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Renin-Angiotensin System (RAS) involvement in the oxidative stress-Induced impairment of retinal neuronal cells

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Abstract

Purpose: We previously reported that neurons in the inner layer of the retina are impaired in diabetes through angiotensin II type 1 receptor (AT1R) signaling and oxidative stress. Although induction of oxidative stress in the downstream of AT1R is well-known, influence of oxidative stress on AT1R signaling in the retinal neurons remains to be elucidated. In this study, we analyze the influence of oxidative stress on AT1R signaling in retinal neuronal cells using a selective culture system of rat retinal ganglion cells (RGCs).

Methods: Rat RGCs were purified by a two-step immunopanning procedure and cultured with or without antioxidant (AO) compounds. Reactive oxygen species (ROS) in RGCs were analyzed using dihyderoethidium. The expressions of angiotensin II, cleaved caspase 3, and netrin-1 were analyzed by immunocytochemistry. Live RGCs were detected by calcein-acetoxymethyl ester. The roles of AT1R signaling and netrin-1 were analyzed using an AT1R blocker (telmisartan) and an anti-netrin-1 neutralizing antibody, respectively.

Results: ROS and Angiotensin II were induced in RGCs cultured without AO compounds (AO-). In these cultures, the number of live RGCs was decreased and the expression of cleaved and activated caspase 3 increased, but these changes were attenuated by the addition of the AT1R blocker. A reduction in netrin-1 expression under the AO- condition was also prevented by the AT1R blocker. The AT1R blocker's effects on RGC survival and reduction in cleaved-caspase 3 positive cells were cancelled by the anti-netrin-1 neutralizing antibody

Biography

Yoko Ozawa M.D., Ph.D. works as a chief of the Medical Retina Division (Age-related macular disease; AMD division) and also a vitreoretinal surgeon, as well as a Lab chief of the Laboratory of Retinal Cell Biology (RCB lab). Her main research interest is the neuroprotection and oxidative stress in the retinal diseases, such as AMD and diabetic retinopathy.