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Session I

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Effects of *Mif* deficiency and fructose-enriched diet on lipid metabolism in the mouse liver

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The macrophage migration inhibitory factor (MIF) is a pro-inflammatory cytokine involved in metabolic inflammation and regulation of energy metabolism in the liver. Genetic deletion of *Mif* may contribute to the development of systemic insulin resistance, while fructose overload can disturb hepatic lipid metabolism leading to steatosis, inflammation and type 2 diabetes. The aim of the present study was to elucidate the impact of combined effects of *Mif* deficiency and fructose-enriched diet on insulin sensitivity and lipid metabolism in the liver of male mice. We analysed the effects of 9-week 20 % fructose-enriched diet on indicators of systemic insulin sensitivity, liver histology and biochemical parameters of lipid metabolism in wild type and MIF deficient ($MIF^{-/-}$) C57Bl/6J mice. The expression of the following lipogenic genes was examined: fatty acid synthase (*Fas*), acetyl-CoA carboxylase (*Acc*) and stearoyl-CoA desaturase-1 (*Scd1*). Levels of insulin-regulated transcriptional factors involved in lipogenesis (sterol regulatory element-binding protein-1c, SREBP-1c and carbohydrate-response element-binding protein, ChREBP), together with the expression of hepatic fatty acid metabolism regulator (peroxisome-proliferator-activated receptor α, PPARα) were also analysed. *Mif* deficiency did not affect plasma free fatty acid and triglyceride levels, but impaired systemic insulin sensitivity regardless of the diet. In $MIF^{-/-}$ animals, liver histological analysis confirmed the presence of lipid droplets and focal necrosis, but these effects were more pronounced in $MIF^{-/-}$ mice on fructose diet. Although *Acc* and *Fas* levels were unchanged, elevated levels of *Scd1*, SREBP-1c and ChREBP, together with decreased PPARα protein level, were most likely responsible for the lipid accumulation observed in the liver of $MIF^{-/-}$ animals. In conclusion, the results show that energy-rich fructose diet potentiates the effects of *Mif* deficiency on development of fatty liver and systemic insulin resistance.

Keywords: *Mif* deficiency, fructose-enriched diet, liver, lipid metabolism, insulin resistance