Heme oxygenase-1 gene transfer protects retinal ganglion cells from ischemia-reperfusion injury

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摘要

Abstract

RGC (retinal ganglion cell) death following ischaemic insult is the major cause of a number of visionthreatening diseases, including glaucoma. The aim of the present study was to evaluate the role of HO-1 (haem oxygenase-1) in the retina against IR (ischaemia/reperfusion) injury. Adenovirusmediated HO-1 gene transfer (Adv-HO-1) was carried out by injection into the vitreous body to induce HO-1 overexpression. At 3 weeks after transfection, levels of HO-1 expression, as measured byWestern blot analysis, immunohistochemical staining and activity assay, were drastically upregulated. Transient retinal ischaemia was induced by raising the intraocular pressure to 150 mmHg for 60 min. Untreated IR caused a significant decrease in RGC numbers at 3 and 7 days after reperfusion (76.1 and 67.2% of control eyes with sham IR respectively; $P<0.001$). Eyes pretreated with Adv-HO-1 had less RGC loss on day 3 and 7 following reperfusion compared with control eyes injected with Adv-GFP (adenovirus containing a gene for green fluorescent protein; 94.3 and 88.2% respectively; $P=0.007$ and 0.001). SnP (tin protoporphyrin), an HO-1 inhibitor, counteracted the effects of Adv-HO-1. In conclusion, these findings provide evidence that augmentation of HO-1 enzyme overexpression by intravitreal injection is able to protect RGCs against IR-induced damage.