Genome-wide Gene Expression Analysis of the Liver from Low Dose-rate-irradiated Mice

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Abstract

Previously we reported life span shortening and increased incidences of cancer and non-cancer diseases in B6C3F1 mice irradiated with gamma-rays at 20 mGy/day for 400 days. In the present study, we investigated the genome-wide gene expression profile of the liver from male and female mice irradiated at 20 mGy/day for 100, 200, 300 and 400 days. In the Ingenuity Pathway Analysis, no significant alteration was found in the “p53 signaling” pathway. Instead, female mice irradiated at 20 mGy/day for 200 and 300 days showed prominent upregulation of several pathways related to lipid metabolism, such as “Cholesterol biosynthesis” and “Adipogenesis” pathways. In male mice, however, alterations in these pathways were not conspicuous. These results may correspond to the increased incidence of fatty liver and obesity, which may promote hepatocarcinogenesis, in low dose-rate-irradiated female mice.

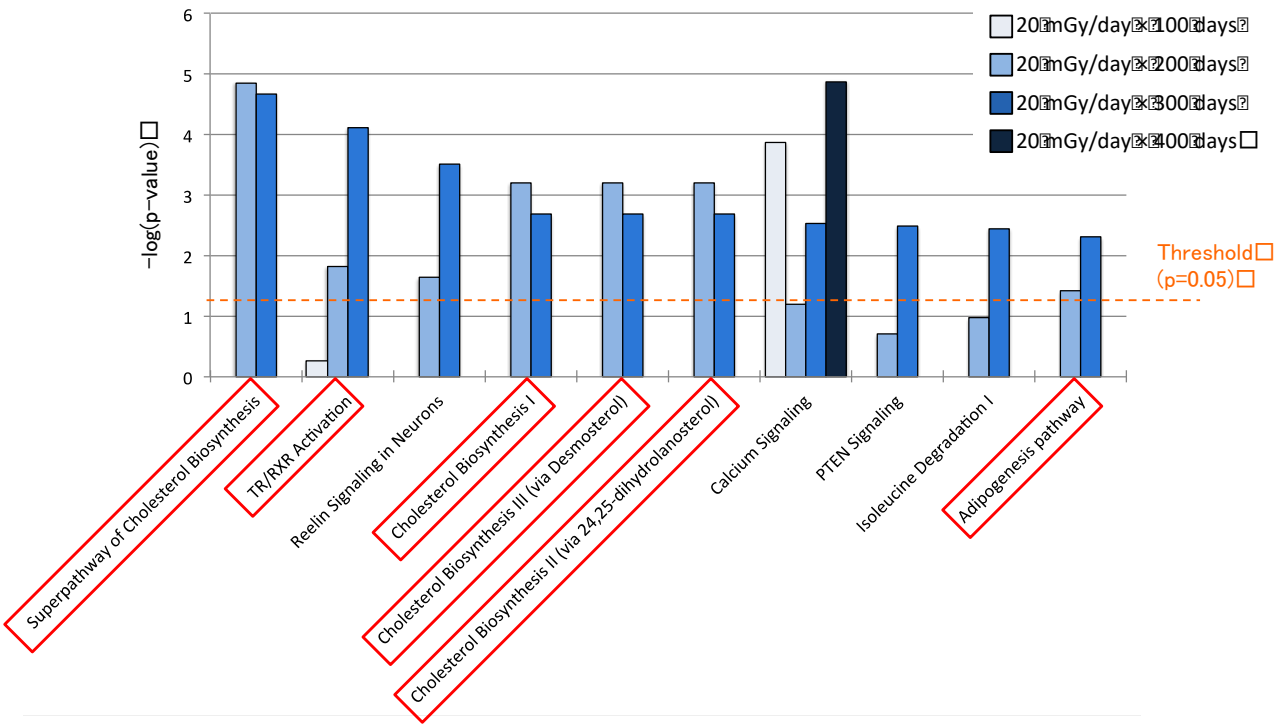

Fig. 1 Alterations in gene expression in low dose-rate-irradiated female mice. Ten most significantly altered canonical pathways in the liver from female mice irradiated for 300 days were identified by the gene ontology algorithm of Ingenuity Pathway Analysis. Columns represent groups with different irradiation periods. The y-axis represents the negative log of the p-value from Fisher's exact test. The dashed line indicates a p value of 0.05 as a threshold of significance. The pathways related to lipid metabolism are marked by red boxes.

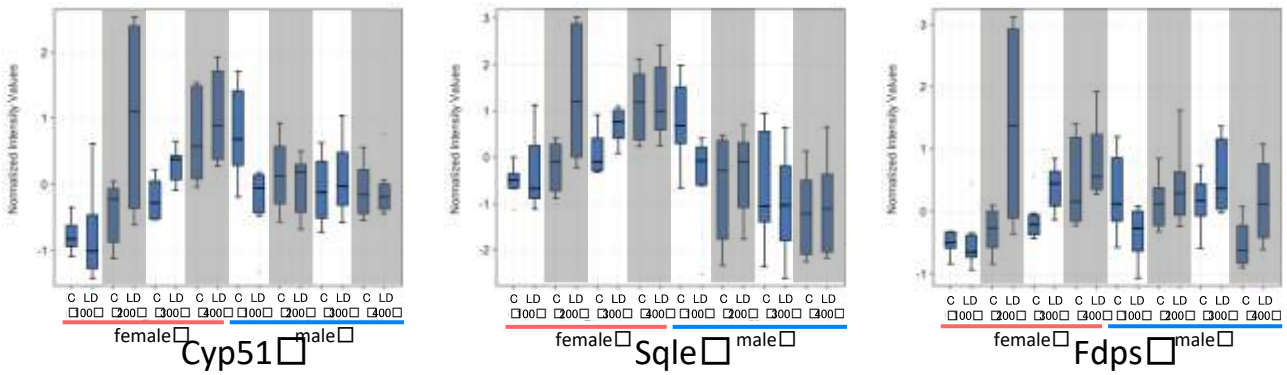

Fig. 2 Box-and-whisker plots of the expression of the genes encoding cholesterol biosynthesis enzymes. The y-axis indicates normalized gene expression signals processed by GeneSpring. Tiny red lines in graph areas indicate outliers.