

# Genetic factors contributing to type 2 diabetes in a Japanese population

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The prevalence of type 2 diabetes is continuously increasing in many countries, including Japan. Although the precise mechanisms underlying the development and progression of type 2 diabetes have not been fully elucidated, a combination of multiple genetic and environmental factors is considered to contribute to the pathogenesis of the disease.

To date, nearly 20 susceptibility genes for type 2 diabetes were identified by several genome-wide and candidate gene association studies. We have examined the relationships between seven susceptibility genes and diabetes in a population-based samples (401 with diagnosed as diabetes and 448 controls with normal glucose levels). We have found that the genotypes of three genes (*KCNQ1*, *KCNJ11* and *SLC30A8*) were associated with diabetes. We then counted the cumulative numbers of susceptible allele of these three genes for each subject. The cumulative numbers of susceptible allele were significantly higher in diabetic subjects than that of control subjects ( $P=0.004$ ).

Next, to examine the interaction between obesity and the cumulative numbers of susceptible allele of three genes for determining diabetes, we have classified the subjects into obesity groups ( $BMI \geq 25 \text{kg/m}^2$ ) and normal weight group ( $BMI < 25 \text{kg/m}^2$ ). The significant associations between diabetes and the cumulative numbers of susceptible allele were observed only in normal weight group ( $P=0.0005$ ), but not observed in the normal weight group ( $P=0.39$ ), although obesity is a major risk factor for diabetes in our subjects.

These data suggest that the cumulative numbers of susceptible allele are risk factors for diabetes independent of obesity, and may become important risk factors of subjects without other risk factors such as obesity.