ABSTRACT

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Title of Diploma Thesis: The impact of endoglin on the activation of liver fibrosis *in vitro*

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Liver fibrosis is a dynamic process characterized by the transformation of hepatic stellate cells (HSC) into proliferative myofibroblasts. Endoglin, which is highly expressed in HSC, is a transmembrane glycoprotein acting as a co-receptor for binding to Transforming Growth Factor β (TGF-β). It is increased expression is associated with pathological conditions and is thus a significant marker for tumor diseases, cardiovascular diseases, and others. For this reason, endoglin is a target molecule for therapeutic interventions. Carotuximab (TRC105) is a monoclonal antibody against endoglin. It binds to the orphan domain of endoglin and affects it is signalling pathway through SMAD phosphorylation.

Aim: The aim of the study was to determine whether carotuximab is capable of reducing endoglin expression and thereby preventing the development or limiting the progression of liver fibrosis in human hepatic stellate cells.

Methods: For the experimental part, we used human HSCs at passage number 3. The cells were cultured until reaching 90% confluence, then exposed to serum-free medium containing 300 µg/ml TRC105 for 4 hours. Subsequently, fibrosis was induced by adding TGFβ at a concentration of 5 ng/ml for 24 hours. To measure selected markers of liver fibrosis and it is signalling pathway, including collagen, αSMA, and SMAD2/3, as well as endoglin, RT-PCR and flow cytometry methods were employed.

Results: The results showed that treatment of the cells with TGF-β led to an increase in fibrosis markers (collagen, αSMA) and endoglin at the mRNA level. Following the addition of the antibody (TRC105), the excessive expression of endoglin induced by TGFβ was prevented, resulting in similar effects on collagen and αSMA, also led to a reduction in the expression of pSMAD2/3. The results show that endoglin may play a role in the process of liver fibrosis and suggest that direct blockade of endoglin and it is signalling pathway could have a protective antifibrotic effect crucial for the treatment of liver pathologies.