Analysis of Metabolism in the Liver of Low Dose-rate-irradiated Mice

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Abstract

To determine the effects of low-dose rate (LDR) radiation on metabolism, we analyzed the amount of low-molecular-weight metabolites (metabolome analysis) and the genome-wide gene expression in the liver of B6C3F1 female and male B6C3F1 mice irradiated at 20 mGy/day LDR for 300 days (total dose 6000 mGy). Both in the irradiated females and in the irradiated males under fasting conditions, when compared to the non-irradiated controls, we observed an increase in the expression of the gene for Srebp1, the master regulator of lipid homeostasis, in the liver and an increase in the level of insulin in the blood. An increase in the amount of acetyl CoA, and an decrease in the expression of the gene for pyruvate dehydrogenase kinase (Pdk4), which regulates the acetyl CoA level, were noted in the liver in the irradiated females but not in the irradiated males. These results suggest that irradiation may play a role in switching of metabolism from the fatty acid synthesis pathway to the cholesterol synthesis pathway in the liver of female mice, and also in the development of fatty liver observed in irradiated females.

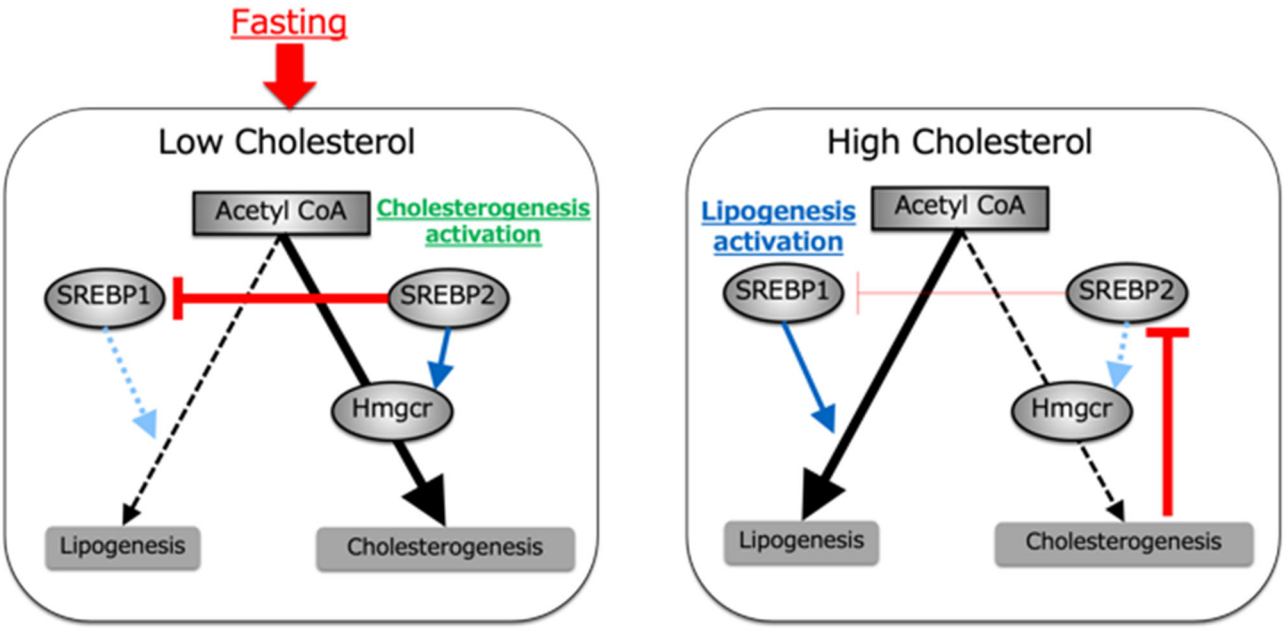

Fig. 1 Regulation of fatty acid and cholesterol synthesis pathways

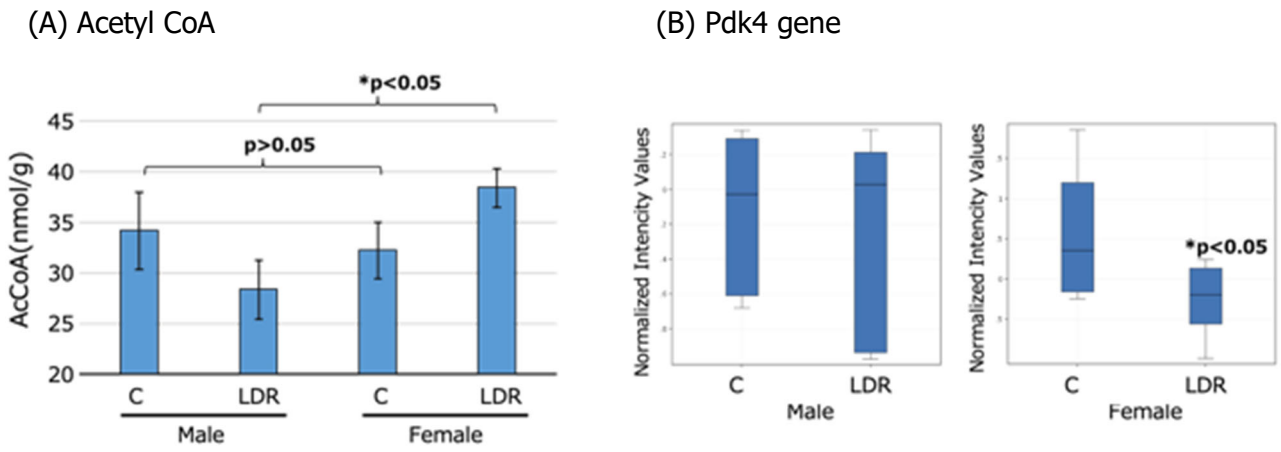

Fig. 2 (A) Amount of acetyl CoA and (B) expression of the gene for pyruvate dehydrogenase kinase (Pdk4) in the liver of male and female, low dose rate (LDR)-irradiated and control (C) mice