

# Lack of association between glutathione s-transferase mu 1 (*GSTM1*) gene polymorphisms and obesity

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Recent researches suggested that personal individual's genetic background is contributed to the susceptibility to obesity. The present of this study is to investigate whether single nucleotide polymorphisms (SNPs) of glutathione s-transferase mu 1 (*GSTM1*) gene are susceptibility to obesity in Korean population. In present study, two SNPs (rs1056806 [Asp142Asp], rs3815029 [promoter]) of *GSTM1* gene were genotyped in 117 overweight/obese subjects with a body mass index (BMI)  $\geq 23$  kg/m<sup>2</sup> and 125 nonoverweight/obese with a BMI of 18.5–23.0 kg/m<sup>2</sup>. Genotyping of two SNPs (rs1056806 and rs3815029) was determined by sequencing after polymerase chain reaction. Logistic regression models (codominant, dominant, recessive, and log-additive models) and allele

analysis were used to calculate odds ratio, 95% confidence interval, and *P*-values. Significant association was considered at  $P < 0.05$ . Tested two SNPs in *GSTM1* genes did not show any significant association with obesity (rs1056806,  $P = 0.24$  in codominant 1 model; rs3815029,  $P = 0.59$  in codominant 1,  $P = 0.09$  in codominant 2,  $P = 0.16$  in dominant,  $P = 0.09$  in recessive, and  $P = 0.07$  in log-additive models). In summary, these results indicate that SNPs of *GSTM1* gene did not associated with susceptibility of obesity in the Korean population.

**Keywords:** Overweight, Obese, Obesity, *GSTM1*, Single nucleotide polymorphism

## INTRODUCTION

Obesity is a state in which excess fat is accumulated in the body to cause abnormalities in health (Goodarzi, 2017). Obesity itself is a cause of many chronic diseases including stroke and is one of the health-threatening factors (Kalantari et al., 2016; Zhou et al., 2017). In recent years, the overall obesity population is rapidly increasing due to a decrease in physical activity and an increase in energy consumption. The increase in the obese population is associated with an increased incidence of diverse diseases such as diabetes (Mutie et al., 2017), cardiovascular disease (Shaw et al., 2017), cancer (colon cancer, breast cancer, prostate cancer, etc.) (Engin, 2017; Fardet et al., 2017), dyslipidemia, and osteoarthritis. Obesity is a burden on individual health care costs and national health care costs (Tremmel et al., 2017). This aspect is a common phenomenon not only in European countries such as England and France, but also in countries around the world including Asia (Hoque et al., 2016; Kim and Basu, 2016).

The cause of obesity has recently been proposed to be related to complex, multifactorial biological and environmental factors (Bell, 2017; O'Rahilly and Farooqi, 2000). From a biological point of view, obesity is known to determine physiological and genetic, race, sex, and age. Regarding to association between obesity and genetic background, when one of the identical twins is obese, the other is much more likely to be obese than the fraternal twin 28845613. In addition, the statistic that obesity correlations between parents and patients are stronger than the relationship between parents and progenitors is evidence that obesity is affected by genetic factors (O'Rahilly and Farooqi, 2000).

Glutathione (*GST*) genes are phase II enzymes involved in the detoxification of intrinsic and extrinsic electrophilic compounds, which protect against oxidative stress by eliminating free radicals by glutathione-dependent peroxidase and affect individual susceptibility to diseases such as hypertension (Ge et al., 2015). Genetic polymorphisms of the glutathione s-transferase mu 1 (*GSTM1*) gene are known to affect DNA and antioxidant levels (Altay and

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Bozoğlu, 2017).

Genetic polymorphisms of specific genes are known to be associated with obesity in recent years and many studies are under way (Akbarian et al., 2017; Liu et al., 2017; Rivera et al., 2017). In present study, we investigated the relationship between *GSTM1* gene polymorphisms and obesity.

## MATERIALS AND METHODS

### Study subjects

Table 1 shows clinical and biochemical characteristics of overweight/obese and control subjects. In the present study, 117 overweight/obese subjects and 125 nonoverweight/obese subjects were recruited. These subjects were recruited among participants that examined a general health check-up program. Subjects with severe diseases such as stroke, psychiatric disorders, and cancers were excluded. The biochemical characteristics of individuals were measured such as fasting plasma glucose, fasted glycated hemoglobin, high-density lipoprotein. Body mass index (BMI) is calculated as weight (kg) divided by the square of height (m). According to the classification of Korean Society for the Study of Obesity (underweight, BMI < 18 kg/m<sup>2</sup>; normal, BMI 18 to < 23 kg/m<sup>2</sup>; moderately obese, BMI 23 to < 25 kg/m<sup>2</sup>; obesity I, BMI 25 to < 30 kg/m<sup>2</sup>; obesity II, BMI ≥ 30 kg/m<sup>2</sup>), subjects were divided into 2 subgroups, the overweight/obese group (BMI ≥ 23 kg/m<sup>2</sup>) and the control group (18 kg/m<sup>2</sup> ≤ BMI < 23 kg/m<sup>2</sup>).

