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Title: Unveiling the Regenerative Potential: Investigating the Role of Neurogenin in Zebrafish Retina Regeneration

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Keywords: Animal Maintenance

Retinal injury, drugs delivery and Harvesting .

RNA Isolation

Reverse Transcription Polymerase Chain Reaction (RT-PCR).

Issue

May-2024

Date:

IISER Mohali

Publisher:
Abstract:

Zebrafish (Danio rerio), owing to its immense regenerative capability, has emerged as a powerful model organism for studying retinal regeneration in depth, a process that holds significant promise for potential therapeutic applications in humans. Unlike mammals, their damaged retinas can be restored through cellular proliferation and differentiation. This process involves the its dedifferentiation of MG (Muller glia) cells into MGPCs (Muller glial proliferating cells), abundant glial cells within the retina, into functional retinal neurons. Müller glia play a pivotal role by dedifferentiating, re-entering the cell cycle, and proliferating. These progenitor cells then undergo a fascinating switch, differentiating into various retinal cell types, including photoreceptors essential for vision. Orchestrating this intricate dance are transcription factors like Ngn, Pax6, and Sox2. These factors act as molecular switches, controlling the expression of genes critical for proliferation and differentiation. Additionally, epigenetic modifications on DNA, chemical adjustments affecting gene expression, might contribute by enhancing the accessibility of these regenerative genes for the transcription factors. In this study, we delve into the role of zebrafish neurogenin1 (ngn1), a basic helixloop- helix protein that is a key player in early neural development. Although its role in formation of neural plate is well studied, its importance in the context of retina regeneration remains underexplored. Ngn1 was shown to localise to the Müller glial nuclei, that were re-established following the regenerative response. Thus, Ngn 1 can be used to mark different cell types at particular stages of retinal regeneration: neuronal progenitor formation, proliferation, and the reestablishment of the Müller glia cells. These markers will be important to further characterize the regeneration response in other retinal damage models and to elucidate the defects associated with mutants and morphants that disrupt the regeneration response. Furthermore, within the Neurogenin subfamily, we observe three major clusters, with Ngn1 and Ngn2 sharing a closer relationship. The analysis on this transcription factor reveals the identification of novel proteins which aligns with the Ngn3 subfamily. By comparing to other known Neurogenin sequences, zebrafish Ngn3 was very similiar to mouse Ngn3 and human NGN3. Although overall sequence similiarities are only 32.7 and 31.7% respectively. Genetic mapping assigns Ngn3 to linkage group (LG) 13, closely related to human chromosome 10, and shared orthologous genes between the two species reinforce the concept of a common.

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