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Micro RNA's As Stemcell Regulators And Therapeutic Targets

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Abstract: ***MicroRNA's play a pivotal role in regulating various functions of the body inclusive of regulating stem cells. This ability of MicroRNA to regulate various functions can be exploited to develop therapeutic modalities for various disease conditions. Understanding the pathophysiology of microRNA is important for the same. Thus, this article deals with elaborating the role of microRNA's as stem regulators and therapeutic targets.***

The hallmark of a stem cell is its capability to self-renew and to produce differentiated cells. This property of these stem cells is controlled by active interplays between extrinsic signaling, epigenetics and transcriptional regulations. Recent research indicates that microRNAs (miRNAs) have an important role in regulating stem cell self-renewal and differentiation by repressing the translation of selected mRNAs in stem cells and differentiating daughter cells. Such a role has been shown in embryonic stem cells, germ line stem cells and various somatic tissue stem cells inclusive of cardiovascular cells. These findings reveal a new dimension of gene regulation in controlling stem cell fate and behavior.(1)

The concept of self-renewal holds good when a stem cell generated one (asymmetric division) or two (symmetric division) daughter cells that tends to have similar developmental potential as the parent cell. The property of stem cell to self-renew themselves depends upon various factors inclusive of epigenetic programs and stem cells. The rate at which this happens depends upon the type of stem cell. Embryonic stem (ES) cells are cell lines derived from the inner cell mass of a developing blastocyst. These cells can self-renew and rapidly multiply thereby leading to production of large amount of tissue for tissue replacement.(2)

miRNAs are scattered throughout the genome. They can be found as isolated transcript units or can be clustered and co-transcribed as polycistronic primary transcripts.(3) In addition to the roles of miRNAs in controlling stem cell differentiation, which have become increasingly well established, several new twists have emerged in the miRNA world. Among them is the notion that miRNAs function in injury or stress situations. Micro RNAs have also been implicated in the regulation of stem cell aging. One such parameter is regulation of Stem cell reprogramming which is another key factor which determines the extent to which this differentiation process can take lead. It is divided into three phases; Initiation, Maturation and Stabilization. Where the initiation phase is controlled by miR-200 family (miR-200b and miR-200c), the miR-106a-363 and miR-302-367 cluster, and miR-93/ 106b. Also, down-regulated miR-30/let-7 family along with up-regulated miR-17, miR-19, miR-290, and miR-8 family miRNAs play important roles in the activation and maintenance of pluripotency.(4)

As stated earlier these microRNA's play a pivotal role in maintaining and regulating various functional aspects of the body there by providing a wider chance to exploit their purpose as therapeutic targets. Opting micro-RNA's as therapeutic Targets can lead to either development of miRNA antagonists or miRNA mimics. Whereas antagonist can lead to inhibiting the miRNAs that cause Disease while mimics can restore the amount of microRNA's lost to contract the disease mechanism. (5)

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The two-striated muscle specific miRNAs that are widely conserved and increasingly expressed in adult heart are miR-1 and miR-133a.Two MADS-box transcription factors, myocyte enhancer factor -2 (MEF2) and serum response factor (SRF) directly regulate the cardiac transcription of miR-1/miR-133a pairs. (6) Adult heart undergoes hypertrophic change which can be physiologic or pathologic in nature. Pathologic hypertrophic condition validates presence of various microRNA's in it. Among which frequently reported to be upregulated includes miR-208, miR-21, miR-125, miR-129 and miR-195, whereas miR-1, miR-133, miR-29, miR-30 and miR-150 is often found to be downregulated. (7)

Innovative MicroRNA-based theraupetic approaches have reached the current state of affairs which is an LNA-modified antimiRNA directed against the liver-specific miRNA miR-122, which is required for replication of the hepatitis C virus (HCV). miR-122. Since most of the mi-RNA's are beneficial rather than pathogenic developing drugs is widely studied. Despite these uncertainties and given the pace of this field, it seems more likely that few of the uncountable miRNAs implicated in cardiovascular disease will emerge as viable biomarkers and drug targets as well as enabling unveiling the mechanisms of various diseases.(8)

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