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Genetic variation at the PRDX3 locus as a risk factor for obesity

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Oxidative stress resulting from excess reactive oxygen (ROS) species and/or deficiencies in antioxidant capabilities plays critical roles in the pathogenesis of lifestyle-related diseases such as hypertension, diabetes, atherosclerosis, obesity and cancer. Genetic variations that affect activity or expression levels of the antioxidant or oxidant enzymes may therefore be associated with susceptibility to lifestyle-related diseases.

We analyzed the genotypes of eleven genetic polymorphisms in eight kinds of genes for antioxidant or oxidant enzymes (*SOD2, CAT, GPX1, MPO, GSTM1, GSTM3, GSTT1, PRDX3*), in 816 randomly selected Japanese men. The mean age of the subjects was 54.0 ± 5.1 years.

Statistically significant association was observed between obesity and the genotypes of the *PRDX3* (Peroxiredoxin 3) (P=0.031). The mean BMI of homozygote of the minor allele were higher than that of the other genotypes (P=0.008). Furthermore, we found a consistent interaction between the genotype in *PRDX3* and dietary fat intake in relation to BMI. Among subjects with high fat diet (≧25% of energy), the strong associations between the genotypes of *PRDX3* and obesity and/or BMI were observed (P=0.0001), but the associations were not observed in subjects with low fat diet (<25% of energy).

It is reported that the increase in fat and glucose intake lead to increased intracellular production of ROS. PRDX3 was suggested to provide a primary antioxidant defense of mitochondrial respiratory chain and protecting mitochondria against oxidative stress. These data suggests that the interaction between genotypes of *PRDX3* and dietary fat intake is important in the development of obesity. Further studies are required to clarify the interaction between oxidative stress and lifestyle-related diseases.