### SNP selection and genotyping

Peripheral bloods of all subjects were collected in ethylenediaminetetraacetic acid or heparin tube. Genomic DNAs were extracted by QIAamp DNA mini kit (QIAGEN, Valencia, CA, USA). We selected two SNPs (rs1056806 [Asp142Asp], rs3815029 [promoter]) in *GSTM1* gene. Genotype of each SNP was performed by sequencing after polymerase chain reaction (PCR).

**Table 1.** Clinical and biochemical characteristics of overweight/obese and control subjects.

Characteristic	Overweight/obese (n=117)	Control (n=125)
Age (yr)	44.2 ± 14.1	35.2 ± 11.3
Body mass index (kg/m <sup>2</sup> )	25.5 ± 2.3	20.6 ± 1.3
Fasting plasma glucose (mg/dL)	91.6 ± 22.7	85.1 ± 8.6
High-density lipoprotein (mg/dL)	49.6 ± 10.7	54.9 ± 11.7
Glycated hemoglobin (%)	5.8 ± 0.7	5.4 ± 0.5
Triglyceride (mg/dL)	191.7 ± 32.9	170.8 ± 26.2

Values are presented as mean ± standard deviation.

The primers used for PCR are as follows; rs1056806, sense, 5'-AAGGAGGAGTGATATGGGGAAT-3', antisense, 5'-GTGGCATGAAACCAGTACTCAA-3'; rs3815029, sense, 5'-TGACACTGTTCTGTGTAGG-3' and antisense, 5'-GATCTGGCTGTGTCTCAAG-3'.

### Statistical analysis

SNPStats (<http://bioinfo.iconcolgia.net/index.php>) and IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, USA) were used to determine the odds ratio (OR), 95% confidence interval (CI), and *P*-value. Logistic regression models (codominant 1 [A/A genotype vs. A/B genotype], codominant 2 [A/A genotype vs. B/B genotype], dominant [A/A genotype vs. A/B genotype+B/B genotype], recessive [A/A genotype+A/B genotype vs. B/B genotype], and log-additive models [A/A genotype vs. A/B genotype vs. B/B genotype]) were applied. The *P*-value below 0.05 was considered significant.

## RESULTS

In order to evaluate the association between *GSTM1* gene and susceptibility of obesity, we genotyped and analyzed the one exonic SNP (rs1056806) and one promoter SNP (rs3815029) of *GSTM1* gene.

Table 2 showed genotypic distributions of two SNPs of *GSTM1* gene in the control group and overweight/obese group. The C/C genotype:T/C genotype:T/T genotype of rs1056806 in the overweight/obese group and the control group were 90.8%:9.2%:0.0% and 93.6%:6.4%:0.0%. And the C/C genotype:C/G genotype:G/G genotype of rs3815029 in the overweight/obese group and the control group were 42.4%:45.6%:12.0% and 48.7%:45.34%:6.0%. In genotypic analysis, two SNPs did not be observed any significant association with susceptibility of obesity (rs1056806: OR, 0.62; 95% CI, 0.28–1.36; *P* = 0.24 in codominant 1 model [C/C genotype vs. C/T genotype] and rs3815029: OR, 0.75; 95% CI, 0.41–1.36; *P* = 0.59 in codominant 1 model [C/C genotype vs. C/G genotype]; OR, 0.36; 95% CI, 0.12–1.07; *P* = 0.09 in codominant 2 model [C/C genotype vs. G/G genotype]; OR, 0.66; 95% CI, 0.37–1.18; *P* = 0.16 in dominant model [C/C genotype vs. C/G genotype + G/G genotype]; OR, 0.42; 95% CI, 0.15–1.19; *P* = 0.09 in recessive model [C/C genotype + C/G genotype vs. G/G genotype]; and OR, 0.66; 95% CI, 0.42–1.03; *P* = 0.07 in log-additive model [C/C genotype vs. C/G genotype vs. G/G genotype]).

