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Title:	Understanding the Role of the Hippo-YAP Signaling Pathway in the Process of Retina Regeneration in Zebrafish
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Abstract:	<p>Sight is probably one of the most important senses that a number of animals rely on in their daily lives. While the exact anatomy of the eye varies among animals, most vertebrates possess retina as the inner most layer that helps them with vision. Needless to say, any injury or disease to the retina can cause severe aberrations in vision or even the loss of it. Hence, the body has an intrinsic regenerative capacity to help in such crises. While mammals like humans have an extremely limited potential for regeneration, naturally regenerative organisms like the zebrafish possess excellent reparative mechanisms that can result in full reconstitution of all retinal layers and hence lead to complete restoration of vision. This process of retina regeneration in zebrafish is mainly characterized by the acquisition of a stem cell-like state by the Muller Glial cells which allows them to generate proliferating progenitor populations that can then differentiate into the different cell types. This process requires the interplay of multiple signaling cascades like the TGF-β, Delta-Notch, JAK-Stat and Wnt signaling pathway. However, one such pathway that is not completely understood in this context is the Hippo-YAP signaling pathway. Though recent reports in mice have shown the Hippo pathway to be associated with the quiescence exit of Muller Glial cells and MG cell reprogramming, little is known about its role in a naturally regenerative organism like the zebrafish. In this study, we try to elucidate the role of the Hippo-YAP signaling pathway by looking at the effects of inhibition of the YAP-TEAD interaction on the proliferative response of the Muller Glial cell-derived Progenitor cells (MGPCs) and on the expression levels of various Regeneration Associated Genes (RAGs) like <i>ascl1a</i>, <i>hdac1</i>, <i>oct4</i>, <i>sox2</i> and <i>tgfb1</i> in the three phases of retina regeneration, namely, the dedifferentiation phase, the proliferation phase and the redifferentiation phase. Furthermore, this study also looks into the effect of this inhibition on the cell fate by quantifying the redifferentiated cell types like the Muller Glial cells, Amacrine cells and the Bipolar cells. In addition, the study has also looked at how the response to injury is affected when the Hippo-YAP pathway is constitutively kept in the ON state in the homeostatic conditions. Together these experiments show that the Hippo pathway plays an important role in the process of zebrafish retina regeneration and has different functions and underlying mechanisms depending on the phase of retina regeneration.</p>
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