Adenovirus-mediated heme oxygenase-1 gene transfer inhibits the development of atherosclerosis in apoE-deficient mice

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摘要

Abstract

BACKGROUND: Increasing evidence supports the role of heme oxygenase-1 (HO-1) in cytoprotective response and iron homeostasis. The object of this study was to investigate whether adenovirus-mediated gene transfer of HO-1 in arteries reduces iron overload and inhibits lesion formation in apolipoprotein E (apoE)-deficient mice. METHODS AND RESULTS: Infection of rat aortic smooth muscle cells with adenovirus carrying the human HO-1 gene (Adv-HO-1) resulted in a high-level expression of HO-1 protein, which effectively reduced the hemin-induced iron overload in these cells. Adenovirus-mediated gene transfer in arteries in vivo was achieved by direct injection of Adv-HO-1 into the left ventricles of anesthetized animals. Transgene was expressed in the endothelium and aortic lesion of apoE-deficient mice after they had received recombinant adenovirus for 1 week and gradually decayed during the next 5 weeks. When young apoE-deficient mice (14 weeks old) received Adv-HO-1 (2.5 x 10(9) pfu) for 6 weeks, lesions that developed in the aortic root or aortic arch were significantly smaller than those in control littermates receiving empty viral vector. Furthermore, the iron deposition as well as tissue iron content was much less in aortic tissue of Adv-HO-1-treated mice. The inhibitory effect of HO-1 gene transfer on the progression of advanced lesions was also observed in older apoE-deficient mice (20 weeks old) receiving Adv-HO-1 intraventricularly. CONCLUSIONS: Overexpression of HO-1 in vascular cells facilitates iron metabolism and attenuates development of atherosclerosis in apoE-deficient mice.