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Cyp2b-Knockdown Mice Poorly Metabolize Corn Oil and Are Age-Dependent Obese

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Abstract

We previously made a RNAi-based cytochrome P450 2b (Cyp2b)-knockdown (Cyp2b-KD) mouse to determine the in vivo role of the Cyp2b subfamily in xenobiotic detoxification. Further studies reported here indicate a role for Cyp2b in unsaturated fatty-acid (UFA) metabolism and in turn obesity. Mice were treated intraperitoneally (i.p.) with 100 μ L corn oil as a carrier or the potent Cyp2b-inducer 3,3',5,5'-Tetrachloro-1,4-bis(pyridyloxy)benzene (TCPOBOP (TC)) dissolved in corn oil. Surprisingly, female Cyp2b-KD mice but not male mice showed increased liver lipid accumulation. Male Cyp2b-KD mice had higher serum triacylglycerols, cholesterol, very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) than wildtype (WT) mice; females had higher cholesterol, LDL, and HDL. Thus, Cyp2b-KD mice are unable to clear a high bolus dose of corn oil, potentially because the Cyp2b-KD mice were unable to metabolize the UFA in the corn oil. Therefore, WT and Cyp2b-KD mice were housed for 35 weeks and necropsies performed to test whether Cyp2b-KD mice develop age onset obesity. Cyp2b-KD mice exhibited a significant increase in body weight caused by an increase in white adipose tissue deposition relative to WT mice. Serum cholesterol, triacylglycerol, LDL, and VLDL were significantly greater in 35-week-old Cyp2b-KD males compared to WT males; only serum triacylglycerol and LDL were higher in females. In conclusion, changes in Cyp2b expression led to perturbation in lipid metabolism and depuration in Cyp2b-KD mice. This suggests that Cyp2b is more than a detoxification enzyme, but also involved in the metabolism of UFA, as Cyp2b-KD mice have increased the body weight, fat deposition, and serum lipids. © 2018 AOCS

Author Keywords

Cyp2b; liver; NAFLD; obesity; P450; PUFA; triacylglycerol

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