



Epigenetic complexes and Notch signaling dynamics in intestinal stem cell plasticity

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ABSTRACT

Intestinal stem cells (ISCs) are crucial for the maintenance and repair of the intestinal epithelium. Their dysregulation is a key factor in the development of various diseases, including cancer and inflammatory bowel disease. We have recently shown that the epigenetic Polycomb Repressive Complex 2 is essential for the proliferative capacity of ISCs in *Drosophila* [1]. Specifically, loss of the catalytic subunit Enhancer of zeste (E(z)), induces premature differentiation of ISCs into enterocytes, a phenotype that requires hyperactivation of Notch signaling. In contrast, increased differentiation to enteroendocrine cells was observed upon loss of Trithorax (trx), the founding member of the activating Trithorax group of genes (TrxG), that antagonizes the repressive Polycomb group of genes (PcG). Following comparative transcriptome analysis, a subset of E(spl)-HLH Notch target genes, was found to be expressed at higher levels in ISCs with reduced levels of trx. These results propose a link connecting epigenetic modifications and Notch signaling. Further elucidation of the molecular mechanisms involved is essential for developing new approaches to promote intestinal health during life.

REFERENCES

[1] Veneti Z, Fasoulaki V, Kalavros N, Vlachos IS, Delidakis C, Eliopoulos AG. Polycomb-mediated silencing of miR-8 is required for maintenance of intestinal stemness in *Drosophila melanogaster*. *Nat Commun*. 2024 Mar 2;15(1):1924.