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

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Introduction: Neurovascular degeneration results in vascular dysfunction, leakage, ischemia, and structural changes that can lead to significant visual impairment. We previously showed the protective effects of peptain-1, a 20 amino acid peptide derived from the αB-crystallin core domain, on retinal ganglion cells in two animal models of glaucoma. Here, we evaluated the ability of peptain-1 to block apoptosis of human retinal endothelial cells (HRECs) in vitro and retinal capillary degeneration in mice subjected to retinal ischemia/reperfusion (I/R) injury.

Methods: HRECs were treated with either peptain-1 or scrambled peptides (200 µg/mL) for 3 h and a combination of proinflammatory cytokines (IFN-γ 20 ng/mL + TNF-α 20 ng/mL+ IL-1β 20 ng/mL) for additional 48 h. Apoptosis was measured with cleaved caspase-3 formation via western blot, and by TUNEL assay. C57BL/6J mice (12 weeks 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) was intravitreally injected immediately after I/R injury and 7 days later. One microliter of PBS was injected as vehicle control, and animals were euthanized on day 14 post-I/R injury. Retinal capillary degeneration was assessed after enzyme digestion followed by periodic acid–Schiff staining.

Results: Our data showed that peptain-1 entered HRECs and blocked proinflammatory cytokine-mediated apoptosis. Intravitreally administered peptain-1 was distributed throughout the retinal vessels after 4 h. I/R injury caused retinal capillary degeneration. Unlike scrambled peptide, peptain-1 protected capillaries against I/R injury. Additionally, peptain-1 inhibited microglial activation and reduced proinflammatory cytokine levels in the retina following I/R injury.

Discussion: Our study suggests that peptain-1 could be used as a therapeutic agent to prevent capillary degeneration and neuroinflammation in retinal ischemia.