Abstract Title:
Glial Hypertrophy and Neuronal Remodeling in Mice Deficient in GFAP and Vimentin Following Experimental Retinal Detachment

Presentation Start/End Time:
Tuesday, May 03, 2005, 4:00 PM - 4:15 PM

Location:
Gr Floridian H

Reviewing Code:
263 retinal detachment - RC

Author Block:

Keywords:
673 retinal detachment, 588 Muller cells, 714 transgenics/knock-outs

Purpose:
Retinal detachment induces Müller cell hypertrophy both within the retina and as cellular membranes in the subretinal space. Structural and immunolabeling data suggest a prominent role for the cytoskeleton in this process. Indeed, glial fibrillary acidic protein (GFAP), vimentin, and tubulin upregulation are all hallmarks of the hypertrophy. There also may be a relationship between Müller cell hypertrophy and neuronal remodeling after detachment. Here we sought to determine if Müller cell hypertrophy was functionally dependent upon the presence of the 2 intermediate filament proteins GFAP and vimentin.

Methods:
Experimental retinal detachments were created in wild-type C57BL/6J mice and mice deficient in GFAP and vimentin (GFAP-/- vim-/-). The retinas were harvested at 7 or 28 days post-detachment. Immunohistochemistry was performed using antibodies to GFAP, vimentin, S100, VAMP, rod opsins, cone opsins, protein kinase C, and neurofilament protein. Images were collected with an Olympus Fluoview confocal microscope.

Results:
Glial cell hypertrophy was observed in both wild-type and GFAP-/- vim-/- mice following detachment. Focal regions of Müller cell growth appeared scleral to the outer limiting membrane in both groups after detachment. These processes were anti-GFAP, -S100, and -vimentin labeled in wild-type mice and only anti-S100 labeled in the GFAP-/- vim-/-. Anti-S100 labeling revealed abnormal Müller cell morphology in the attached GFAP-/- vim-/- retina, which was exaggerated after detachment. Extensive neuronal remodeling also occurred both in the GFAP-/- vim-/- and wild-type animals. These events included the sprouting of neurites from bipolar and horizontal cells into the outer nuclear layer.

Conclusions:
These studies demonstrate that the intermediate filament proteins GFAP and vimentin are not required for the hypertrophy of Müller cells nor does their absence prevent neuronal remodeling/sprouting in the GFAP-/- vim-/- retinas. The results suggest that other cytoskeleton protein(s) may play a critical role in initiating Müller cell hypertrophy.

Commercial Relationship:
M.R. Verardo, None; G.P. Lewis, None; M. Takeda, None; B.M. Wardak, None; M.D. Rabena, None; D.F. Chen, None; S.K. Fisher, None.

Support:
NEI EY0088 (SKF), NSF0331697 (SKF), NEI EY012983 (DFC), Dept. of Defense (DFC)