

INDUCED MESENCHYMAL STEM CELLS AS A NEXT-GENERATION THERAPEUTIC TOOL IN REGENERATIVE MEDICINE

Marta Kot

Department of Transplantation, Institute of Pediatrics, Faculty of Medicine, Jagiellonian University Medical College, Kraków, Poland

Mesenchymal stem cells (MSCs) represent a promising tool for regenerative medicine due to their multipotent differentiation capacity and immunomodulatory properties. Induced mesenchymal stem cells (iMSCs), derived in vitro from induced pluripotent stem cells (iPSCs), offer a reproducible and scalable alternative to tissue-derived MSCs. The ability to standardize their generation and ensure cellular homogeneity makes iMSCs an increasingly attractive option for clinical applications.

In this study, iMSCs were differentiated from commercial human iPSCs and evaluated for their morphological, immunophenotypic, and functional properties. The cells displayed a typical fibroblast-like morphology and expressed key mesenchymal markers CD73, CD90, and CD105 (>99%), while lacking hematopoietic markers CD3 and CD45. They demonstrated the capacity for trilineage differentiation and did not show signs of senescence (SA- β -Gal assay), maintaining high proliferative potential.

A key aspect of the study was high-throughput transcriptomic profiling (RNA-seq) to assess gene expression and cellular identity. Over 11,400 active genes were identified in iMSCs, including 395 uniquely expressed in iMSCs, 420 shared with iPSCs, and 1,072 overlapping with tissue-derived MSCs. Differential gene expression analysis confirmed high similarity to classical MSCs, and clustering analyses demonstrated high reproducibility across independently derived iMSC lines. Genes upregulated in iMSCs were associated with tissue regeneration (e.g., LRRN1, PAX3), immune response (e.g., TRIML2, RUNX3), extracellular matrix remodelling (e.g., MMP9), and lineage specification (e.g., NKX6-1, DLX1). Functional enrichment analysis revealed significant activity in biological pathways including chemotaxis, adhesion, angiogenesis, and ERK1/2 kinase signalling, critical to tissue repair, self-renewal, cell survival, and morphogenesis.

The obtained iMSCs meet International Society for Cell Therapy (ISCT) criteria and exhibit a stable molecular profile with therapeutic potential. The ability to derive iMSCs from patient-specific iPSCs enables a scalable, standardized, off-the-shelf, and personalized cell source for regenerative medicine and advanced cell-based therapies.

Acknowledgements: This study was supported by research grant K/MNT/000260 from National Science Centre.