# Association of Ghrelin Gene Polymorphisms with Obesity in Japanese Children

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P3-D1-760

## Background

Recently, ghrelin (GHRL) has attracted attention as a hormone connected with energy metabolism and appetite. The relationship between ghrelin gene polymorphisms and obesity has been analyzed in adults, but the influence of these SNPs on childhood obesity is uncertain.

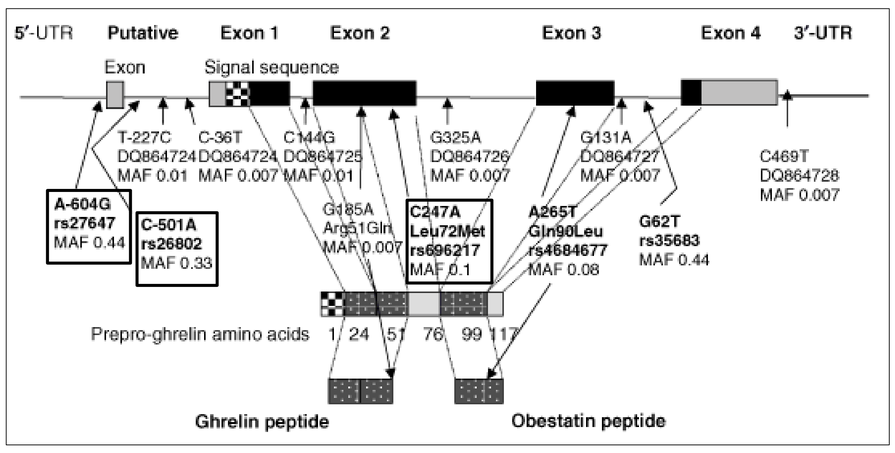
## Objective

We performed SNPs analysis of the GHRL gene and examined its relationship with childhood obesity.

## Population and Methods

We analyzed 44 patients (31 boys, 13 girls) treated in our clinic from 2010 to 2014. The average age at the first visit was 11.4 years old (range, 5.9–17.8 years old) (Table 1).

We selected three SNPs of the ghrelin gene: g.A-604G (rs27647), g.C-501A (rs26802), and g.C247A (rs696217, Leu72Met) (Fig.1). The SNPs were genotyped using the ABI 7500 Fast Real-Time PCR System and Taqman® SNP Genotyping Assays.




Ghrelin gene (GHRL, chromosome 3p25.3) (#1)

## Discussion

- Our study suggested that g.C247A (rs696217, Leu72Met) of GHRL gene polymorphism was related to hypercholesterolemia in obese Japanese children (Table 2, Fig. 2).
- The relationship between the SNPs of GHRL gene and HOMA-IR index was not seen in Japanese childhood obesity, although g.A-604G and g.C247A (Leu72Met) of GHRL polymorphism were related to insulin resistance in Caucasian adults (#2,#3,#4, Fig.3). The probability that childhood obesity could translate to adulthood obesity is known to be 40-85%.The patient having the specified SNPs of GHRL gene may show insulin resistance when they grow up.
- The ratio of these SNPs almost accorded with the ratio of East Asian people (#5, Fig1). But because there is a race difference, we cannot discuss these SNPs among all races.

## Conclusions

- Our study suggests that Met/Met of g.C247A (rs696217, Leu72Met) could be a risk factor for hypercholesterolemia in childhood obesity in Japan.
- We could not find the relationship between BMI, BMI-Z score and GHRL gene polymorphisms. In addition, the relationship between insulin resistance and GHRL gene polymorphisms was not observed.
- We are planning to examine the relationship between diet and GHRL gene polymorphisms in childhood obesity on a larger sample size for definitive conclusion.

Our work was supported with
JSPS KAKENHI Grant Number 24650427.

## Results

| | Mean ± SD | Range |
|---|---|---|
| n (M / F) | 44 (31 / 13) | |
| Age (years) | 11.4 ± 2.9 | (5.9-17.8) |
| Total cholesterol (mg/dL) | 180.8 ±33.4 | (123-266) |
| LDL-cholesterol (mg/dL) | 109.6 ±31.2 | (55.8-191.6) |
| HDL-cholesterol (mg/dL) | 52.7 ±13.4 | (24-91.7) |
| Triglycerides (mg/dL) | 129.6 ±76.4 | (29-346) |
| obesity index (%) | 49.1 ±13.4 | (21.9-79.3) |
| BMI (kg/m$^2$) | 27.3 ±4.3 | (19.4-37.2) |
| BMI Z- score (SD) | 2.2 ±0.4 | (1.5-3.0) |
| Fasting glucose (mg/dL) | 95.9 ±12.4 | (82-133) |
| Fasting insulin (μU/mL) | 32.9 ±45.5 | (2.2-244) |
| HOMA-IR | 8.8 ±14.5 | (0.5-80.1) |
| HbA1c (NGSP) (%) | 5.6 ±0.6 | (4.1-8.4) |

