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EDITORIAL
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Editorial: Epigenetic Regulation of Stem Cells Derived From Craniofacial Tissues

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Editorial on the Research Topic

Epigenetic Regulation of Stem Cells Derived From Craniofacial Tissues

The function regulation of mesenchymal stem cells (MSCs) is a complex process, and the effects of the directed differentiation of mesenchymal stem cells and the craniofacial tissue regeneration under micro-environmental conditions such as inflammation, hypoxia and aging are not clear, in which epigenetics plays a significant role (1). In this special topic, we have included seven articles that reviewed recent progress in epigenetic regulation of stem cells derived from craniofacial tissues.

Li et al. summarized epigenetic influence on stem cells derived from dental tissues (DSCs). They discussed the important role of epigenetics in odontogenic/osteogenic differentiation of DSCs, DNA methylation, histone modifications, histone acetylation and non-coding RNAs are emphatically introduced. Further, Li illustrated epigenetics affects the odontogenic and osteogenic differentiation of DSCs by regulating signaling pathways.

Han and Fan review of the recent work on the relationship of miRs and osteogenic differentiation of mesenchymal stem cells. MicroRNAs are broadly expressed and involved in stem cell renewal, differentiation, cell cycle and cell apoptosis and other biological processes. miRNAs generally act as an inhibitory molecule by post-transcriptional targeting downstream genes, leading to translational inhibition or mRNA decay. In this review, Fan et al. summarized targeting osteogenic genes regulated by miRNA, in which the major osteogenic transcription factors RUNX2 and OSX were described in detail. Then the authors discussed the influence of miRNAs on the expression levels of Wnt signaling pathway, TGF-β/BMP signaling pathway, MAPK signaling pathway and Notch signaling pathway, which regulate osteogenic differentiation.

Microenvironment also play critical roles in tissue regeneration. Li et al. discussed immune microenvironment and bone regeneration process in oral and maxillofacial region. Bone is composed of osteoblasts, osteoclasts, osteocytes, and other basic elements. Bone resorption and bone formation are largely regulated by a variety of immune responses under normal and pathogenic conditions. In addition to the traditional bone cells, immune cells containing neutrophils, B cells, macrophages and T cells, were also implicated in remodeling of bone. Therefore, interaction between local stem cells and immune cells in the oral microenvironment may modify the regenerative process. Cytokines are derived from immunocompetent cells such as TNFα, IL-1, IL-6 and interferon-γ (IFN-γ). At last, Yu revealed the effects of these inflammatory cytokines on both osteoclasts (OC) and osteoblasts.

Hypoxia is an important cellular stress mechanism with significant pathological implications in numerous diseases. Ye et al. also discussed that tissue regeneration is modulated by different Non-coding RNAs (ncRNAs) in hypoxia. They summarized the effects of hypoxia on the proliferation and differentiation potential of odontogenic MSCs, and also pointed out the results are uncertain

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due to the differences of cell sources and experimental conditions. The authors further discussed the effect of hypoxia-induced ncRNAs on differentiation of mesenchymal stem cells. Studies of ncRNAs and their interaction can promote or reverse the effects of hypoxia microenvironment on MSCs, and provide good conditions for better modified stem cells for *in vivo* transplantation.

In addition, ncRNAs derived from extracellular vesicle has become the focus of cell-to-cell communication, which play an essential role in regulating different biological processes. Yan et al. reviewed the research progress of extracellular vesicle (EV) secreted by MSCs (MSC-EVS) in tooth and maxillofacial tissue repair and regeneration. They reviewed the achievement and methodology of EV derived ncRNA. They discussed the expression of ncRNA in EV cells from different MSCs and cell modification triggers EV transfer of ncRNAs. Emerging evidence confirmed that EV-derived ncRNA can efficiently modulate the differentiation of MSC. These EV derived non-coding RNAs have the potential to be used as drug vehicle.

MSCs are promising candidates for cellular therapy of different diseases in humans and in animals. Zhang et al. reviewed the literature on stem cell therapy in chronic periodontitis and summarized limitations from the host and coping strategies that influence resident or transplanted stem cell-mediated periodontal regeneration. PDLSCs have been proved to possess the periodontal regenerative property *in vitro* and animal studies, however the clinical application of autologous PDLSCs to treat periodontal intrabony defects is not satisfactory, which indicates continuous inflammation in the periodontal tissue induces functional impairments of endogenous P-PDLSCs. The prerequisite for stem cell therapy in chronic periodontitis is the improvement of local stem cell niche. Small molecular drugs, herbal extracts, and accessory extracellular vesicle products, can effectively improve the extracellular environment and promote stem cell function. And they also mentioned that active treatments for systemic diseases would also assist in recovering the limited stem cell function on the basis of amelioration of the inflammatory periodontal microenvironment.

Another type of MSCs that have been broadly mentioned is stem cells derived from human exfoliated deciduous teeth. Guo et al. state the multipotency of SHEDs in their review, presenting the immense potential for tissue regeneration engineering. And they emphatically introduce the paracrine activity and immunomodulatory of SHEDs, it can interact with the local inflammatory microenvironment through multiple paracrine functions, and the modulatory functions of SHEDs-CM or SHED-EVs to immunocyte have been proved as well. All these biological properties indicate SHEDs will be widely used in clinical application in regenerative medicine.

AUTHOR CONTRIBUTIONS

ZF: design and conception, manuscript writing, manuscript revising, financial support, final approval of the manuscript, and approved publication.

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