Peptain-1 blocks ischemia/reperfusion-induced retinal capillary degeneration in mice

CJ Hougen (M.D., SOM), MH Nam, RB Nahomi, and RH Nagaraj, Department of Ophthalmology, University of Colorado, Denver, CO.

Purpose: Diabetic retinopathy (DR) is characterized by abnormalities of retinal neuronal and capillary cells. Peptain-1 was shown to be protective against retinal ganglion cell death in animal models of glaucoma. Here we evaluate the ability of peptain-1 to block apoptosis of human retinal endothelial cells (HRECs) in vitro and retinal capillary cells in mice after retinal ischemia/reperfusion (I/R) injury. *Methods:* HRECs were treated with peptain-1 or scrambled peptide (200 μg/ml) for 3 h and a combination of pro-inflammatory cytokines (IFN-γ 50U/ml +TNF-α 20ng/ml + IL-1β 20ng/ml) for 48 h. C57BL/6J mice (12-week-old) were subjected to I/R injury by elevating the intraocular pressure to 120 mmHg for 60 min followed by reperfusion. Peptain-1 or scrambled peptide (0.5 μg of in 1 μl of PBS) were injected intravitreally immediately after I/R injury and after one week. Contralateral eyes were used as vehicle controls and animals were euthanized on day 14 post-I/R injury. Abnormalities in the retinal capillaries were evaluated by Periodic acid-Schiff staining of elastase-digested retinal blood vessels. *Results:* Our data suggest peptain-1 entered HRECs without any transfer reagents. Peptain-1 blocked caspase-3–mediated apoptosis in HRECs but scrambled peptides did not. Intravitreally injected peptain-1 was distributed throughout the retina after 4 h. The I/R injury caused the loss of retinal capillary cells. A similar pattern was observed in the scrambled peptide injected group. Intravitreally injected peptain-1 protected retinal cells from I/R injury. *Conclusion:* Our study demonstrated that peptain-1 protects retinal capillary cells from I/R injury and suggests that peptain-1 could be used as a therapeutic agent to prevent the death of capillary cells in DR.