Title:	Unlocking the molecular mechanisms underlying Zebrafish Retina Regeneration: the crucial role of egr-1
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Abstract:	Unlike higher vertebrates, where retinal injury leads to scar formation, Zebrafish possess the remarkable capability to regenerative response in the retina by restoring the retinal structure and function. This regenerative capability is driven by Muller Glia, the only glial cell type in the retina. Upon sensing injury, MG cells de-differentiate into Muller glial-driven progenitor cells (MGPCs), which exhibit stem cell-like characteristics, proliferate, migrate to the various layers and differentiate into respective cell types to restore the retinal physiology with the help of various factors that assist tissue remodeling. Previously, it was reported that Wnt signaling pathway play key role in retina regeneration and − catenin stabilization was shown to be one of the key factors driving proliferation. Following injury, in a cascade of signaling events many regeneration associated genes like ascl1a, lin28, mycb, mmp9, hdac, her4.1, insm1a, cytokines like i11b were reported to be regulated. Although the roles of many genetic and epigenetic regulators have been identified in retinal regeneration but that of developmentally important growth factors remains under- explored. In this study, we explored one component of growth factor i.e., egr-1 and understand the significance of its expression and localization.Lethality rate and phenotype of egr-1 knockdown morphants embryos suggests the relevance of egr-1 in embryonic developmental. Upon checking the temporal expression pattern by q-RT-PCR, we found out the egr-1 transcript levelto be up-regulated during initial proliferation phase of retina regeneration, when Muller glia just begins proliferating. In-situhybridisation and Immunostaining revealed that egr-1 transcripts are expressed in Inner nuclear cell layer (INL) andinhibiting its localization regulates the proliferation of MGPCs. Thus, we hypothesize that egr-1 has critical role in proliferation of MGPCs. Knocking down egr-1 during later phase of regeneration confirms the essential function of egr-1 in post MGPCs proliferation phase. Further, we also aimed towards establishing a mechanistic involvement of egr-1 with other regeneration associated genes like mmp9, lin28, zic2b, her4.1, c-fos, insm1a. Lastly, upon inhibiting and over-expressing one of the well established pro-proliferative signaling pathways TGF-, the levels of egr-1 were down-regulated, suggesting that egr-1 might be playing the crucial role in regeneration by providing feedback mechanism and hence system tries to regulate them in order to maintain homeostasis.
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