Absence of Fas receptor signaling reduces photoreceptor cell death and improves retinal function in a mouse model of P23H autosomal dominant retinitis pigmentosa

David Zacks, MD, PhD
Ann Arbor, MI

Purpose:
Fas receptor activation has been implicated in cell death in a variety of retinal diseases. In this work we tested the hypothesis that preventing Fas receptor signaling will reduce photoreceptor (PR) cell death in the P23H mouse model of autosomal dominant retinitis pigmentosa (adRP).

Methods:
We crossed the P23H mouse with the Fas-lpr mouse, which contains a functional knockout of the Fas receptor, to generate the P23H/Fas-lpr mouse. We assessed the extent of PR loss and retinal degeneration, as well as the level of microglia/macrophage activation in the P23H/Fas-lpr mouse as compared to P23H litter-mate controls.

Results:
The P23H mouse retina had increased Fas expression in the outer retina, as compared to wild-type controls. Lack of Fas signaling in the P23H mouse resulted in improved PR survival as well as function, as assessed by ERG. This improved survival was associated with reduced infiltration of Iba1+ cells (microglia/macrophages) into the outer retina, as well as reduced expression of inflammatory cytokines.

Conclusions:
Absence of Fas signaling can prevent PR cell death in the P23H mouse retina. Our data supports the postulate that Fas serves an important role in regulating PR cell death during disease.