Title:	Understanding the role of Neuregulin during zebrafish retina regeneration
Authors:	Chakraborty, Trirupa
Keywords:	zebrafish Neuregulin regeneration retina
Issue Date:	Apr-2020
Publisher:	IISER Mohali
Abstract:	It has long been the goal of vision researchers to find a key to diseases like glaucoma, diabetic retinopathy, etc which cause vision impairment and loss. While the Müller Glial cell comprises the major glial component of the retina and can form progenitors that give rise to all the retinal cell types in Danio rerio, mammalian Müller glia is limited by way of regeneration as despite expressing genes required for acquiring stem-cell fate, they fail to act as progenitors in vivo. Since retina regeneration is a complex interplay of a number of signaling pathways like Delta- Notch, FGF2-FGFR-MAPK, Insulin-IGF1-PI3K (Goldman, 2014), the key to unraveling ways of coaxing the mammalian Müller glia to act as progenitors for the retinal cell types in vivo, might be held in understanding how the different signaling pathways regulate the regeneration associated genes. In our study we explored the nerve-derived factor, Neuregulin (Nrg) and Nrg1- ErbB Signaling in context of zebrafish retina regeneration. The Nrg1-ErbB Signaling has already been shown to have a positive regulation on proliferation of stem cells in regenerating axolotl limb, and in neurogenesis from neural progenitor cells of the developing zebrafish brain as well as for cardiomyocyte proliferation during embryogenesis (Farkas, Freitas, Bryant, Whited, & Monaghan, 2016; Sato et al., 2015; Yaniz-Galende & Hajjar, 2014). Moreover, since the Neuregulins are nerve-derived factors and the ErbB are transmembrane receptors, we hypothesized that the signal of an injury might be mediated to the nucleus of Müller glial cell by Neuregulins via the Nrg1/ErbB signaling cascade, thereby initiating regeneration. From our study we observed that both the Nrg1 and the ErbB receptors showed a similar peak in expression during the proliferative phase. By pharmacological inhibition of the Nrg1-ErbB1 signaling and the Nrg1-Erb2 signaling, we showed a reduction in the number of proliferating cells, thereby suggesting a positive role in proliferation. Additionally, we found that the inhibition of the Nrg1/ErbB1 signaling cascade resulted in a differential expression of ascl1a which required for the proliferation of Müller glial cells. Interestingly however, upon drug inhibition, we found a decrease in the protein expression of Hdac1, whose upregulation during the dedifferentiation phase (0-2dpi) was previously shown to be essential for successful proliferation in zebrafish fin regeneration (Mitra et al., 2018). Overall this study suggests a role of Nrg1 and its ErbB receptors in regulating some known regeneration-associated genes during the proliferative phase of zebrafish retina regeneration.
URI:	http://hdl.handle.net/123456789/1482
Appears in Collections:	MS-15

Files in This Item:

File	Description	Size	Format	
MS15204.pdf		1.16 MB	Adobe PDF	View/Open