Genes Related to Caloric Restriction (CR) and Lifestyle- Related Diseases

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Calorie restriction (CR) is the only experimental manipulation that is known to extend the lifespan of a number of organisms. 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 blood pressure, triglyceride (TG) level, cholesterol level, and so on.

Nampt is an enzyme plays an important role in NAD biosynthesis pathway, and it decreases blood glucose level. It also increases the activity of Sirt1, which is a key enzyme of physiological effect of CR. In addition, Sirt1 is closely related to signaling pathway of insulin. Sirt1 repress the insulin transcription. Insulin is the hormone which is important for glucose and lipid metabolism. Therefore, it is very likely that variations of CR-related gene are related to lipid metabolism. In this study, I focused on genes related to NAD biosynthesis pathway and signaling pathway of insulin.

The genotypes of 27 SNPs in the 10 genes related to CR (*ADH*・*NAMPT*・*NMNAT*・*SIRT1*・*INS*・*INSR*・*IRS2*・*PI3KR1*・*FOXO1*・*FOXA1*) in 2485 subjects (age: 54.8±6.5 years old) were determined. Next, I investigated whether the interaction of between genetic polymorphisms in such genes and dietary fat intake affect lipid metabolism.

In this study, a significant association was observed between *NMNAT* genotypes and triglyceride (TG) level. In addition, a significant relationship was observed between *FOXA1* genotypes and TG level. Furthermore, when analyzed in relation to fat intake, in the group of people with high fat intakes, these relationships become stronger. These results suggest that the genetic difference in the genotypes of *NAMNAT* and *FOXA1* gene affect the inter-individual variations of TG level.