Researchers elucidate cause of death of photoreceptor cells in retinitis pigmentosa

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Research conducted at the Angiogenesis Laboratory at Massachusetts Eye and Ear Infirmary, has for the first time, identified the mode of death of cone photoreceptor cells in an animal model of retinitis pigmentosa (RP).

This groundbreaking study, led by Demetrios G. Vavvas, M.D., Ph.D., and including Joan W. Miller, M.D., Mass. Eye and Ear/Mass General Hospital Chief of Ophthalmology and Chair of Ophthalmology at Harvard Medical School, has further identified the receptor interacting protein (RIP) kinase pathway as a potential target for developing treatment for vision loss in patients with retinitis pigmentosa. The study is expected to be published the week of Aug. 20 in the Proceedings of the National Academy of Sciences Early Edition.

Retinitis pigmentosa is an inherited condition that causes irreversible vision loss due to the degeneration of photoreceptor cells in the eye called "rods" and "cones." Rods are responsible for night vision, while cones are responsible for daylight and central vision. Vision loss from RP often begins with loss of night vision, due to death of rods, followed by loss of peripheral and central vision, due to death of rods and cones. Such vision loss can have a significant impact on people's daily lives, such as affecting their ability to read or drive a car. RP affects more than 1 million people around the world.

Research conducted by Eliot L. Berson, M.D., of the Berman-Gund Laboratory for the Study of Retinal Degenerations at Mass. Eye and Ear,

has shown that Vitamin A supplementation and an omega-3 rich diet can slow visual decline resulting from RP; they do not completely stop disease progression, however. For most patients, RP results in irreversible vision loss.

Previous studies have identified mutations in more than 50 genes that cause RP, but the mechanisms by which rods and cones die remain to be completely defined. Since many of the genes associated with RP produce proteins that are used specifically in rod cells, it is still a puzzle why and how cones, which in some cases do not use the mutant proteins, die after rods degenerate. Using an animal model of RP, the investigators studied whether RIP kinase mediated necrosis is involved in the death of photoreceptor cells, finding for the first time that it is involved in cone degeneration and that a deficiency of RIP kinase reduced cone loss. Moreover, the study found that treatment with a drug that inhibits RIP kinase significantly delayed cone cell death and preserved cone photoreceptors.

"Though the precise mechanisms involved in RIP kinase inducing necrosis remain unknown, our finding that necrosis results in cone cell death puts us one step closer to understanding this disease and, more importantly, moves us one step closer to being able to provide novel therapies to millions of patients with vision loss," said Dr. Vavvas.

More information: www.pnas.org/cgi/doi/10.1073/pnas.1206937109

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