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MicroRNA engineering improved therapeutic function of human mesenchymal stem cells

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Mesenchymal Stem Cells (MSCs) are attractive sources for cell therapy. However, MSCs have limited expansion capacity. Cellular senescence induced by long-term culture results in the loss of self-renewal property and disrupts their therapeutic functions. MicroRNAs (miRNAs) have been demonstrated as crucial regulators of senescence. In this study, we identified the core miRNA that regulated self-renewal of MSCs from human Umbilical Cord (UC). By a high-throughput deep sequencing, we first investigated the miRNA expression changes of UCMSCs, after a long-term ex vivo expansion. We found the expression of miR-18a was markedly down-regulated in late passaged UCMSCs. To verify miR-18a's role in preventing senescence, we performed a knock down and overexpression analysis. Inhibition of miR-18a blocked the cell cycle process, repressed expression of "stem genes" including Oct4 and Nanog, and induced expression of senescence marker. Moreover, enforced expression of miR-18a promoted expression of Oct4 and Nanog and prevented senescence. Bioinformatics analysis identified CTDSPL and VEGFB as putative targets of miR-18a. Western blot and reporter assay confirmed miR-18a inhibited CTDSPL expression by binding its 3'UTR site. Furthermore, miR-18a improved VEGFB expression by targeting its promoter region. Finally, we designed a lentivirus vector to stably express miR-18a in MSCs. MSCs with stably expressed miR-18a had improved proliferation ability and differentiation potential. Taken together, these findings suggested that the expression of miR-18a is crucial for maintaining self-renewal of human MSCs.

Biography

Xianhui Meng is a Doctoral student of Southeast University, China. His research interest is microRNA's regulatory role in cellular senescence, self-renewal and therapeutic function of human mesenchymal stem cells.

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