Unlocking the Potential to Regenerate Lost Neurons and Visual Function

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Research into regenerative medicine capabilities is producing new insights into restoring neural function particularly through the control of Müller cell differentiation. Fischer et al.\(^1\) demonstrated that Müller glia can re-enter the cell cycle, express progenitor cell markers, and differentiate into retinal neurons in vertebrates. While the mammalian regenerative capabilities of Müller glia are more limited relative to birds and amphibians, Karl et al.\(^2\) discussed the possibilities of neural and visual regeneration in humans through the use of Müller cell manipulation. However, this prospective therapeutic could only become possible through greater understanding of the signaling processes that limit glial regenerative capabilities in humans.

In a study that reveals signaling processes that could be utilized to unlock neural regeneration through glial cells, Liu et al.\(^3\) explored the ability of Wnt signaling to influence mammalian Müller cell dedifferentiation, proliferation, and neurogenesis in the post injury retina. They demonstrate this by first establishing and characterizing the glial cell response, proliferation, apoptosis, and ultimate gliosis in laser-injured retinal tissue of wild type mice. Cleverly, the authors utilize Axin2\(^{LacZ/\_}\) mice and Axin2\(^{LacZ/LacZ}\) mice, repeating the laser injury in the mutant animals. As Axin2 is an inhibitor of Wnt signaling in progenitor cells, Axin2\(^{LacZ/LacZ}\) mice have an increased sensitivity to Wnt stimulus and a prolonged Wnt signaling duration. These experiments demonstrated a decrease in apoptotic cells in the Axin2\(^{LacZ/LacZ}\) mice after laser injury. Additionally, the authors show increased proliferation in the outer nuclear layer in the Axin2\(^{LacZ/LacZ}\) mice. The proliferating cells are also positive for either a Müller cell marker or a progenitor/stem cell marker indicating some regenerative capacity in these animals likely through the Müller cells. Ultimately, the authors display long term survival and rhodopsin expression by these initially proliferative cells. This finding stresses the probable ability of Wnt-pathway manipulation to confer real, long term neural regeneration and visual recovery after injury.

References


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