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Topological analysis of regulatory networks reveals functionally key genes and miRNAs involved in the differentiation of mesenchymal stem cells

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Abstract

Background: The details of molecular mechanisms underlying the differentiation of Mesenchymal Stem Cells (MSCs) into specific lineages are not well understood. Objectives: We aimed to construct the interactome network and topology analysis of bone marrow mesenchymal stem cell of CAGE data. Applying the enrichment results, we wanted to introduce the common genes and hub-microRNA and hub-genes of these giant network. Materials and Methods: In this study, we constructed gene regulatory networks for each non-mesenchymal cell lineage according to their gene expression profiles obtained from FANTOM5 database. The putative interactions of TF-gene and protein-protein were determined using TRED, STRING, HPRD and GeneMANIA servers. In parallel, a regulatory network including corresponding miRNAs and total differentially expressed genes (DEGs) was constructed for each cell lineage. Results: The results indicated that analysis of networks' topology can significantly distinguish the hub regulatory genes and miRNAs involved in the differentiation of MSCs. The functional annotation of identified hub genes and miRNAs revealed that several signal transduction pathways i.e. AKT, WNT and TGFβ and cell proliferation related pathways play a pivotal role in the regulation of MSCs differentiation. We also classified cell lineages into two groups based on their predicted miRNA profiles. Conclusions: In conclusion, we found a number of hub genes and miRNAs which seem to have key regulatory functions during differentiation of MSCs. Our results also introduce a number of new regulatory genes and miRNAs which can be considered as the new candidates for genetic manipulation of MSCs in vitro.

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Keywords

Differentiation, MiRNA, MSCs, Regulatory network, Topological analysis

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