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Title:	Leptin and IL-6 Family Cytokines Synergize to Stimulate Müller Glia Reprogramming and Retina Regeneration
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Abstract:	Unlike mammals, zebrafish can regenerate a damaged retina. This remarkable regenerative response is mediated by Müller glia (MG) that undergo a reprogramming event that drives their proliferation and the generation of multipotent progenitors for retinal repair. The mechanisms that drive MG reprogramming are poorly understood. Here, we report that Leptin and Gp130-coupled receptors, acting via a Jak/Stat signaling pathway, stimulate MG reprogramming and progenitor formation in the injured retina. Importantly, we find that ascl1a gene expression, which drives MG reprogramming in fish and mammals, is regulated in a Jak/Stat-dependent manner and requires consensus Stat-binding sites for injury-dependent activation. Finally, we identify cytokines that areinduced by retinal injury and exhibit a remarkable synergy in their ability to activate Jak/Stat signaling and MG reprogramming in the uninjured retina. Our study not only furthers our understanding of retina regeneration in zebrafish but also suggests new strategies for awakening retina regeneration in mammals.
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