Abstract

The liver plays a central role in human physiology, and its vulnerability to metabolic disorders such as non-alcoholic steatohepatitis (NADH) underscores the need for effective therapeutic interventions. This thesis investigates the potential of M1043, a monoclonal antibody targeting endoglin (ENG), in mitigating liver injury associated with NASH progression.

ENG, a coreceptor for transforming growth factor (TGF)-β, is implicated in various pathological processes, including fibrosis and angiogenesis. Elevated levels of soluble ENG (sENG) and transmembrane ENG are observed in NASH, suggesting its involvement in disease progression. Additionally, intracellular adhesion molecule-1 (ICAM-1) and vascular cellular adhesion molecule-1 (VCAM-1) play crucial roles in inflammation and endothelial dysfunction, key features of NASH.

In this study, male mice were divided into control, choline-deficient L-amino acid defined high fat diet (CDAA)+rat IgG, and CDAA+M1043 groups, with the latter two groups fed a CDAA-HFD inducing NASH changes. Mice were treated with M1043 for four weeks, and liver samples were analyzed for protein expression of ENG, ICAM-1, and VCAM-1. Results showed that CDAA-HFD induced liver injury, as evidenced by elevated liver enzymes, and upregulation of ENG, ICAM-1, and VCAM-1. Importantly, M1043 treatment significantly prevented CDAA-HFD induced increase in the expression of these markers, suggesting its potential therapeutic efficacy in NASH.

Our findings highlight the promising role of M1043 in mitigating liver injury associated with NAFLD. Further research is needed to elucidate the underlying mechanisms and evaluate the translational potential of M1043 as a therapeutic agent for liver diseases.