



IOP-LOWERING AND NEUROPROTECTIVE EFFECTS OF RHO/ROCK INHIBITORS

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Background: Rho-associated protein kinase (ROCK) plays important roles in diverse cellular behaviors. In our studies, we aimed to elucidate the role of Rho-ROCK signaling in regulation of intraocular pressure (IOP) and outflow facility.

Design: Experimental animal study

Materials: Bovine and rat tissue studies

Main Outcome Measures: IOP and outflow facility in rat glaucoma model and alteration of cellular structures and cell survival after ischemia

Results: Our results showed that administration of a specific ROCK inhibitor showed a reduction in IOP and an increase in outflow facility in experimental eyes. Western blot analysis revealed the presence of p160ROCK in trabecular meshwork (TM) cells and ciliary muscle (CM) tissues. In cultured TM cells, exposure to Rho/ROCK inhibitor caused retraction of cell bodies as well as disruption of actin bundles and impairment of focal adhesion formation. Also, Rho/ROCK inhibitor inhibited carbachol-induced contraction of isolated bovine CM strips. Similar IOP-lowering and outflow facility-increasing effects were found in experiments using non-selective protein kinase inhibitors and myosin light chain kinase inhibitors. In addition, we conducted studies on neuroprotective effects of Rho/ROCK inhibitor on retinal neurons in rats with pressure-induced transient retinal ischemia.

Conclusions: Our TUNEL experiments and morphometric analysis demonstrated neuroprotective effects of Rho/ROCK inhibitor against cell death (apoptosis) of retinal ganglion cells in rats with high IOP. ROCK inhibitors have potential as a treatment modality for glaucoma.