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MEETING ABSTRACTS

HIGH-FAT DIET INDUCES CHANGES IN ACTIVITY AND EXPRESSION OF DRUG-METABOLIZING ENZYMES IN MOUSE LIVER

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Non-alcoholic fatty liver disease (NAFLD) is a multifactorial, complex, and chronic liver disease with increasing worldwide prevalence. Metabolic syndrome and obesity are the main risk factors associated with NAFLD. High-fat diet causes an excessive fat accumulation in the liver referred to as simple steatosis, which can further progress to more severe stages of NAFLD including non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma. As NAFLD has been reported to cause changes in the liver homeostasis and metabolism of xenobiotics (1), the objective of this study was to investigate NAFLD-induced changes in the expression and/or activity of selected phase I drug-metabolizing liver enzymes. For our study, liver samples from wild type mice fed with standard or high-fat diet were used. The mRNA and protein expression as well as the specific activity of several cytochrome P450 (CYP), carbonyl reductase (CBR), and aldo-keto reductase (AKR) enzymes were determined by using real-time quantitative PCR, western blotting, and spectrophotometric methods, respectively. High-fat diet caused significant induction of mRNA as well as protein expression and specific activity of CYP1A1/2. The mRNA expression of CYP3A11 and CYP3A13 (orthologs of human CYP3A4) was decreased, while its protein expression remained unchanged. Induction was observed also for AKR1C6 and AKR1C20 (orthologs of human AKR1C1) at mRNA and protein level.

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Keywords: non-alcoholic fatty liver disease; steatosis; high-fat diet; phase I drug-metabolizing enzymes

References

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