ABSTRACT

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Title of diploma thesis: Evaluation of gene expression of selected ABC and OATP transporters in the HTR-8/SVneo cell line during stimulation with pro-inflammatory cytokines

Placenta is the first and the largest fetal organ that gradually develops during pregnancy and plays an essential role in the development of the fetus. It fulfills the entire spectrum of functions, ensures the transport of nutrients to the fetus and the removal of waste substances back into the maternal circulation, protects the fetus from toxins, and at the same time fulfills a certain mechanical and especially immunological barrier between mother and fetus. One of the main functions of the placenta is the transport function which is made possible by membrane transporters present mainly in the syncytiotrophoblast layer of the placenta. Transporters in the human placenta can be divided into two families, SLC and ABC which are further divided into several subfamilies. The expression of transporters changes physiologically during pregnancy, but pathological conditions such as inflammation can also influence the expression. At the beginning of pregnancy and during childbirth, inflammation plays a physiological role, but if there is an excessive inflammatory response during pregnancy, it can lead to complications that can result even to spontaneous abortion or premature birth. It has been shown that the expression of transporters can be affected in the case of infection or inflammation. This work investigates the effect of the inflammatory response on the expression of ABC and SLC placental transporters, using the first-trimester placental cell line HTR-8/SVneo and its pro-inflammatory stimulation with selected mediators, namely IL-6, TNF-α, IFN-γ, LPS and HMBG1. Namely, the transporters encoded by

the *ABCB1, ABCC1, ABCC2, ABCC4*, *ABCC5 and ABCG2* genes were included and from SLC, the genes encoding the OCTN (OCTN1 and OCTN2) and OATP (OATP2A1, OATP2B1, OATP3A1, OATP4A1) transporters were included.

The results of this work pointed out that certain pro-inflammatory mediators can affect the gene expression of selected ABC and SLC transporters. Based on the evaluated data, we achieved significant changes in the gene expression of ABCC2, ABCC4, ABCG2, OCTN1, OCTN2 and OATP2A1 transporters following stimulation with IFN-γ. A change in the gene expression for ABCC2, ABCC4, OCTN1 and OATP2B1 transporters was further observed with TNF-α stimulation. Deregulation of gene expression was also noted after IL-6 stimulation of ABCC4 and ABCG2 transporter. A change in the gene expression of ABCG2 transporter occurred also after stimulation with LPS. These results may contribute to a better understanding of gene expression changes in the inflammatory environment. However, it would be appropriate to verify these results with the help of further experiments and possibly extend them with samples of villous explants from placentas ideally obtained during the first trimester.

Keywords: placenta, inflammation, gene expression, transporters, pro-inflammatory cytokines