
Wnt signaling promotes Muller cell proliferation and survival after injury.

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Public Summary:

PURPOSE: Muller glia respond to retinal injury by a reactive gliosis but only rarely do mammalian glial cells re-enter the cell cycle and generate new neurons. In the non-mammalian retina, however, Muller glia act as stem/progenitor cells. Here, we test the function of Wnt signaling in the post-injury retina, focusing on its ability to influence mammalian Muller cell de-differentiation, proliferation and neurogenesis. **METHODS:** A Nd:YAG laser was used to create light burns on the retina of Axin2(LacZ/+) Wnt reporter mice. At various timepoints after injury, retinas were analyzed for evidence of Wnt signaling as well as glial cell response, proliferation, and apoptosis. Laser injuries were also created in Axin2(LacZ/LacZ) mice, and the effect of potentiated Wnt signaling on retinal repair was assessed. **RESULTS:** A subpopulation of mammalian Muller cells are Wnt responsive and when Wnt signaling is increased these cells showed enhanced proliferation in response to injury. In an environment of heightened Wnt signaling, caused by the loss of Wnt negative regulator Axin2, Muller cells proliferate after injury and adopted the expression patterns of retinal progenitor cells (RPCs). The Wnt-responsive Muller cells also exhibited long-term survival and in some cases, expressed the rod photoreceptor marker, Rhodopsin. **CONCLUSIONS:** The Wnt pathway is activated by retinal injury, and prolonging the endogenous Wnt signal causes a subset of Muller cells to proliferate and de-differentiate into RPCs. These data raise the possibility that transient amplification of Wnt signaling after retinal damage may unlock the latent regenerative capacity long speculated to reside in mammalian neural tissues.

Scientific Abstract:

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