1761667 and rs1527483) were selected based on previous studies that had identified significant associations with OFP[7]. We aimed to investigate the associations between the genotypes of these two *CD36* SNP and dietary fat intake and metabolic phenotypes in a Japanese population.

Materials and methods

Study subjects

A total of 525 community-dwelling individuals participated in a health check-up carried out in Hokkaido, Japan, at the end of August 2015. This cross-sectional study was conducted based on clinical information and lifestyle data collected during the health check-up. Twenty-nine participants were excluded, due to incomplete lifestyle information in the questionnaire (n 3) or lack of informed consent to participate in the present study (n 26). Genotyping was unable to be successfully performed in another individual, who was therefore excluded. As a result, a total of 495 residents (228 men and 267 women) were analysed. The study protocol was approved by the Ethics Committee at Nagoya University School of Medicine.

Data collection

Anthropometric indices (height, weight and waist circumference) were measured during the health check-up to determine BMI (kg/m^2) and obesity status. Obesity was defined as waist circumference ≥ 85 cm in men or ≥ 90 cm in women. Blood pressure was measured using an automatic sphygmomanometer. Mean blood pressure (MBP) was calculated using systolic blood pressure (SBP) and diastolic blood pressure (DBP) via the following formula: MBP = DBP + (SBP − DBP)/3. Hypertension was defined as SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg, or use of antihypertensive medications. Participants were instructed to fast overnight. Fasting blood samples were collected and centrifuged within an hour of sampling. Biochemical analyses of blood samples were performed in the laboratory of Yakumo General Hospital. Diabetes mellitus was defined as fasting blood glucose ≥ 100 mg/dl (5·55 mmol/l) or use of medications for diabetes mellitus. Dyslipidaemia was defined as TAG ≥ 150 mg/dl (1·69 mmol/l), HDL-cholesterol ≤ 40 mg/dl (1·03 mmol/l) or use of medications for dyslipidaemia. The self-reported questionnaire in this study included questions on medical history and lifestyle habits of participants, including smoking status (current, former or never), alcohol consumption (current, former or never) and exercise habit (almost none, 1–2 h/week, 3–4 h/week or ≥ 5 h/week). Dietary intake of energy, total fat, SFA, MUFA, PUFA, n-3 PUFA and n-6 PUFA was estimated using a valid and reliable short FFQ[30–33]. Energy-adjusted nutrient intake using the residual method was utilised in our analyses to avoid effects of body size and weight on nutritional intake[34]. Because all items used for dietary fat intake showed positively skewed distributions, logarithmically transformed values were applied in our statistical analyses.

DNA collection and genotyping

Individual whole blood samples (350 µl) were collected at the health check-up and stored at 4°C until DNA extraction was performed. DNA was automatically extracted from the whole blood sample using a commercial kit and the BioRobot M48 Workstation (QIAGEN). In the genotyping step, we used PCR with confronting two-pair primers (PCR-CTPP) method, which is suitable for manually genotyping a number of samples in an epidemiological study in terms of running time and cost. To explain the PCR-CTPP method briefly, two pairs of allele specific primers (four primers: forward 1 (F1) and reverse 1 (R1) for X allele and F2 and R2 for Y allele) with different lengths are used. As shown in Supplementary Fig. S1, a PCR product with a length of a-bp, including X allele, is amplified between F1 and R1, although a product with a length of b-bp, including Y allele, is amplified between F2 and R2. A common band with a length of c-bp ($a + b - 1$) is amplified between F1 and R2. Therefore, a- and c-bp bands are observed in the XX genotype. Similarly, b- and c-bp bands are observed in the YY genotype. For the heterozygotes, all three bands are observed. The length of PCR products (a-bp and b-bp) should be different enough to distinguish by electrophoresis gel. Details and applications of this genotyping method have been reported elsewhere[35,36]. PCR primers for genotyping rs1761667 were: F1, 5'-TTG CCC TTT TTC CAT CTT CTG TGA-3' and R1, 5'-CCA GGC TTT GAG CAT GG**T**-3' for amplifying the *A* allele (155 base pairs (bp)); and F2, 5'-TTC ATC TTT GCA TGC CAG C**G**-3' and R2, 5'-AGT CCA AGC TTC TAT CCT TCC TA-3' for amplifying the *G* allele (341 bp). Primers for rs1527483 were: F1, 5'-TTC TGT ATG CAA GTC CTG ATG TT-3' and R1, 5'-TCA CTT CAT AAA CCA TAG GAA GAA AT**C**-3' for amplifying the *C* allele (259 bp); and F2: 5'-TCT TGA AAG TTA CTG AAA CTT AGG TC**A**-3' and R2: 5'-TGC CCA ATC GAA TGT CAA-3' for amplifying *T* allele (422 bp). These primers were obtained from Hokkaido System Science Co., Ltd. A total volume of 26 µl of PCR mixture comprising 17·4 µl of distilled water, 2·5 µl of 10× PCR Buffer (including 15 mM $MgCl_2$, 2·0 µl dNTPs, 0·5 µl of each primer, 0·1 µl AmpliTaq Gold (Thermo Fisher Scientific Japan)) and 2·0 µl of template DNA was used to amplify specific DNA regions for rs1761667 and rs1527483. PCR amplification was performed using the Veriti Thermal Cycler (Applied Biosystems). Amplification for rs1761667 and rs1527483 was initiated with pre-denaturalisation at 95°C for 10 min, followed by 30 cycles of denaturalisation at 95°C for 1 min, annealing at 61°C (rs1761667) or 60°C (rs1527483) for 1 min and extension at 72°C for 1 min and finalised by post-extension at 72°C for 5 min. A 2 % agarose gel with 2 µl/100 ml of ethidium bromide was used to visualise all PCR products and determine the genotypes at each locus. Representative gels for the genotyping of rs1761667 and rs1527483 are shown in Fig. 1(a) and (b), respectively.

