Endoglin is crucial for atorvastatin induced eNOS expression in endothelial cells in vitro

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Objectives: Endoglin was shown to be co-expressed with eNOS in aortic endothelium in atherosclerotic plaques and upregulated by atorvastatin (ATV) treatment in mice. In this study, we focused on endoglin and eNOS expression during inflammation and after ATV treatment. We hypothesized whether inflammation modulates ATVdependent induction of endoglin and eNOS expression in vitro in endothelial cells and whether ATV-induced eNOS expression is regulated via endoglin.

Methods: Human umbilical vein endothelial cells (HUVECs) were exposed to TNFa or/and ATV treatment. In ATV pretreatment model, cells were treated 24 h by ATV, and then cultured with TNFalpha for 16 h. The protein expression of selected markers was examined by flow cytometry and Western blot analysis and soluble endoglin levels in medium were measured by means of ELISA. Gene expression of endoglin was examined by qRT-PCR.

Results: ATV treatment significantly increased endoglin and eNOS expression, and interestingly it was able to prevent its TNF-alpha-mediated down regulation. Suppression of endoglin using small interfering RNA (siRNA), but not inhibition of TGF-beta signaling with SB431542, abrogated ATV-induced eNOS expression. ATV treatment did not change the expression of p-Smad2.

Conclusions: Our results showed that inflammation results in reduced expression of endoglin and eNOS in HUVECs, which could be prevented by ATV treatment. Moreover, ATV induced eNOS expression seems to be dependent on endoglin expression, but not on Smad2. Possible implications of this finding might be reflected in pathological conditions characterized by reduced levels of endoglin and eNOS as for example in hereditary hemorrhagic telangiectasia or in other endothelial dysfunctions.

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