

Potential of Integration-free Induced Pluripotent Stem Cells in Musculoskeletal Regeneration

Potencial de Células Madre Pluripotentes libres de integración en la regeneración músculo-esquelética

Wan-Ju Li¹

¹ Laboratory of Musculoskeletal Biology and Regenerative Medicine, Department Orthopedics and Rehabilitation, University of Wisconsin-Madison, USA. Email: li@ortho.wisc.edu

Abstract

Stem cell therapies hold promise for the treatment of musculoskeletal disorders. Mesenchymal stem cells (MSCs) derived from adult tissues are the most common type of stem cells being investigated for biomedical applications among all stem cell types. However, studies have shown that MSC properties and functions are largely affected by age and health condition of the donor, which often causes inconsistency in therapeutic outcomes. This is a critical challenge that needs to be addressed before the promise of stem cells for therapies can be fulfilled. Our group has worked on tackling the challenge for more than a decade by developing strategies such as priming the cell with regulatory molecules or hypoxia culture. Recently, we successfully reprogrammed human and pig somatic cells into induced pluripotent stem cells (iPSCs) using the integration-free episomal method and subsequently derived MSCs from iPSCs for evaluation of potential orthopedic applications. Our study results showed that through cellular reprogramming the capacity of cell propagation and multilineage differentiation of MSCs was greatly enhanced and the expression of aging-associated markers in the cell was significantly downregulated, suggesting that cellular reprogramming can rejuvenate MSCs to increase the regenerative capability, and our approach converting MSCs into iPSCs is promising for addressing the challenge of reduced therapeutic potential associated with MSC aging. In addition, we found that during chondrogenic induction reprogrammed MSCs increasingly differentiated into hyaline chondrocytes expressing cartilage-specific markers, compared to control parental cells, suggesting that iPSC-derived MSCs are promising therapeutic agents for articular cartilage regeneration. In general, our findings highlight the potential of iPSCs in better understanding aging-associated musculoskeletal disorders and providing biological options for the treatment.

References

Li, W.J., Jiao, H. & Walczak, B.E. 2019. Emerging opportunities for induced pluripotent stem cells in orthopedics. *J. Orthop. Translat.* 17: 73-81. DOI: 10.1016/j.jot.2019.03.001