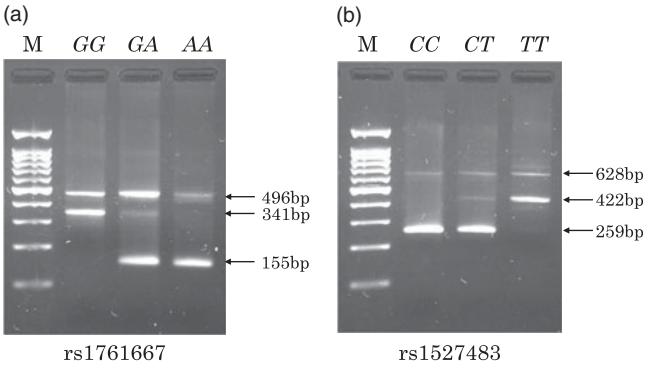

Fig. 1. Typical gels for genotyping the two cluster of differentiation 36 (*CD36*) polymorphisms (rs1761667 and rs1527483). Lane M contains a 100-bp ladder. For rs1761667 (a), lane *GG*, 341 bp band; lane *GA*, 341- and 155-bp bands; lane *AA*, 155-bp band. For 1527483 (b), lane *CC*, 259-bp band; lane *CT*, 259- and 422-bp bands; lane *TT*, 422-bp band.

Statistical analysis

The primary purpose of this study was to detect differences in dietary fat intake and metabolic profiles between three genotypes in rs1761667 and rs1527483. The required sample size for our analysis was calculated using the R package of pwr. For a type I error rate (α) of 0·05, the total sample size of 159 participants offered 80 % power ($1 - \beta$) to detect a moderate effect size ($f = 0{\cdot}25$) of genetic variants on metabolic profiles and dietary fat intake[37]. Although normally distributed variables are expressed as mean values and standard deviations, TAG, HDL-cholesterol and all variables for dietary fat intake are presented as medians and 1st–3rd quartiles because of the skewed distributions. Fisher's exact test was used to confirm the consistency of Hardy–Weinberg equilibrium in this population[38,39]. Associations between the genotypes of two *CD36* SNP, dietary fat intake and metabolic profiles were assessed using multiple linear regression analysis. Multiple logistic regression analysis was performed to estimate the OR for metabolic disorders, according to the genotypes. These regression analyses were performed after adjusting for sex and age and all statistical analyses were performed using R version 3.5.0 (R Foundation). Values of $P < 0{\cdot}05$ were considered statistically significant.

Results

Basic characteristics of participants

The basic clinical profiles of study subjects are summarised by the three genotypes of rs1761667 and rs1527483 (Table 1). No significant differences were observed between the genotypes of each polymorphism. The minor allele frequency (MAF) of rs1761667 and rs1527483 was 0·267 and 0·209, respectively, which was consistent with the result from a Japanese public database (Japan Multi Omics Reference Panel: JMorp) (MAF = 0·275 and 0·220, respectively)[40]. Genotype distributions of each SNP in this population were in accordance with Hardy–Weinberg equilibrium ($P = 0{\cdot}73$ and 0·89, respectively). Table 2 shows dietary fat and fatty acid intake, according to the genotypes in the present study.

