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Title: Elucidating the Role of Histone Demethylases underlying tissue regeneration in zebrafish

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Abstract:

Zebrafish possess tremendous regenerative potential compared to mammalian counterparts and are able to regenerate and restore their various tissue structures, such as the retina and caudal fin. This regeneration potential is attributed to specialized cells known as progenitor cells which undergo reprogramming in the mass of proliferating cells and restore lost tissue. Reprogramming of a cell requires precise gene regulation as lineage-specific genes must be turned off to change the identity of the cell to a progenitor cell. This regulation is achieved by the activity of various Epigenetic regulators, which modify histone proteins and, in turn, regulate the transcription of genes. Epigenetic eraser removes the active modification on chromatin and thus influences transcription. Kdm1a encodes for Lsd1, which is a methyl group eraser, and erases methyl modification on H3K4 and H3K9 on histones. H3k4me3 is an active mark, while H3k9me3 is a repressive modification, so the activity of Lsd1 on these sites is repressive and activating in nature.Lsd1 is abundantly expressed in Neural tissues as seen by whole mount In-situ hybridization, and upon inhibition by irreversible drug (Gsk-Lsd1), we observe various developmental defects in the developing embryo, particularly the majority of the defects are observed in the spinal cord, which indicates towards the importance of Lsd1 activity in neural tissues. We also observe a reduction in blastema formation and Muller glial progenitors cell population in the caudal fin and retina upon injury upon inhibition of LSd1 activity, which suggests a Pro-proliferative role of Lsd1 activity during the regeneration process in tissue upon injury.Further, to access how Lsd1 controls Reprogramming and proliferation in progenitor cells, we are currently developing a transgenic line where the Kdm1a promoter will drive the expression of GFP(Kdm1a:eGFP).

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