Local statin therapy differentially interferes with smooth muscle and endothelial cell proliferation and reduces neointima on a drug-eluting stent platform.

OBJECTIVE: Therapeutic strategies to provide local inhibition of mitogen mediated proliferation and migration of human coronary artery smooth muscle cells (CASMC) by means of drug-eluting stents have been shown to enable effective limitation of neointimal hyperplasia. However, currently available drug-eluting stents utilize compounds that may also adversely affect endothelial regrowth, thus possibly precipitating subsequent cardiac events. Accordingly, identification of compounds that differentially inhibit smooth muscle and endothelial cell migration and proliferation could be of substantial clinical usefulness. METHODS AND RESULTS: In addition to lipid lowering, statins are known to display auxiliary pleiotropic activities. The purpose of this study was to evaluate the effect of local administration of cerivastatin on proliferation, migration and cytotoxicity of CASMC as well as coronary artery endothelial cells (CAEC) and to evaluate the effect of cerivastatin-coated stents on the inhibition of neointima formation as well as endothelial regrowth within the stented vessel. Cerivastatin displayed a differential effect on CASMC as compared to CAEC with regard to proliferation and migration; both were more profoundly inhibited in CASMC. Appreciable cytotoxicity and pro-apoptotic effects were low in both cell lines at therapeutic
concentrations. Cerivastatin-elution led to significant inhibition of neointima formation in the rat carotid stent model, endothelial coverage of in-stent vascular tissue was similar with control and cerivastatin-eluting stents. CONCLUSIONS: As proof of principle, our study provides evidence that local application of a HMG-CoA reductase inhibitor on a drug-eluting stent platform can efficiently limit neointima formation. Consequently, these compounds warrant further clinical evaluation to confirm this finding. Our data further suggest that the anti-restenotic effect of local statin administration might be associated with a more protective interaction with the endothelium than that observed with compounds currently employed on drug-eluting stents.