Genotypes of two CD36 polymorphisms and dietary fat intake

Table 3 shows the results of adjusted linear regression analyses for associations between three genotypes of two *CD36* polymorphisms (rs1761667 and rs1527483) and dietary fat intake. Individuals with the *AA* genotype showed higher fat and MUFA intake (standardised $\beta = 0{\cdot}110$ and 0·087, $P = 0{\cdot}01$ and 0·05, respectively) compared with the *GG* and *GA* genotypes, whereas no significant associations between the genotypes of rs1761667 and intake of other fatty acids were observed in the present study. For rs1527483, SFA intake in the *TT* genotype was significantly lower compared with the *CC* and *CT* genotypes (standardised $\beta = -0{\cdot}087$, $P = 0{\cdot}05$, respectively). However, no significant association was observed between the genotypes of rs1527483 and intake of other dietary fat.

Genotypes of two CD36 polymorphisms and metabolic phenotypes

In adjusted linear regression analyses, the *AA* genotype of rs1761667 was significantly associated with 7·0 mmHg lower MBP compared with the *GG* genotype (standardised $\beta = -0{\cdot}123$, $P = 0{\cdot}02$), while the *GA* genotype was not significantly associated with lower MBP (standardised $\beta = -0{\cdot}053$, $P = 0{\cdot}32$) (Table 4). No significant association was observed between the genotypes of *CD36* polymorphisms and other metabolic profiles (Supplementary Tables S1 and S2). Multivariable logistic regression also showed that the adjusted OR for hypertension was marginally lower in the *AA* genotype in rs1761667 than in the *GG* genotype (OR = 0·49, 95 % CI 0·24, 1·02, $P = 0{\cdot}06$), but not in the *GA* genotype (OR = 0·85, 95 % CI 0·57, 1·28, $P = 0{\cdot}44$) (Table 5). No significant associations between hypertension and the genotypes of rs1527483 were observed in our logistic regression analysis. Associations between the genotypes of *CD36* polymorphisms and other metabolic disorders can be seen in Supplementary Tables S3 and S4.

Discussion

The primary goal of this study was to elucidate the associations of the genotypes of *CD36* polymorphisms with dietary fat intake and metabolic phenotype. We found that the *AA* genotype of rs1761667 in the *CD36* was significantly associated with higher fat and MUFA intake and lower blood pressure in the Japanese population.

The two polymorphisms (rs1761667 and rs1527483) examined in the present study are non-coding intronic SNP located at chromosome 7, and do not cause structural changes in the *CD36* protein. The *AA* genotype of rs1761667 is known to be involved in reduced *CD36* mRNA expression[5]. Furthermore, previous studies in humans and experimental animals have reported *CD36* expression level as significantly associated with individual differences in OFP[6]. According to these results, rs1761667 is assumed to play an important role in human OFP. Keller *et al.*[8] originally reported that African American participants with the *AA* genotype of rs1761667 had a preference for adding fats and oils. In a similar finding described by Pepino *et al.*[6], the threshold for detecting oleic acid, one of the major

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Table 1. Clinical characteristics of participants (*n* 495) according to the three genotypes of cluster of differentiation 36 (*CD36*) SNP (Mean values and standard deviations; numbers of participants and percentages; medians and interquartile ranges)