**Table 1.** Clinical characteristics of obese children in Japan (Kyoto).

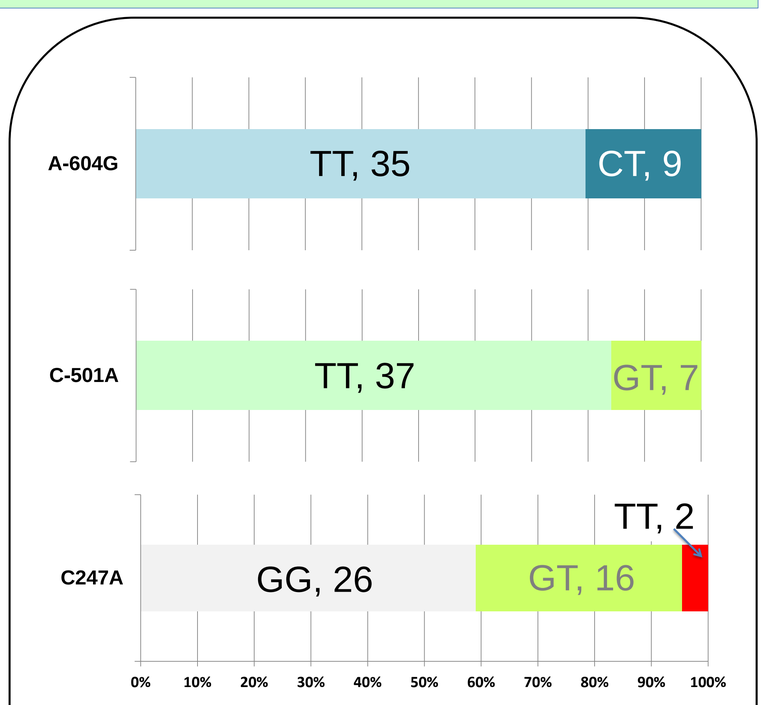



**Figure 1.** The number of each genotype of GHRL gene polymorphism (n) .

**Table 2.** Association between GHRL gene polymorphisms and clinical parameters on obese children (n=44) in Japan (P-value).

| SNP | Age | T cho | LDL-cho | HDL-cho | TG | obesity index | BMI | BMI z | BS | insulin | HbA1c | HOMA-IR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A-604G, rs27647 [a] | 0.1 | 0.3 | 0.3 | 0.4 | 0.8 | 0.4 | 0.7 | 0.3 | 0.8 | 0.4 | 0.4 | 0.4 |
| C-501A, rs26802 [a] | 0.2 | 0.4 | 0.8 | 0.1 | 0.7 | 0.2 | 0.6 | 0.1 | 0.2 | 0.4 | 0.7 | 0.4 |
| C247A, rs696217 [b] | 0.7 | 0.002 | 0.03 | 0.2 | 0.8 | 0.6 | 0.7 | 0.9 | 0.6 | 0.5 | 0.4 | 0.5 |

([a] Mann-Whitney U test, [b] multiple comparison)

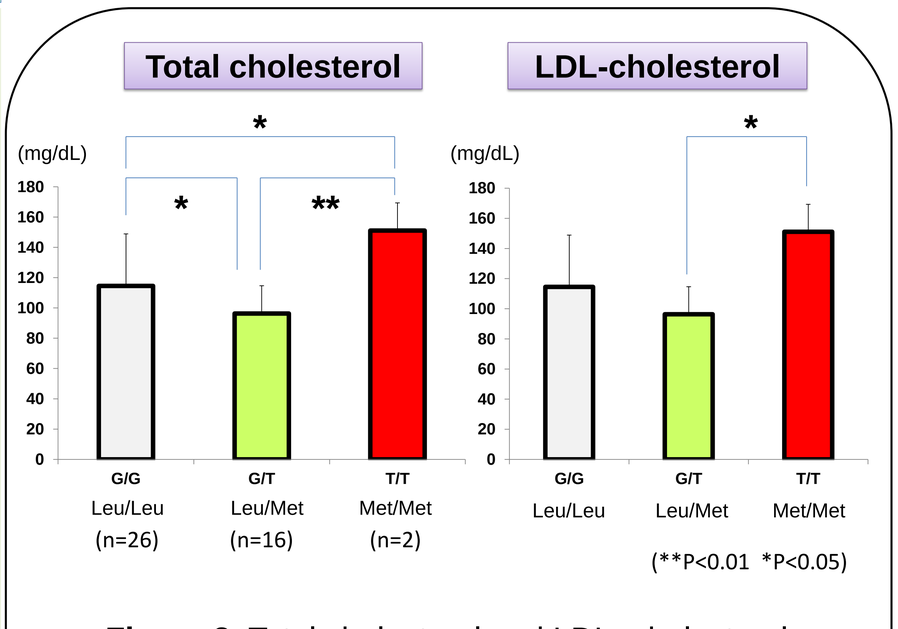



**Figure 2**. Total cholesterol and LDL- cholesterol according to g.C247A (Leu72Met) genotypes.

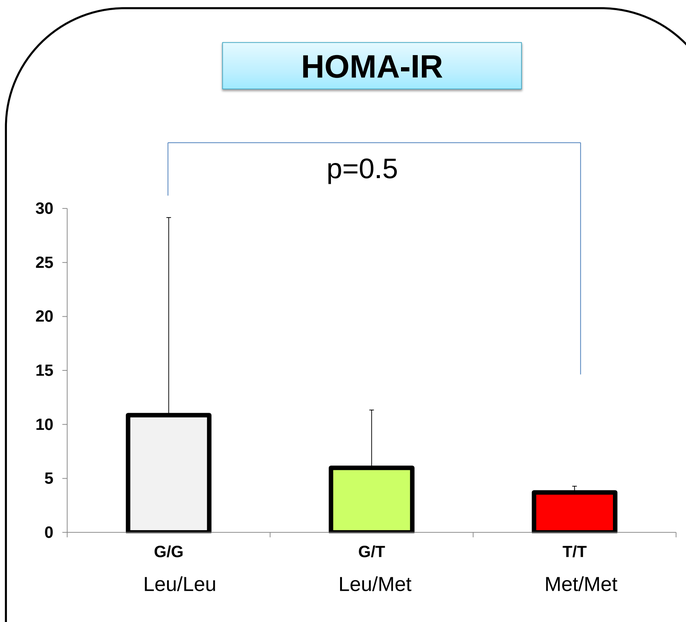



**Figure 3.** HOMA-IR according to g.C247A (Leu72Met) genotypes.

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