Abstract

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Title of diploma thesis: Study of gene expression regulation in kidneys

During evolution, each organism was forced to create its complex defense system to prevent the accumulation of endogenous and foreign substances, including drugs, in the body. These defense systems are composed of Phase I and Phase II enzymes and transport proteins. One of the main roles in the metabolism of endogenous and biotransformation of exogenous substances is ensured by the constitutive androstane receptor (CAR).

This work aimed to determine the effect of activation of the human constitutive androstane receptor (hCAR) on the gene expression of drug transporters and biotransformation enzymes in the kidneys of humanized mice. Additionally, to examine the effect of CAR on the expression of selected genes in the HK2 cell line. In both cases, the isolation of mRNA was performed using the classic phenol-chloroform extraction followed by reverse transcription and the qRT-PCR reactions.

Firstly, we studied the influence of CITCO, an agonist of hCAR, on the expression of biotransformation and transport protein genes in the kidneys of humanized mice. The expression of *Ugt1a1* and *Slc22a1* genes was increased with statistical significance. In the second part, we focused on the influence of genes in the human HK2 cell line after the addition of substances affecting the CAR. In only one case, a significant increase of the *CYP2B6* gene after administration of CITCO 10 μM + PK11195 10 μM was apperent. A significant reduction of expression was observed for the *CYP3A4* gene after administration of phenobarbital 500 μM and the combination PK11195 10 μM + CITCO 10 μM.

A comparison of the results with studies investigating the regulation of gene expression by CAR in the liver suggests that CAR also plays a significant role in kidneys, however, it differs and its exact definition requires further research.