	rs1761667						rs1527483					
	GG (*n* 268)		*GA* (*n* 190)		*AA* (*n* 37)		*CC* (*n* 310)		*CT* (*n* 163)		*TT* (*n* 22)	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Age (years)												
Mean	62·9		64·0		64·9		63·1		64·0		63·9	
SD	9·7		10·1		9·9		9·9		9·6		12·3	
Men	114	42·5	94	49·5	20	54·1	142	45·8	74	45·4	12	54·5
BMI (kg/m^2)												
Mean	23·6		23·7		23·4		23·8		23·3		23·8	
SD	3·4		3·4		2·8		3·5		3·2		2·4	
WC (cm)												
Mean	82·1		82·2		81·8		82·5		81·5		81·3	
SD	9·8		10·3		10·0		10·2		9·9		8·1	
HDL-C* (mmol/l)												
Median	1·45		1·47		1·53		1·47		1·50		1·45	
1st–3rd quartiles	1·24–1·76		1·24–1·73		1·29–1·71		1·24–1·76		1·29–1·76		1·20–1·69	
TAG* (mmol/l)												
Median	1·02		0·99		0·91		0·99		1·12		1·04	
1st–3rd quartiles	0·78–1·48		0·72–1·46		0·70–1·22		0·75–1·43		0·75–1·51		0·72–1·45	
SBP (mmHg)												
Mean	131·2		131·7		123·8		130·5		130·8		135·6	
SD	20·1		20·7		19·1		20·7		20·1		17·2	
DBP (mmHg)												
Mean	76·4		76·3		71·5		76·1		75·4		79·6	
SD	13·9		13·5		12·9		13·9		13·2		15·1	
Glucose (mmol/l)												
Mean	4·93		5·0		5·04		5·01		4·93		4·85	
SD	0·86		0·84		0·73		0·92		0·73		0·49	
Smoking status												
Never	144	53·7	86	45·3	14	37·8	145	46·8	87	53·4	12	54·5
Former	83	31·0	73	38·4	18	48·6	122	39·4	45	27·6	7	31·8
Current	41	15·3	31	16·3	5	13·5	43	13·9	31	19·0	3	13·6
Alcohol consumption												
Never	139	51·9	89	46·8	15	40·5	152	49·0	82	50·3	9	40·9
Former	5	1·9	6	3·2	0	0·0	8	2·6	3	1·8	0	0·0
Current	124	46·3	95	50·0	22	59·5	150	48·4	78	47·9	13	59·1
Exercise habit												
<1 h/week	152	56·7	117	61·6	25	67·6	184	59·4	94	57·7	16	72·7
1–2 h/week	52	19·4	37	19·5	4	10·8	57	18·4	33	20·2	3	13·6
3–4 h/week	37	13·8	16	8·4	8	21·6	44	14·2	16	9·8	1	4·5
>5 h/week	27	10·1	20	10·5	0	0·0	25	8·1	20	12·3	2	9·1
Hypertension	170	63·4	118	62·1	19	51·4	195	62·9	97	59·5	15	68·2
Dyslipidaemia	115	42·9	75	39·5	12	32·4	127	41·0	66	40·5	9	40·9
Diabetes	27	10·1	26	13·7	5	13·5	42	13·5	15	9·2	1	4·5
Obesity	86	32·1	69	36·3	13	35·1	115	37·1	48	29·4	5	22·7

WC, waist circumference; HDL-C, HDL-cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.
* HDL-C and TAG are presented as medians and 1st–3rd quartiles because of skewed distributions.

Table 2. Dietary fat and fatty acid intakes of participants according to the three genotypes of cluster of differentiation 36 (*CD36*) SNP (Medians and interquartile ranges)

	rs1761667						rs1527483					
	GG (*n* 268)		*GA* (*n* 190)		*AA* (*n* 37)		*CC* (*n* 310)		*CT* (*n* 163)		*TT* (*n* 22)	
	Median	25 %–75 %	Median	25 %–75 %	Median	25 %–75 %	Median	25 %–75 %	Median	25 %–75 %	Median	25 %–75 %
Total fat (g/d)	42·5	36·9–48·1	41·7	36·7–48·7	44·5	39·1–53·2	42·3	36·7–49·1	43·6	38·3–49·)	38·2	34·0–43·8
SFA (g/d)	11·5	9·5–13·1	10·9	9·5–12·6	12·0	10·2–13·8	11·3	9·5–12·9	11·6	9·9–13·)	10·0	8·8–11·7
MUFA (g/d)	15·2	13·3–18·2	14·9	13·2–17·9	15·5	13·6–20·1	15·3	13·3–17·9	15·4	13·3–18·7	14·3	12·9–15·9
PUFA (g/d)	12·3	10·6–14·7	12·1	10·9–14·9	12·5	11·1–15·5	12·2	10·6–14·7	12·7	10·9–15·2	11·9	10·7, 13·2
n-3 PUFA (g/d)	2·16	1·88–2·54	2·18	1·90–2·48	2·12	1·93–2·62	2·17	1·88–2·5)	2·18	1·89–2·54	2·05	1·85–2·26
n-6 PUFA (g/d)	10·4	8·87–12·4	10·3	8·95–12·4	11·1	9·48–13·4	10·4	8·90–12·4	10·4	9·03–12·8	10·2	8·80–10·6

