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THE ROLE OF MACROPHAGE MIGRATION INHIBITORY FACTOR IN LIVER INFLAMMATION, OXIDATIVE STRESS, AND APOPTOSIS IN MICE ON A FRUCTOSE DIET

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Macrophage migration inhibitory factor (MIF) is a pleiotropic cytokine that plays an essential role in the inflammatory response and various other biological effects such as activation of apoptosis and oxidative stress. Fructose-enriched diets have previously been associated with the development of low-grade inflammation leading to metabolic stress. The aim of the present study was to investigate the combined effects of deletion of the *Mif* gene and a 9-week 20% fructose-enriched diet on metabolic inflammation, apoptosis, and oxidative stress in the liver of wild-type (WT) and *Mif* knockout ($MIF^{-/-}$) male C57Bl/6J mice. We analyzed liver histology and expression of pro-inflammatory genes: Tumor necrosis factor (TNF), interleukin 1β (IL-1β), and IL-6. Antioxidant activity was estimated by the protein levels of antioxidant enzymes catalase (CAT), superoxide dismutase (SOD1), mitochondrial MnSOD (SOD2), glutathione reductase (GR) and glutathione peroxidase (GPX). The results showed that antioxidant protection was activated in the liver of MIF-deficient mice. Increased hepatic expression of the cytokines IL-6 and IL-1β was observed in the same animals. Histologic analysis confirmed the presence of apoptosis, inflammation, enlarged Kupffer cells, and regenerative changes, such as binucleated hepatocytes, anisonucleosis, and anisocytosis. In addition, confluent and focal necrosis was observed in the liver of $MIF^{-/-}$ mice, which was even more pronounced in the animals consuming fructose. In conclusion, MIF may play a protective role in metabolic stress, as inflammation, oxidative stress, apoptotic and necrotic changes occur in the liver in its absence.