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saturated FA overload can be reduced by local desaturation. Thus, the stearoyl-CoA desaturase-1 (SCD1) enzyme is an important member in the cellular defense mechanism against lipotoxicity. The regulation of SCD1 is well characterized, but SCD5, the other human isoform has barely been studied yet. The present work aimed to assess the tissue-specific expression of the SCD5 promoter. Due to the marked central nervous system expression of the isoenzyme, the promoter activity of SCD5 constructs was planned to measure in neuronal cells. We also aimed to investigate the effect of two naturally occurring SNPs in the 5' region of SCD5 on gene expression. The promoter activity of SCD5 constructs were measured by luciferase assays in transiently transfected HEK293T, HepG2 and SK-N-FI cells. Promoter SNPs were generated by site-directed mutagenesis and characterized by luciferase reporter system. Putative transcription factor (TF) binding sites were analyzed using JASPAR online database. Consistent with our previous results, the 1 kb long 5' region showed the highest promoter activity in SK-N-FI cell line. While 5-fold higher luciferase activity was measured in HepG2 cells and 10-fold higher in HEK293T cells, but the increment was 30-fold in neuronal cells compared to the control. Endogenous SCD5 mRNA levels in the three cell lines and in samples from human liver, kidney and brain tissues showed the same pattern as promoter activities of different strengths measured on cell lines. rs6841081 and rs3811792 SNPs reduced luciferase activity. Based on in silico prediction of transcription factor binding sites, rs3811792 may attenuate the binding of CEBPA on the promoter. Further research is needed to elucidate the mechanism of the observed cell type specificity of SCD5 promoter, as well as the potential contribution of SNPs in human diseases.

P-04.1-133

Antipsychotic clozapine binds catalase and preserves its activity in oxidative environment

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Oxidative stress undoubtedly accompanies mental disorders, and the pleiotropic effects of atypical antipsychotics, recommended drugs in the treatment of psychosis, are not clarified at the molecular level. Catalase is one of the key enzymes of the primary antioxidant protection system. This work studied the binding of second-generation antipsychotic drug Clozapine to commercial bovine liver catalase. Using various spectroscopic methods under simulated physiological conditions, we found moderate binding affinity of clozapine for catalase ($K_a \sim 2 \times 10^5 \text{ M}^{-1}$), the binding influenced the secondary and tertiary structure of protein (according to UV-VIS and CD spectroscopy) and it managed to slightly increase its thermal stability. In AAPH induced oxidation experiments, we found that clozapine efficiently protects catalase from free-radicals oxidation and preserves its activity. Clozapine affects catalase activity in dose dependant manner, having no significant effect at lower concentrations but significantly inhibiting enzyme at saturating concentrations. In conclusion, our results indicate that the effect of direct binding of clozapine to catalase can be both beneficial and harmful and that this effect is dose dependent.

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The endoplasmic reticulum (ER)- associated degradation system regulates the intracellular level of amyloid precursor protein (APP)

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Alzheimer's disease (AD) is one of the most common dementia and neurodegenerative diseases manifested by behavioral disorders and loss of short-term memory. The pathophysiology of AD is characterized by the formation of brain senile plaques from amyloid- β peptide. The accumulation of plaques destroys brain cells and blocks cell-to-cell signaling at synapses. Neurotoxic amyloid- β is formed by sequential cleavage of the amyloid precursor protein (APP) by β -secretase and γ -secretase. APP is a transmembrane glycoprotein which serves a variety of functions related to cell adhesion and migration. Like all plasma membrane proteins, APP is processed in the endoplasmic reticulum (ER) and in the Golgi complex, before being transported to the cell surface. Aberrant processing of APP in the ER may result in overproduction of amyloidogenic products. The endoplasmic reticulum (ER)- associated degradation (ERAD) proteins, such as EDEMs and Derlin-3, support transport of proteins from the ER to the cytosol for degradation by the 26S proteasome. Our research focus on studies of the intracellular level of amyloid precursor protein (APP) dependent on ERAD proteins. The results strongly suggest that the level of APP can be regulated by Derlin-3 and EDEM proteins.

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Peroxidases in green chemistry

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Peroxidases are a widespread group of enzymes belonging to a few families which can be found in plants, animals and microorganisms. They have the ability to catalyze reactions in which various organic or inorganic substances are oxidized using a hydrogen peroxide (H_2O_2) as a substrate. In addition, the family of catalases-peroxidases possesses the ability to decompose hydrogen peroxide to water and oxygen. They often provide protection against reactive oxygen species (ROS) and are therefore an important part of the antioxidant defence system. In our work we focused on production different peroxidases, namely thermostable catalase AfKatG, dye-decolorizing DypB and C-domain of MagKatG2, in *E. coli*. We mutated these enzymes on selected sites and studied effects on activities and/or stabilities (chemical or thermal). We also observed different effects of ions on activity of some enzymes. We tried several compounds as substrates. All of these studies are parts of a project which focuses on biotransformation, mainly use of different enzymes in such reactions, to prepare interesting substances, e. g. aromas as vanillin.

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