The atorvastatin effect on the expression of cytokines in the mouse model of atherosclerosis.

Atherosclerosis is an inflammatory and degenerative disease of blood vessels, characterized by narrowing of the vessel lumen by atherosclerotic plaques. VCAM-1 is a cell adhesion molecule that strongly participate on the development of endothelial dysfunction and the progression of atherogenesis. Endoglin is a transmembrane protein that plays critical role in many physiological and pathological states including angiogenesis, wound healing, myocardial infarction, and cancerogenesis.

The aim of this thesis was to describe the expression of endoglin in the atherosclerotic lesions in apoE/LDL-receptor deficient mice. Moreover we wanted to demonstrate its colocalization with VCAM-1 in the atherosclerotic lesions and furthermore determine the effect of atorvastatin treatment.

ApoE/LDLR-deficient mice on were subdivided into 2 groups. The control group of animals was fed with the western type diet. The same atherogenic diet was used in ATV group, where atorvastatin was added to the atherogenic diet at the dosage of 100 mg/kg per day. Biochemical analysis of lipids, immunohistochemical analysis of endoglin and VCAM-1 expression in light and fluorescence microscopy and western blot analysis were performed.

The results of this thesis confirmed the expression of VCAM-1 and ICAM-1 in the atherosclerotic plaques in ApoE/LDLR-deficient mice. The expression of VCAM-1 was observed in blood vessel intima (atherosclerotic lesion) and in endothelium covering atherosclerotic lesion as well as in endothelium outside the lesion. Moreover strong VCAM-1 expression was visible in smooth muscle cells of tunica media in areas under the lesions. The expression of endoglin was located on the aortic vascular endothelium and in other smaller vessels and capillaries of surrounding myocardium. Moreover fluorescence microscopy revealed colocalization of endoglin and VCAM-1 in the endothelium covering the plaque and outside it. Atorvastatin treatment resulted in strong hypolipidemic effect. In addition western blot analysis showed significant reduction of VCAM-1 expression in atorvastatin treated mice. On the other hand endoglin expression was significantly increased after atorvastatin treatment.

In conclusion these results demonstrate different role of endoglin and VCAM-1 in atherogenesis suggesting possible protective role of endoglin in atherogenesis.