Table 3. Multiple linear regression analysis* for the association between two cluster of differentiation 36 (*CD36*) SNP and dietary fat intake (β-Coefficients and 95 % confidence intervals)

	rs1761667 (*GG* + *GA* as reference)				rs1527483 (*CC* + *CT* as reference)			
	Standardised *β*	Unstandardised *β*†	95 % CI	*P*	Standardised	Unstandardised *β*†	95 % CI	*P*
Total fat	0·110	0·122	0·027, 0·217	0·01	–0·047	–0·066	–0·188, 0·056	0·29
SFA	0·083	0·074	–0·002, 0·150	0·06	–0·087	–0·099	–0·196, –0·002	0·05
MUFA	0·087	0·081	0·000, 0·161	0·05	–0·041	–0·048	–0·151, 0·055	0·36
PUFA	0·058	0·074	–0·036, 0·184	0·19	–0·013	–0·021	–0·162, 0·120	0·77
n-3 PUFA	0·036	0·036	–0·050, 0·122	0·41	0·001	0·001	–0·109, 0·111	0·98
n-6 PUFA	0·076	0·099	–0·013, 0·211	0·09	–0·015	–0·025	–0·169, 0·118	0·73

* Adjusted for sex and age.
† The *β*-coefficient indicates an increase/a decrease of dietary fat intake (g/d) for the *AA* (rs1761667) or *TT* genotype (rs1527483).

Table 4. Multiple linear regression analysis* for associations between the genotypes of cluster of differentiation 36 (*CD36*) SNP and mean blood pressure (*n* 349)
(β-Coefficients and 95 % confidence intervals)

		Unadjusted				Sex and age adjusted			
		Standardised *β*	Unstandardised *β*†	95 % CI	*P*	Standardised *β*	Unstandardised *β*†	95 % CI	*P*
rs1761667	*GG*		Reference				Reference		
	GA	–0·043	–1·357	–4·793, 2·078	0·44	–0·053	–1·689	–5·009, 1·631	0·32
	AA	–0·102	–5·707	–11·75, 0·337	0·07	–0·123	–6·877	–12·75, –1·007	0·02
rs1527483	*CC*		Reference				Reference		
	CT	0·013	0·042	–3·054, 3·937	0·81	0·015	0·487	–2·897, 3·872	0·78
	TT	0·069	4·939	–2·711, 12·59	0·21	0·050	3·595	–3·829, 11·02	0·34

* This analysis was performed after excluding those who took antihypertension medications (*n* 146).
† The *β*-coefficient indicates an increase/a decrease of blood pressure (mmHg) in each genotype compared with the *GG* (rs1761667) or *CC* (rs1527483) genotype.

Table 5. Multiple logistic regression analysis for the associations between the genotypes of two cluster of differentiation 36 (*CD36*) SNP and hypertension (HT)
(Odds ratios and 95 % confidence intervals)

			Unadjusted			Sex and age adjusted		
		HT/non-HT (*n*)	OR	95 % CI	*P*	OR	95 % CI	*P*
rs1761667	*GG*	170/98	1·00	–	–	1·00	–	–
	GA	118/72	0·94	0·64, 1·39	0·77	0·85	0·57, 1·28	0·44
	AA	19/18	0·61	0·30, 1·22	0·16	0·49	0·24, 1·02	0·06
rs1527483	*CC*	195/115	1·00	–	–	1·00	–	–
	CT	97/66	0·87	0·59, 1·28	0·47	0·81	0·54, 1·22	0·32
	TT	15/7	1·26	0·52, 3·39	0·62	1·21	0·46, 3·43	0·71

