

## 6-3

### 日本人のアルコール消費に関わる遺伝子多型のスクリーニング

○黄 鶴、ロペスヨスバニ、日野 公洋、伊佐治麻実子

ジェネシスヘルスケア株式会社

### Screening of novel germline variants related to alcohol consumption in the Japanese population

He Huang, Yosvany Lopez, Kimihiro Hino, Mamiko Isaji

Genesis Healthcare Co.

Background: Alcohol intoxication/abuse has been historically linked to accidents and violence. Despite its negative impact, many Japanese still consume alcohol on a daily basis, without regarding their genetic sensitivity to alcohol intake. Therefore, there is a need for comprehensive studies aimed at discovering those unknown genetic variants associated with alcohol sensitivity and metabolism. These studies could assist in advising Japanese individuals on the right doses of alcohol to be consumed based on their genetic makeups.

Design: To address this issue, we screened the genotypes of Japanese consumers for significant variants related to alcohol consumption. Our cohort of samples included 11,321 males and 16,183 females. Their genotype information was obtained via their purchase of our personalized genetic kit Genesis 2.0, and the later analysis using our customized Illumina microarray chip. As for the lifestyle information, we relied on our customers' self-assessment regarding their alcohol intake habits. This information was finally used to perform a comprehensive genome-wide association study analysis and uncover potentially significant variants.

Results: When the quality control for the genome-wide association analysis was performed, 308,736 variants for males and 308,428 variants for females were retained. The association results of drinking behavior (drinking frequency per week) showed a cluster of single nucleotide polymorphisms at 12q24 ( $p$ -value  $< 5 \times 10^{-8}$ ). In addition, a well-studied functional variant in ALDH2 at 12q24 ( $p$ -value  $< 1.2 \times 10^{-193}$  for males and  $p$ -value  $< 4.9 \times 10^{-224}$  for females), which has been reported to have a strong association in the Japanese population, was observed. However, unknown variants associated with alcohol drinking behavior were detected in genes such as BRAP, ACAD10, NAA25, HECTD4, MYO1H, UBE3B, MMAB, MYL2, RPH3A, OAS3, and OAS2. Additionally, the variants in genes BRAP, ACAD10, NAA25, HECTD4 were also in linkage disequilibrium with that detected in ALDH2. Although genes MYL2, RPH3A, OAS3 have been reportedly associated with alcohol consumption in Korean men, they have gone unreported for the Japanese population.

Conclusion and Perspective: In this study, we have identified new loci and alleles highly associated with alcohol consumption in the Japanese population. Our results suggest that many genes in 12q24 appear to play an important role in alcohol consumption for the Japanese population. A well-known alcohol metabolizing gene ADH1B did not show any significant association with drinking behavior in our analysis. One possible cause for this omission could be the use of lifestyle information which included drinking frequency instead of alcohol dependence. To expand the scope of future studies, we will focus on collecting more lifestyle data that includes alcohol dependency and alcohol abuse. As the pioneering genetic testing and research company in Japan, Genesis Healthcare Co. always aspires to contribute to the well-being of the Japanese population. Given the fast pace at which the population is ageing, we feel more than ever a strong sense of responsibility to share new discoveries with researchers, healthcare professionals, and the general public.