# Genes for NAD Biosynthesis Pathway and Lifestyle-Related Diseases.

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In mammals, nicotinamide phosphoribosyltransferase (NAMPT1) and nicotinamide mononucleotide adenylyltransferase 1 (NMNAT1) constitute a nuclear NAD(+) salvage pathway which regulates the functions of NAD(+)-dependent enzymes such as the protein deacetylase SIRT1. NAMPT1 is an enzyme plays an important role in this pathway, and several recent reports have shown a positive association between genotypes of NAMPT1 and high-density lipoprotein cholesterol (HDL-C) level in various populations. Other reports have shown NAMPT1 also increases the activity of SIRT1, which is closely related to longevity and Calorie restriction (CR). CR has been shown to reduce the incidence of age-related disorders in mammals. It induces metabolic changes, improves insulin sensitivity and alters neuroendocrine function in animals. That can lead to a fall in triglyceride (TG) level, low-density lipoprotein cholesterol (LDL-C) level, a rise in HDL-C level, and so on. Therefore, it is likely that variations of genes for NAD biosynthesis pathway are related to lipid metabolism.

In this study, I have examined the relationships between genetic variations of genes for NAD biosynthesis pathway and lipid levels (HDL-C, LDL-C, and TG). The genotypes of 11 SNPs in the 3 genes for NAD biosynthesis pathway (*NAMPT1, NMNAT1, SIRT1*) were determined in 2769 subjects (53.9±7.5 years old). Next, I investigated whether the interaction between genetic polymorphisms in such genes and dietary fat intake affect lipid metabolism. Statistically significant association was observed between HDL-C level and the genotypes of the *SIRT1* and *NMNAT1* (P=0.032, 0.024). Furthermore, we found a consistent interaction between the genotype in *SIRT1* and dietary fat intake in relation to HDL-C. Among subjects with high fat diet (≧25% of energy), the strong associations between HDL-C and the genotypes of *SIRT1* was observed (P=0.0089), but the association was not observed in subjects with low fat diet (＜25% of energy). These results indicate that the genetic difference of NAD biosynthesis pathway affect the inter-individual variations of HDL-C level.