ISER 2024

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PROGRAM ABSTRACTS

XXVI Biennial Meeting of the International Society for Eye Research
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Conclusion
RXR-based therapy shows promise for the treatment of diabetes. Not only could it lower hyperglycemia effectively for diabetic patients, but it could also balance retinal lipid metabolism and reduce anti-inflammatory cytokine expression resulting in the slowing of the progression of DR.

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Retinoid X receptors (RXR): Potential therapeutic targets in retina neurodegenerative diseases

Section: Retinal Degeneration

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Retinal neurodegenerative diseases share the death of photoreceptors (PR) as a common final step and still now lack effective treatments. Oxidative stress, degeneration or altered functionality of the retinal pigment epithelium (RPE) cells and inflammatory processes involving immunomodulatory cell types such as these RPE cells or Müller glial cells (MGCs) also play pivotal roles. Current therapeutic strategies aim to identify factors and signaling pathways to prevent neuronal death, modulate inflammation, and promote neuronal regeneration. Retinoid X receptors (RXRs), nuclear receptors governing multiple cellular functions, have attracted attention for their potential therapeutic efficacy. Since their roles in the retina are scarcely known, we investigated whether RXRs might prevent retina cell death and control inflammation.
In *in vitro* models of retinal degeneration induced by oxidative damage or BMAA, a cyanotoxin linked to retinal neurotoxicity, we demonstrated that RXR activation promoted neuronal survival and protected RPE cells from cell death, preventing reactive oxygen species (ROS) formation and loss of mitochondrial function. In neuro-glial cultures from retinas of *rd1* mouse, a model of Retinitis Pigmentosa, we evidenced that RXR activation enhanced the survival of *rd1* PR, preserving mitochondrial function, simultaneously decreasing MGC reactivity and promoting an anti-inflammatory environment, supporting a novel protective effect of RXR activation on *rd1* PR. To expand comprehension of the impact of RXR activation in immune response modulation in retina neurodegeneration, we studied whether this activation affected the immune and antiviral drug-response. We demonstrated that RXR agonists reduced the expression of proinflammatory cytokines induced by H2O2 (IL-6 and TNFα) and BMAA (COX-2), while promoting anti-inflammatory cytokine expression (IL-10 and TGFβ). Moreover, RXR activation may modulate the response to HSV-1 viral infection in retinal cells.
Overall, our results suggest that activation of RXRs protects retina cell types from multiple injuries by acting, at least on a shared point in death pathways, such as ROS generation and mitochondrial dysfunction, while also promoting an anti-inflammatory response and modulating viral infection dynamics, offering novel insights for ocular therapeutic drug development.

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