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