IS NEUROGLOBINE (NGB) A PERSPECTIVE FOR GLAUCOMA?

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BACKGROUND AND AIMS

Glaucoma is an optic neuropathy characterized by optic disk cupping and visual field loss. It is usually associated with elevated intraocular pressure (IOP). The exact cause of optic nerve damage from glaucoma is not fully understood, but involves mechanical compression and decreased blood flow of the optic nerve. Besides several medical, surgical or laser treatments to control the IOP, there is no specific therapy for the neural injury induced by glaucoma so far.

Neuroglobin (Ngb) is a recently discovered globin, which is expressed predominantly in the central and peripheral nervous system and has a possible role as an endogenous neuroprotectant. (1) Several publications have shown that neuroglobin plays a neuroprotective role in cerebral ischemia. (2) The concentration of Ngb in the retina is about 100-fold higher than in the brain and Ngb was even shown to be upregulated in eyes of patients with advanced glaucoma. (3)

The aim of our study is to further explore the mechanisms of Ngb function in the retina, and investigate the possible neuroprotective potency of this O_2-binding protein in glaucoma.

MATERIAL AND METHODS

1) *In vitro:* We will set up cultures for primary retinal ganglion cells (RGCs). The cultured RGCs will be subjected to hypoxia by incubation in a controlled-atmosphere incubator. Cell survival and apoptosis will be assessed using MTT method and TUNEL staining. Ngb expression in normoxic and hypoxic cells will be compared. Additionally, the RGCs will be transfected with plasmids expressing Ngb mRNA to evaluate the neuroprotective effect of Ngb.

2) *In vivo:* The ischemia/reperfusion model and the staurosporine intravitreal injection model cause acute RGC loss. We will also use a laser model to induce chronic elevated IOP by obstructing the aqueous outflow pathway. We will first analyze upregulated Ngb expression in these models. The localization of both Ngb mRNA and protein will be assessed. Ngb-Tg mice will be subjected to the glaucoma models. We will measure cell density or retinal thickness. We will also analyze the possible contribution of oxidative stress via immunostainings for ROS and determine possible effects on NO scavenging by evaluating the expression of NOS. Furthermore, we will transfect RGCs in vivo using intravitreal injections of a Ngb expressing adeno-associated virus to test the therapeutic potential of Ngb.

CONCLUSION

Our project will go from in vitro to in vivo, from the induction of Ngb expression to its neuroprotective role and from lab research to potential clinical therapeutic strategy. Thus it will not only provide us with an improved understanding of neuroglobin, but also open a new perspective for the treatment of retinal ganglion cell apoptosis and glaucomatous neuropathy.

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