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Title: Understanding the Role of DNA methyltransferases (Dnmts) in Zebrafish Retina Regeneration

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Abstract: Retinal damage is a serious problem that affects mankind. Unfortunately, there are no feasible solutions available to alleviate this problem. However, lower vertebrates like fishes and frogs mount a very robust regenerative response after retinal damage culminating in functional restoration of vision. Previously published studies reveal hundreds of genes that are up/down regulated post injury. It is probable that most of these genes have CpG islands in their corresponding promoter sequences that are susceptible to DNA methylation events by DNA methyltransferases (Dnmts). Such events modify gene expression epigenetically. Therefore it would be interesting to find out how Dnmts are regulated post-retinal injury during retinal regeneration in zebrafish. If so, then we can also try to understand the proliferative genes whose expression and induction are regulated post injury, by Dnmt mediated methylation events. It is also essential to evaluate the functionality of the identified genes in earlier dedifferentiation of the retina using, cell biological, genetic and pharmacological approaches during regeneration. One can also try to address the question of whether or not Dnmt mediated gene regulation is involved/necessary and sufficient for retina regeneration by trying to block the action of Dnmts using pharmacological inhibitors. Epigenetic mode of silencing like DNA methylation may be required for maintaining various pro-proliferative genes in check in the uninjured condition in the retina. A reversal of this by DNA de-methylation is necessary for initiating the Muller glia de-differentiation necessary for normal regeneration. Later once regeneration is completed, the retinal homeostasis is restored back through epigenetic mechanism of gene silencing. So understanding this hierarchy mediated by Dnmts becomes inevitable for these studies. This study tries to answer the above questions. Till date, a specific pathway by which Dnmts acts during retina regeneration is not known, however the proposed study might provide us some directions to understand it.

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