Why does the blood cholesterol level increase in mice exposed to stressful housing environment?

Yutaka Takahashi[2], Hiroyuki Sakakibara[2], Yoshitaka Ojima[2], Akio Kobayashi[2], and Kayoko Shimoi[1,2]

[1]Global COE Program, [2]Department of Environmental Health Sciences, Graduate School of Nutritional and Environmental Sciences, University of Shizuoka

It is noted that daily exposure to social and psychological stress is associated with lifestyle-related diseases such as hyperinsulinemia, hyperglycemia, cardiovascular diseases, and cancer, as well as mental disorders. We have previously reported that chronic stressful housing environment affected the expression levels of genes related to lipid metabolism in mice, followed by increase of blood cholesterol level and induction of visceral fat-related obesity. In this study, we investigated the mechanism on increase of the blood cholesterol level in mice exposed to stressful housing environment using hepatic gene expression analysis. Male C57BL/6 NCrSlc mice (4 weeks old) were housed at 5 per cage. After acclimatization for 10 days, mice were exposed to stressful housing environment for 90 days. The weights of organs and the biochemical indices of blood were measured. Moreover, the hepatic gene expression of 3-hydroxy-3-methylglutaryl coenzyme A reductase (Hmgcr), cholesterol 7 α -hydroxylase (Cyp7a1), bile salt export pump (Bsep), multidrug resistance-associated protein 3 (Mrp3), and low density lipoprotein receptor (Ldlr) were determined in real-time quantitative PCR method.

Body weight, visceral fat weight, and blood cholesterol level in the mice exposed to stressful housing environment were significantly higher than those in the control mice. There was no difference in the expression levels of Hmgcr, which is related cholesterol synthesis, between two groups. However, the mice exposed to stressful housing environment showed significant reduction in the expression levels of Cyp7a1 related to cholesterol metabolism and Ldlr related to hepatocellular reuptake of cholesterol. On the contrary, the expression level of Mrp3, which is related to excretion of bile acid into blood, was significantly higher in the mice exposed to stressful housing environment. These results suggested that chronic stressful housing environment may cause abnormalities of the system for cholesterol metabolism, excretion, and hepatocellular reuptake, in consequence, increase the blood cholesterol level in mice.