Potential role of P2X7 receptor in neurodegenerative processes in a murine model of glaucoma

Pérez de Lara MJ1, Avilés-Trigueros M2, Guzmán-Arángez A1, Valiente-Soriano FJ2, de la Villa P3, Vidal-Sanz M4, Pintor J1

1 Department of Biochemistry and Molecular Biology IV, Faculty of Optics and Optometry, Complutense University of Madrid, c/Arcos de Jalón 118, E-28037, Madrid, Spain.
2 Laboratory of Experimental Ophthalmology, Dept. of Ophthalmology, Faculty of Medicine, University of Murcia and Murcia Institute of Bio-Health Research (IMIB), E-30120, El Palmar, Murcia, Spain.
3 Systems Biology Department, Faculty of Medicine, University of Alcalá, Alcalá de Henares, Madrid, Spain.
4 Laboratory of Experimental Ophthalmology, Dept. of Ophthalmology, Faculty of Medicine, University of Murcia and Murcia Institute of Bio-Health Research (IMIB), E-30120, El Palmar, Murcia, Spain. Electronic address: manuel.vidal@um.es

Glaucoma is a common cause of visual impairment and blindness, characterized by retinal ganglion cell (RGC) death. The mechanisms that trigger the development of glaucoma remain unknown and have gained significant relevance in the study of this neurodegenerative disease. P2X7 purinergic receptors (P2X7R) could be involved in the regulation of the synaptic transmission and neuronal death in the retina through different pathways. The aim of this study was to characterize the molecular signals underlying glaucomatous retinal injury. The time-course of functional, morphological, and molecular changes in the glaucomatous retina of the DBA/2J mice were investigated. The expression and localization of P2X7R were analysed in relation with retinal markers. Caspase-3, JNK, and p38 were evaluated in control and glaucomatous mice by immunohistochemical and western-blot analysis.

Furthermore, electroretinogram recordings (ERG) were performed to assess inner retina dysfunction. Glaucomatous mice exhibited changes in P2X7R expression as long as the pathology progressed. There was P2X7R overexpression in RGCs, the primary injured neurons, which correlated with the loss of function through ERG measurements. All analyzed MAPK and caspase-3 proteins were upregulated in the DBA/2J retinas suggesting a pro-apoptotic cell death. The increase in P2X7Rs presence may contribute, together with other factors, to the changes in retinal functionality and the concomitant death of RGCs. These findings provide evidence of possible intracellular pathways responsible for apoptosis regulation during glaucomatous degeneration.

Copyright © 2019 The Authors. Published by Elsevier Inc. All rights reserved.


PMID: 31102752