MUFA, was eightfold higher in a Caucasian population with the *GG* genotype than in those with the *AA* genotype[5]. Obese women with the *AA* genotype exhibited a lower sensitivity for oleic acid compared with those with the *G* allele[10]. Such results have suggested that individuals with the *AA* genotype of rs1761667 have reduced sensitivity to fat content, which can lead to increased fat intake. In fact, Hispanic subjects with the *AA* genotype of rs1761667 showed higher fat intake compared with subjects with the *GG* genotype[15], although few studies have reported no significant association between the genotypes of rs1761667 and dietary fat intake in Asian populations. Given these previous studies, greater dietary intake of fat and MUFA in the *AA* genotype of rs1761667 appears reasonable. With regard to rs1527483, we found no significant associations with dietary fat and fatty acid intake. In a Malaysian population that consisted mostly of ethnic Chinese, individuals with the *TT* genotype perceived significantly greater fat content independent of fat concentrations than *C* allele carriers[12]. One study in African Americans also found that participants with the minor allele of rs1527483 (*T*) rated fat content higher than those with the *CC* genotype[8]. A recent study among Czech young adults reported that the *CC* genotype of rs1527483 had higher sensitivity for linoleic acid detection than the *CT* and *TT* genotypes[13]. On the other hand, the genotypes of rs1527483 was not significantly associated with the capability in a Caucasian population to detect oleic acid[9]. Compared with rs1761667, the association of rs1527483 with OFP seems invalid, and comprehensive studies are needed to better characterise the relationship between the genotypes of rs1527483, OFP and dietary fat intake in either ethnic group.

Previous studies in rodents found that *Cd36* genetic background was linked to the regulation of blood pressure[41,42].

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Abnormal expression of *CD36* in the kidney was involved in the genetic basis of hypertension[43]. In humans, *CD36* polymorphisms have been reported to be associated with CVD such as ischaemic stroke[25,26], CHD[27,29] and essential hypertension[28] in Asians. Such findings supported consistent evidence of a significant association between *CD36* and CVD in both humans and animals. In the present study, the *AA* genotype of rs1761667 had a lower blood pressure than the *GG* genotype, but no significant relationship was observed in the genotypes of rs1527483. Taking our findings together, the *AA* genotype of rs1761667 was associated with higher dietary intake of MUFA, which may be associated with decreased blood pressure and lower risk of CVD[44,45]. Although significant associations between the genotypes of *CD36* polymorphisms (rs1761667 and rs1527483) and anthropometric and lipid indices have been observed in many studies in Caucasian[17,18] and African American populations[21,22], we did not find any such associations among community-dwelling Japanese adults in Japan. Our result is in line with previous studies in Asians, showing no significant relationship between the two polymorphisms and those phenotypes[12,25]. These discrepancies could be attributable to different ethnicities, which may indicate that rather than obesity or dyslipidaemia, hypertension based on the genotypes of rs1761667 plays an important role in CVD onset in Asian populations.

The strength of this study was the comprehensive analysis used to examine the associations of *CD36* polymorphisms with individual dietary intake and clinical profiles in an Asian population. However, several limitations must also be considered. The key consideration in this study was that *CD36* deficiency is relatively common in Asian populations (2–3 %) but not in Caucasians (less than 0·3 %)[46–48]. *CD36* deficiency has been well investigated for several pathophysiological conditions[49–52]. One study in a Japanese population demonstrated that patients with *CD36* deficiency showed an atherogenic effect[53]. Future work in Asian populations is thus needed to clarify the effects of *CD36* deficiency on blood pressure and hypertension. In our study, subjects were genetically homogeneous and community-dwelling people living within a single administrative area. The sample size was relatively small for exploring the influences of genetic variants on several indices, but the estimated sample size seemed sufficient. Our results must therefore be confirmed in other Asian populations with larger sample sizes. Furthermore, transethnic studies are warranted to clarify the molecular mechanism underlying the associations between *CD36* polymorphisms and diseases across different ethnicities.

In conclusion, we found that the *AA* genotype of rs1761667 was significantly associated with higher dietary fat and MUFA intake and a lower blood pressure compared with the *GG* genotype. This result could shed light on the individual differences in dietary fat intake based on the genotypes of *CD36* polymorphisms and its effect on blood pressure in an Asian population.

Acknowledgements

The authors thank Mrs. Yoko Mitsuda and Mrs. Keiko Shibata from the Department of Preventive Medicine at Nagoya University Graduate School of Medicine for their technical assistance. The authors are also grateful to Mr. Kensuke Suzuki at the Department of Economics, Pennsylvania State University, for his expert advice in statistical method. We are also grateful to the participants and staff of the health examination programme for residents of Yakumo Town, Hokkaido, Japan.

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

R. F. drafted the article and performed statistical analyses; R. F., A. H., K. S., K. W. and T. K. contributed for data acquisition; N. H. and K. W. were responsible for the conception and design; N. I. and C. G. contributed to the interpretation of results. All the authors reviewed the manuscript.

The authors declare no conflicts of interest with respect to this study.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114519000679

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