Title:	Understanding Cross-Talk Between Polycomb Repressive Complex 2(PRC2) And Histone Deacetylases (Hdacs) During Zebrafish Retina Regeneration
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Abstract:	“Regeneration—the reactivation of development in later life to restore missing tissues—is so “unhuman” that it has been a source of fascination to humans since the beginnings of biological science.” 1 . Planaria, salamanders, zebrafish, African spiny mice etc. are some of the animals that show remarkable ability to regenerate their body parts. Amongst these, zebrafish is one of the best model organisms to explore regeneration because of its ability to regrow almost all damaged body parts like liver, fin, heart and even the central nervous system (CNS). CNS regeneration is almost nil in mammals, therefore a lot of information can be elucidated by studying regeneration of the retina of zebrafish, one of the most accessible part of its CNS. Signalling pathways like Notch, Mapk–Erk, Jak–Stat pathway etc. have been shown to be turned on in the phases post retinal injury. Epigenetics of zebrafish retina regeneration has been studied mainly in terms of DNA methylation and underexplored in terms of histone modifications. In this study we have explored the crosstalk between Polycomb repressive complex 2(PRC2) and Histone deacetylases (Hdacs) during zebrafish retina regeneration. We found that both PRC2 (Ezh2; its catalytic subunit) and Hdacs affect each other’s expression levels and that combined pharmacological blockade of Ezh2 and Hdacs reduce cell proliferation compared to control and keep it similar to exclusive Hdac blockade. We have shown that Hdacs function predominantly during the de-differentiation phase to keep a check on proliferation whereas Ezh2 plays its role during the pre-proliferative phase of regeneration. During the pre-proliferative phase Ezh2 controls cell proliferation with the help of functional Hdacs. As a preliminary result, we also report that the effects of Ezh2 and Hdacs on proliferation is mediated by regulating the expression of regeneration associated genes like ascl1a and mmp9 and ezh2. Interestingly, at the peak of proliferative phase (4dpi) Ezh2 and Hdac1 were found to physically interact. Hence, this study sheds some light on the roles of two histone modifiers to regulate the proliferative phase of zebrafish retina regeneration.
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