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Induction by perfluorinated carboxylic acids with different carbon chain length of peroxisomal α -oxidation in the liver of rats

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The potency of the induction of peroxisomal α -oxidation was compared between perfluorinated fatty acids (PFCAs) with different carbon chain lengths in the liver of male and female rats. In male rats, perfluoroheptanoic acid (PFHA) has little effect, although perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA) and perfluorodecanoic acid (PFDA) potentially induced the activity. By contrast, PFHA and PFOA did not induce the activity of peroxisomal α -oxidation in the liver of female rats while PFNA and PFDA effectively induced the activity. The induction of activity by these PFCAs was in a dose-dependent manner, and there is a highly significant correlation between the induction and hepatic concentrations of PFCAs in the liver regardless of their carbon chain length. These results strongly suggest that the difference in their chemical structure is not the cause of the difference in the potency of the induction. Hepatic concentrations of PFOA and PFNA were markedly higher in male rats compared with female rats. Castration of male rats reduced the concentration of PFNA in the liver and treatment with testosterone entirely restored the reduction. In contrast to the results obtained from the *in vivo* experiments, the activity of peroxisomal α -oxidation was induced by PFDA and PFOA to the same extent in cultured hepatocytes prepared from both male and female rats. These results,

taken together, indicate that difference in accumulation between PFCAs in the liver was responsible for the different potency of the induction of peroxisomal -oxidation between PFCAs with different carbon chain lengths and between sexes.