Title:	Epigenome organization during development and regeneration
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Abstract: In the first part, how CTCF-mediated genome architecture is regulating the dosage of mitotically stable mono-allelic expression of autosomal genes is studied. CTCF was found to insulate the domains of assorted mono and bi-allelically expressed genes, and the dosage of mono-allelically expressed genes were more sensitive to CTCF depletion. Also, after CTCF depletion there was alteration in TAD insulation of inactive alleles of mono-allelic genes. To confirm this, single molecule nascent RNA-FISH experiments on candidate MAE genes in CTCF-AID mESCs were performed. These genes showed significant switch from mono-to bi- allelic expression after CTCF depletion. So via multiple lines of analyses, it is established that CTCF insulated and maintained repressive transcriptional states of inactive alleles of MAE genes, highlighting an allele-specific regulatory role of CTCF. Vision is important to connect us with our surroundings. Various traumatic injuries or diseases of the mammalian retina often lead to irreparable blindness. On the other hand, teleost fish such as zebrafish have remarkable retina regeneration capacity which is mainly because of one retinal cell type-the Muller glia (MG) that is present in all vertebrate retinas. In response to retinal injury, Muller glia undergo reprogramming into progenitor cells that exhibit stem-cell characteristics, proliferate and re-differentiate into all retinal cell types and restore vision. In the second part, the roles of Ezh2 and H3K27me3 during zebrafish retina regeneration were elucidated. Enhancer of zeste homolog 2 (Ezh2) is a catalytic subunit of polycomb repressive complex 2 (PRC2) which helps in the catalysis of H3K27me3 repressive modification via a canonical pathway. Many reports suggest that Ezh2 also plays a critical role in cancer progression by working as a transcriptional co-activator via non-canonical pathways, independent of H3K27me3 function. Thus, the role of Ezh2 and H3K27me3 during zebrafish 3retina regeneration was investigated. In this study, both canonical and non-canonical pathways of Ezh2 during zebrafish retina regeneration were explored. It is found that Ezh2 gets upregulated post retinal injury and is present in Muller glial progenitor cells (MGPCs). Ezh2 is very critical for Muller glial cell proliferation because its pharmacological inhibition and morpholino-mediated knockdown lead to a decline in proliferation. Canonical role of Ezh2 along with PRC2 complex is to write H3K27me3 modification. In the exploration of canonical roles of Ezh2 the H3K27me3 modification and its connection with CTCF was studied. Also, Ezh2 is playing a critical role in MG reprogramming and formation of progenitors by the suppression of Wnt antagonists and also by regulating the PTEN-Akt pathway. This study identifies Ezh2 as a key regulator of retina regeneration, working mechanistically via Wnt/b- Catenin and PTEN-Akt pathway. In the third part, the role of CTCF and genome architecture during zebrafish retina regeneration was explored. CTCF was found to be downregulated post retinal injury and significantly declined in MGPCs. Its knockdown led to a decline in proliferation of MGPCs and was found to affect reprogramming events of regeneration. Further the 3D genome architecture of retina was explored using Hi-C technique to understand how chromatin interactions change during the zebrafish retina regeneration.

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