ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Biochemical Sciences

Candidate: Bc. Klára Osobová

Supervisor: doc. PharmDr. Iva Boušová, Ph.D.

Consultant: Mgr. Gabriela Svobodová

Title of diploma thesis: Changes in epigenetic regulation in the *in vivo* model of NAFLD

This diploma thesis deals with non-alcoholic fatty liver disease (NAFLD), a group of liver diseases with varying degrees of damage to liver tissue, from simple steatosis (NAFL) to steatohepatitis (NASH), liver fibrosis and cirrhosis. The diploma thesis focuses on the description of the pathogenesis of NAFLD and the epigenetic changes associated with it. The aim of this thesis was to map the changes in epigenetic regulation in *in vivo* mouse models of NAFLD, which was induced by a high fat, fructose, and cholesterol (FFC) diet, the application of monosodium glutamate (MSG) or a combination of these factors. The effect of treatment with liraglutide and the peptide LipR31 was also investigated in mouse models. Changes in hepatic mRNA expression for enzymes regulating epigenetic modifications (histone deacetylase, DNA-methyltransferase, histone acetyltransferase) and microRNA expression (miR) were determined using quantitative PCR (polymerase chain reaction). The immunoblot method was used to determinate the protein expression of HDAC8 (histone deacetylase 8) and HDAC3 (histone deacetylase 3). Statistically significant changes were observed in particular between the control group on the standard diet (K STD) and the MSG STD group in expression of HDAC2, HDAC3, HDAC5, Sirt2 and Ep300. Expression of HDAC5 was reduced by both FFC diet (control and MSG mice) and MSG administration. The FFC diet caused an increase in expression of mIR-200a-3p and miR-200b-3p in control and MSG mice. Due to both liraglutide and LiPR administration, expression of miR-200a-3p was decreased in the K FFC group, while in MSG STD mice it was increased by administered substances.