AB041. A novel IL-1 receptor modulator prevents photoreceptor loss in a model of age-related macular degeneration

Rabah Dabouz[1,2], José Carlos Rivera[1,3], Sylvain Chemtob[1,2,3]

[1]Maisonneuve-Rosemont Hospital Research Centers University of Montreal, QC, Canada; [2]Department of Pharmacology and Therapeutics, McGill University, Montreal, QC, Canada; [3]CHU Sainte-Justine Research Centre, University of Montreal, Montreal, QC, Canada

Correspondence to: Sylvain Chemtob, MD, PhD, FRCPC, FAAP. Sainte-Justine Research Center, 3175 Chemin Côte-Sainte-Catherine, Montréal, QC H3T 1C5, Canada.
Email: sylvain.chemtob@umontreal.ca.

Background: The objective of this study is to evaluate the implications of interleukin-1β (IL-1β) in photoreceptor degeneration using a model of blue light in rodents.
Methods: CD-1 mice (12–16 weeks-old) were exposed to blue LED light (6000 lux at 450 nm) for 1 hour and then sacrificed at day 3 post-illumination. Mice were intraperitoneally treated or not with a peptide antagonist of the IL-1β receptor, named Rytvela (or 101.10) twice per day until sacrifice. Several markers related to the inflammatory process such as F4/80, NLRP3, Caspase-1, IL-1β and glial fibrillary acidic protein (GFAP) were evaluated by immunohistochemistry. Photoreceptor cell death was assessed by TUNEL assay and Caspase-3 immunofluorescence.
Results: Immunofluorescence experiments revealed an infiltration of positive F4/80 cells (microglia and macrophages) into the subretinal space in mice exposed to blue light, which was significantly ($P<0.01$) abrogated with Rytvela treatment. Co-localization of NLRP3, Caspase-1, and IL-1β with F4/80 positive cells was clearly detected in the subretinal space, suggesting that these inflammatory cells are the main source of IL-1β. Interestingly, GFAP immunoreactivity, a marker of stress in Müller cells, was augmented in retinas exposed to the blue light, and reduced with Rytvela administration. The TUNEL assay showed that Rytvela prevents photoreceptor apoptosis in the retina of mice exposed to blue light. Likewise, co-culture of retinal explants with LPS-ATP activated bone marrow-derived macrophages resulted in a high number of TUNEL positive photoreceptors, which was reduced by treatment with Rytvela.
Conclusions: These results show that Rytvela attenuated the inflammatory response and prevented the death of photoreceptors in a model of dry AMD. Modulation of IL-1β signaling would be a useful therapeutic avenue for dry AMD, for which no approved treatment currently exists.

Keywords: Inflammation; interleukin-1β (IL-1β); apoptosis; retina; age-related macular degeneration (AMD)

doi: 10.21037/aes.2019.AB041
Cite this abstract as: Dabouz R, Rivera JC, Chemtob S. A novel IL-1 receptor modulator prevents photoreceptor loss in a model of age-related macular degeneration. Ann Eye Sci 2019;4:AB041.