

Does DNA Methylation Plays a Critical Role in Osteoblastic Differentiation of Mesenchymal Stem Cells (MSCs)?

Najmaldin Saki¹, Majid Farshdousti Hagh^{2,*}, Esmaeil Mortaz³, Abdolreza Ardeshiry Lajimi⁴

¹Research Center of Thalassemia and Hemoglobinopathy, Jundishapur University of Medical Sciences, Ahvaz, IR Iran

²Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, IR Iran

³Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, Netherlands

⁴Young Researchers Club, Science and Research Branch, Islamic Azad University, Tehran, IR Iran

*Corresponding author: Majid Farshdousti Hagh, Hematology and Oncology Research Center, Tabriz University of Medical Sciences, Tabriz, IR Iran, Tel: +98-4113364665, Fax: +98-4113364665, E-mail: m.farshdousti@gmail.com.

Received: February 27, 2012; **Revised:** January 16, 2013; **Accepted:** Jun 14, 2013

Keywords: Mesenchymal Stromal Cells; Cell Differentiation; Osteoblastic

Dear Editor,

Mesenchymal stem cells (MSCs) are characterized by ability to differentiate into several cell types and self-renewability. These stem cells have a limited capacity in cell lineage differentiation including osteogenic, adipogenic, chondrogenic, or myogenic lineage differentiations (1). Regarding their ease of isolation and specific characteristics, MSCs have been used widely in regenerative medicine and tissue engineering (2). In spite of identification of several signaling molecules in MSCs differentiation, controlling mechanisms in MSCs differentiation has not well been described. Recently, epigenetic mechanisms have been identified as the master regulatory mechanism in MSCs differentiation such as DNA methylation, histone modification and regulatory micro RNAs (2-4). In this report, we investigate DNA methylation status of ROR2 gene in osteoblastic differentiation of MSCs. We also show that ROR2 promoter was hypomethylated during osteoblastic differentiation for which the details can be found in Noruzinia et al. (5); While other important osteoblastic specific genes did not evaluate. RUNX2 and OSX are two of the most known osteoblast specific transcription factors (6, 7). However, several other non-osteoblast specific transcription factors have been identified to control osteoblast differentiation, including TWIST1 (twist homolog 1), ZBTB16 (zinc finger and BTB domain containing 16), DLX5 and MSX2 (MSH homeobox homolog 2) (8, 9). Therefore, we suggest that those genes (such as RUNX2 and OSX) could be considered as a subject for future investigations.

Besides, it can be postulated that osteoblastic differentiation of MSCs may be influenced by mechanisms other than DNA methylation (10). Therefore, we suggest that other epigenetic mechanisms including histone modification and regulatory micro RNAs regarded in osteoblastic differentiation of MSCs could be considered for future studies.

Acknowledgements

None declared.

Authors' contribution

None declared.

Financial Disclosure

There is no financial disclosure.

Funding Support

There is no funding or supports.

References

1. Saki N, Abroun S, Farshdousti Hagh M, Asgharei F. Neoplastic Bone Marrow Niche: Hematopoietic and Mesenchymal Stem Cells. *Cell J.* 2011;**13**(3):131-6.
2. Caplan AI. Mesenchymal stem cells and gene therapy. *Clin Orthop Relat Res.* 2000;(379 Suppl):S67-70.
3. Boquest AC, Noer A, Sorensen AL, Vekterud K, Collas P. CpG methylation profiles of endothelial cell-specific gene promoter regions in adipose tissue stem cells suggest limited differentiation potential toward the endothelial cell lineage. *Stem Cells.* 2007;**25**(4):852-61.

Implication for health policy/practice/research/medical education:

This article discusses the role of DNA methylation in osteoblastic differentiation of mesenchymal stem cells.

Copyright © 2013, Iranian Red Crescent Medical Journal; Licensee KowsarKowsar Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

4. Aranda P, Agirre X, Ballestar E, Andreu EJ, Roman-Gomez J, Prieto I, et al. Epigenetic signatures associated with different levels of differentiation potential in human stem cells. *PLoS One*. 2009;**4**(11).
5. Tarfiei G, Noruzinia M, Soleimani M, Kaviani S, Mahmoodinia Maymand M, Farshdousti Hagh M, et al. ROR2 Promoter Methylation Change in Osteoblastic Differentiation of Mesenchymal Stem Cells. *Cell J*. 2011;**13**(1):11-8.
6. Nakashima K, Zhou X, Kunkel G, Zhang Z, Deng JM, Behringer RR, et al. The novel zinc finger-containing transcription factor Osterix is required for osteoblast differentiation and bone formation. *Cell*. 2002;**108**(1):17-29.
7. Gollner H, Dani C, Phillips B, Philipsen S, Suske G. Impaired ossification in mice lacking the transcription factor Sp3. *Mech Dev*. 2001;**106**(1-2):77-83.
8. Harada S, Rodan GA. Control of osteoblast function and regulation of bone mass. *Nature*. 2003;**423**(6937):349-55.
9. Holleville N, Mateos S, Bontoux M, Bollerot K, Monsoro-Burq AH. Dlx5 drives Runx2 expression and osteogenic differentiation in developing cranial suture mesenchyme. *Dev Biol*. 2007;**304**(2):860-74.
10. Bradley EW, McGee-Lawrence ME, Westendorf JJ. Hdac-mediated control of endochondral and intramembranous ossification. *Crit Rev Eukaryot Gene Expr*. 2011;**21**(2):101-13.