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Rho-GTPase activators mediated regulation of fluid dynamics as a novel target for the pathophysiology of glaucoma

Janardan Kumar
Becker College, USA

The emerging evidence on Rho-GTPase studies in the field of glaucoma research has reinforced a growing understanding of the molecular mechanism(s) of aqueous humor outflow resistance and provided new drug targets for glaucoma therapy. Several laboratories, including our research team suggested that the increased outflow facility was as a result of the cellular contractions in outflow pathway cells. Even perfusion of thrombin with impurities in porcine eyes, initially misled us to a conclusion that the Rho-GTPase activation with thrombin leading to cellular contraction might increase the outflow facility. Furthermore, investigation of pure thrombin and Lysophosphatidic Acid (LPA) perfusion in porcine eyes led us to conclude that Rho-GTPase activation, in fact, decreased the outflow facility. A number of studies have focused on to the regulation of outflow, however, very little is known about the regulation of fluid dynamics in the eye and the role of outflow pathway cells for maintaining aqueous humor outflow resistance. The simple reason is that the physiologically compromised fluid dynamics measuring device at constant pressure and the fluid medium for perfusion, similar to the aqueous humor, are not fully developed. Hence, measurement of the fluid dynamics at constant pressure is warranted to determine if aqueous flow is continuous or discontinuous, and could be directly correlated with the function of outflow pathway cells. Moreover, we hypothesize that the measurements of LPA and/or thrombin in the aqueous humor of glaucomatous eyes might provide a rationale to the pathophysiology of glaucoma. We anticipate that this new knowledge will ultimately lead to the development of new therapeutic alternatives in the management of glaucoma.

Biography

Janardan Kumar, PhD is a Professor of Microbiology and Chemistry at Becker College. He served as a Chair of the Natural Science Department. Prior to joining Becker College, while working as a Research Associate/Assistant Professor at Duke University, he first proposed at the ARVO international conference, Fort Lauderdale, that the Rho-GTPase activation mediated through LPA and thrombin perfusion caused increase outflow resistance in porcine eyes. In 2001 while at Duke University, he filed for intellectual property in the U.S. on RGD-containing peptides as safe therapeutic alternatives for glaucoma therapy. The same molecule has been filed for patent in Japan, with additional international applications to follow.

janardan.kumar@becker.edu

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