tion, San Diego, CA, USA) according to manufacturer's recommendations. The intraperitoneal injections of LVVYPW and hemorphin-7 (1 mg/kg) into fasting STZ-induced diabetic rats (male, Wistar line, 180–220 g) significantly decrease the expression level of NFκB/p65, increased in nuclear fraction of brain tissue of STZ-induced diabetic rats. In contrast, the significant increase in expression level of NFκB/p65 was found in the brain tissue cytoplasmic fraction, obtained from hemorphin-treated diabetic rats. It should be noted that we didn't observed such an increase in NFκB/p65 expression level in the brain tissue cytoplasmic fraction of rats, which didn't received hemorphin treatment.

Recently, we have demonstrated the involvement of Ca^{2+}/calmodulin/calcineurin signaling pathway in the molecular mechanisms of antidiabetic effect of LVVYPW. Calcineurin was reported to regulate the activity of NFκB by affecting the phosphorylation of IκBs (nuclear factor κB inhibitors). Earlier it has also been reported the involvement of calcineurin/NFκB pathway in pathophysiology of diabetes. Thus, data obtained indicate that hemorphins, by modulation of Ca^{2+}/calmodulin/calcineurin signaling pathway, are able to regulate the activity of NFκB in pathophysiology of diabetes. It should be emphasized that one of the molecular mechanisms of antidiabetic effect of famous antidiabetic drug metformin is inhibition of nuclear translocation of NFκB as well.

Acknowledgment: The study was partially supported by National Foundation of Science and Advanced Technologies (NFSAT), State Committee of Science of the Ministry of Education and Scienceof the Republic of Armenia (SCS MES RA) and U.S. Civilian Research & Development Foundation (CRDF) Grant ■ ECSP-09-31_GRSP.

Keywords: diabetes mellitus, hemorphin, NFkB.

TUE-415
Hepatic mitochondrial content in malondialdehyde may be a marker of sea lamprey contact with atrazine

M. Candeias[1,2], I. Alves-Pereira[1,2], M. J. Lança[1,3], P. R. Almeida[4,5], A. F. Ferreira[5], B. Quintella[5,6], R. Ferreira[1,2]

[1]Instituto de Ciências Agrárias e Ambientais Mediterrânicas, Universidade de Évora, [2]Departamento de Química, [3]Departamento de Zootecnia, [4]Departamento de Biologia, Escola de Ciências e Tecnologia, Universidade de Évora, Évora, [5]Centro de Oceanografia, [6]Departamento de Biologia Animal, Faculdade de Ciências, Universidade de Lisboa, Lisboa, Portugal

The atrazine attracts special attention as pollutant because of its persistence in the aquatic environment. Although this herbicide has been studied in teleost, its toxicity in the sea lamprey, *Petromyzon marinus* is still poorly understood. Oxidative stress may occur if chemical pollutants contribute to block the capacity of mitochondria to generate ATP with continuous production of reactive oxygen species (ROS), disturbing the success of *P. marinus* seawater acclimation. So, the aim of this study was to evaluate how atrazine influences the malondialdehyde (MDA), glutathione (GSH) and glutathione disulfide (GSSG) contents of gills and liver mitochondria of juveniles from Lima river basin, Portugal during salt acclimation. Sampling occurred at the beginning of the *P. marinus* downstream migration. The sampled juveniles were transported alive to the laboratory and maintained in 200 l tanks with LSS 8life support system. Two groups of 40 specimens were hold in tanks with 50 or 100 μg/l atrazine, during 30 days. The salinity was gradually increased from 0 to 35 psu, following a three step procedure during a 30 days period. The control group was maintained in freshwater without atrazine. Mitochondria obtained by centrifugation at 15000 *g*, 30 min, 4°C, of tissues homogenates prepared in 50 mM Tris-HCl pH 7.5 buffer were used in determination of ROS, MDA, GSH and GSSG by fluorescence. The statistical analysis were performed by ANOVA I and Duncan ($p < 0.05$), using SPSS 22 for Windows. The results showed that in *P. marinus* juveniles, no significant changes in the markers of oxidative stress and cell damages were detected in the mitochondrial gills. Nevertheless, in the animals exposed to 50 μg/l atrazine the content in glutathione and GSSG increased. A similar pattern of stress markers was detected in hepatic mitochondria. However, in the presence of atrazine, the MDA level of the mitochondria of liver increased threefold in the animals during salt acclimation. The high level of mitochondrial damages, detected in the hepatic mitochondria of macrophthalmia treated with atrazine, suggests that herbicide exposure caused metabolic failures which can disturb the adaptation of these specimens to the oceanic feeding phase. The hepatic mitochondrial MDA levels of *P. marinus*, may eventually detect sea lamprey contact with chlorine herbicides.

Keywords: Cell damages, Petromyzon marinus, Triazines.

TUE-416
Hepatocyte-specific knockout of Cyp51 from cholesterol synthesis results in sex-specific metabolic adaptations and liver pathologies

D. Rozman[1], G. Lorbek[1], M. Perše[2], J. Jeruc[2], P. Juvan[1], S. Horvat[3]

[1]Faculty of Medicine, Institute of Biochemistry, [2]Faculty of Medicine, Institute of Pathology, [3]Department of Animal Science, Biotechnical Faculty, University of Ljubljana, Ljubljana, Slovenia

Cholesterol is a key molecule in mammals serving as a major component of cell membranes and a precursor of various signaling molecules. The most striking examples of cholesterol deficiency are the inborn errors of cholesterol biosynthesis that, when compatible with life, manifest with severe whole body phenotypes. Surprisingly, liver as the principal site of cholesterol homeostasis has rarely been investigated in these pathologies. We focus on the hepatocyte-specific deletion of lanosterol 14α-demethylase (CYP51) catalyzing the rate-limiting step in the post-squalene part of cholesterol synthesis. The hepatic loss of *Cyp51*

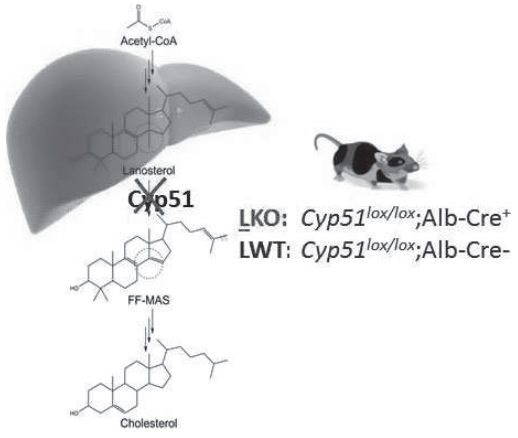

Fig. 1. Hepatocyte-specific ablation of Cyp51 from the cholesterol synthesis pathway leads to accumulation of immediate substrates lanosterol and 24,25 dihydrolanosterol and diminished hepatic cholesterol production.