In allele analysis, allele frequencies of the each SNP in *GSTM1*

**Table 2.** Genotypic distributions of single nucleotide polymorphisms of glutathione s-transferase mu 1 (*GSTM1*) gene in the control group and overweight/obese group

SNP	Genotype	Control	Overweight/obese	Models	OR (95% CI)	P-value
rs1056806	C/C	102 (81.6)	102 (87.2)	Codominant 1	0.62 (0.28–1.36)	0.24
	C/T	23 (18.4)	15 (12.8)	Codominant 2	NA	NA
	T/T	0 (0.0)	0 (0.0)	Dominant	NA	NA
				Recessive	NA	NA
				Log-additive	NA	NA
rs3815029	C/C	53 (42.4)	57 (48.7)	Codominant 1	0.75 (0.41–1.36)	0.59
	C/G	57 (45.6)	53 (45.3)	Codominant 2	0.36 (0.12–1.07)	0.09
	G/G	15 (12.0)	7 (6.0)	Dominant	0.66 (0.37–1.18)	0.16
				Recessive	0.42 (0.15–1.19)	0.09
				Log-additive	0.66 (0.42–1.03)	0.07

Genotype distributions are presented as number (%).

P-values were from logistic regression analyses with the codominant, dominant, recessive, and log-additive models.

SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval; NA, not applicable.

**Table 3.** Allele distributions of single nucleotide polymorphisms of glutathione s-transferase mu 1 (*GSTM1*) gene in the control group and overweight/obese group

SNP	Allele	Control	Overweight/obese	OR (95% CI)	P-value
rs1056806	C	227 (90.8)	219 (93.6)	1	
	T	23 (9.2)	15 (6.4)	0.68 (0.34–1.33)	0.26
rs3815029	C	163 (65.2)	167 (71.4)		
	G	87 (34.8)	67 (28.6)	0.75 (0.51–1.10)	0.15

Genotype distributions are presented as number (%).

P-values were from logistic regression analyses.

SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval; NA, not applicable.

gene were compared between the control group and the overweight/obese group by logistic regression analysis in Table 3. The C allele:T allele of rs1056806 in the overweight/obese group and the control group were 90.8%:9.2% and 93.6%:6.4% and C allele:G allele of rs3815029 in the overweight/obese group and the control group were 65.2%:34.8% and 71.4%:28.6%. The differences of each SNP distributions in two groups also did not show any significant association with obesity.

## DISCUSSION

The most famous gene related to genetic polymorphism and obesity is known as *FTO* gene and there are many studies (Moghanloo et al., 2017; Rivera et al., 2017; Zhou et al., 2017). Although genetic polymorphism alone affects certain diseases, a combination of polymorphisms of several genes is known to affect disease. Therefore, it is necessary to identify candidate genes for obesity.

*GSTM1* is known to be associated with oxidative stress. Excessive oxidative stress results in cellular damage and physiological anomalies. This oxidative stress is considered to have a direct impact on the pathogenesis and progression of major diseases such as

obesity, cancer, arteriosclerosis, coronary artery disease, and rheumatoid arthritis, which frequently occur in modern society (Niemann et al., 2017; Reho and Rahmouni, 2017).

There were several studies about *GSTM1* gene polymorphisms and diseases. The rs1056806 SNP was previously included in the study of *GSTM1* deletion and bladder cancer association using SNP-array, however the researchers did not found any significant association of rs1056806 with bladder cancer (Marenne et al., 2012). The second SNP in this research rs3815029, was studied in the study of allergy or asthma of urban dwelling African American (Joubert et al., 2011), however rs3815029 SNP itself was not significant with general development of allergy, asthma or related diagnostic values. Additionally, rs3815029 was studied in a bladder cancer study, by another group of researchers. The rs3815029 SNP itself was not significant, and the researchers showed that rs3815029 may be influenced by a haplotype which is consisted along with rs412543 and -471C>T which are also in chromosome 1 (1p13.3) (Zhang et al., 2012). Besides, each study results were not showing replicated results of SNPs (Zhang et al., 2012) The present study was also observed that tested two polymorphisms (rs1056806 and rs3815029) of *GSTM1* gene were not

significantly associated with development of obesity.

Our study has limitations. Only a small Korean population of obesity was analyzed, and other polymorphisms were not integrated in this study. In summary, the results of present study suggest that polymorphisms of *GSTM1* gene did not associated with susceptibility of obesity in Korean population.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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