

A novel mechanism for BPA-triggered hepatic steatosis

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Exposure to Bisphenol A (BPA) has been linked to the increased incidence of Non-Alcoholic Fatty Liver Disease (NAFLD): The hepatic manifestation of metabolic syndrome. However, the related underlying mechanisms remain unknown. Given that microRNAs (miRNAs) are widely recognized as the key regulators of lipid metabolism and the potential mediators of environmental effects, this study aimed to examine whether exposure to BPA triggered hepatic lipid accumulation and to further determine if adverse effects of BPA may be modulated in part through miRNAs. Male post-weaning C57BL/6 mice were exposed to 50 µg/kg/day BPA or corn oil for 90 days by oral gavage. We found that insulin resistance, and impaired hepatic lipid accumulation and increased serum triglycerides (TG) existed concomitantly in the BPA exposed mice. In addition, BPA exposure caused significant reduction in miR-192 expression in both mice liver tissues and human HepG2 cells, which were accompanied by significant up-regulation of SREBF1 (a key transcription factors that is capable of activate lipid synthesis) and subsequent expression of lipogenic genes. Bioinformatic and *in vitro* studies suggested that miR-192 acted to the 3'UTR of SREBF1 directly, resulting in profound dysregulation in hepatic lipid homeostasis. Inhibition of miR-192 led to higher TG levels and increased hepatic lipid accumulation by enhancing SREBF1 processing. In contrast, the opposite results were observed with overexpression of miR-192, which downregulated SREBF1 expression. Most importantly, we also showed that *in vivo* and *in vitro* overexpression of miR-192 effectively prevented BPA induced hepatic lipid accumulation, which was independently of insulin resistance. In conclusion, this study showed a novel mechanism that exposure to BPA may up-regulate SREBF1 through inhibition of miR-192 in the liver, thereby contributing to NAFLD.

Biography

Sijun Dong has completed his PhD in 2004 in Biochemistry and Biotechnology, Tokyo University of Agriculture and Technology, Japan. He is the Professor of Environmental Sciences, Chinese Academy of Sciences. He has published more than 50 papers in reputed journals. His research interest is about Environmental Molecular Toxicology and Chinese Medicines and Environmental Health.

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