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Regulatory Noncoding RNA Mediated Alterations and its Effects in Stem Cell Derivatives

Abstract

The versatility of human induced pluripotent stem cells (iPSCs) to self-renew and differentiate into three germ layers makes them invaluable for regenerative therapy. However, certain differentiated derivatives of pluripotent stem cells exhibit oncogenic characteristics, limiting their regenerative potential. This phenomenon may be attributed to dysregulation in gene expression, particularly at the transcriptional level, mediated by small regulatory noncoding RNAs (rncRNAs) such as microRNAs (miRNAs) and PIWI-interacting RNAs (piRNAs).

Main focus of my thesis lies on understanding how miRNAs influence the gene expression landscape in iPSC derivatives, particularly in driving cells towards an oncogenic state. The study utilized both computational (in silico) and experimental (wet lab) approaches to identify key miRNAs involved in this process, thereby unraveling the miRNA mediated molecular mechanisms underlying oncogenic transformation in iPSC derivatives corresponding to any of the three germ layers as well as irrespective of the reprogramming methods used to generate their parental iPSCs.

Additionally, the study involved updating and expanding the knowledge base on piRNAs through the development of piRNAQuest V.2. It provided valuable insights regarding tissue specific piRNAs as well as their involvement in different disease systems. Further, this information served as the backbone to explore the role of piRNAs in differentiating iPSCs towards endothelial lineage. Overall, my work aimed to deepen our understanding of how small regulatory ncRNAs, particularly miRNAs and piRNAs, contribute to transcriptional regulation and influence the fate of stem cell derivatives. By elucidating these intricate regulatory networks, the study aimed to pave the way for safer and more effective stem cell-based regenerative therapies.

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