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iPSZÜRICH

A Lecture Series Focused on Induced Pluripotent Stem Cells

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iMSC: DERIVATION, CHARACTERIZATION AND APPLICATION IN REGENERATIVE MEDICINE

MSCs isolated from both fetal (fMSCs) and adult (aMSCs) tissues adhere to plastic, express the cell surface markers- CD44, CD90, CD105, CD106, CD166, and Stro-1, lack the expression of hematopoietic markers, and can be differentiated into osteogenic, adipogenic, and chondrogenic lineages in vitro. However, transcriptome analysis identified overlapping and distinct gene expression patterns and revealed that fMSCs express more genes in common with pluripotent stem cells than with aMSCs.

Pluripotent stem cell-derived MSCs (iMSCs) from embryonic stem cells (ESCs-H1) and iPSCs (derived from dermal fibroblasts and MSCs isolated young and elderly individuals) met the criteria set out for MSCs by the International Society for Cellular Therapy. Furthermore, dendrogram analyses confirmed that the transcriptomes of all iMSCs (irrespective of cell source) clustered together with the parental MSCs and distinct from pluripotent stem cells.

iMSCs acquired a rejuvenation-associated 50-gene signature (eg, *INHBE, DNMT3B, POU5F1P1* and *CDKN1C*) which are also expressed in pluripotent stem cells but not in the parental MSCs. Significantly, in terms of regenerative medicine, iMSCs acquired a secretome similar to that of primary MSCs, thus highlighting their ability to act via paracrine signalling.

The iMSC concept has enabled circumventing the drawbacks associated with the properties of aMSCs (limited expansion and early senescence) and thus provide a promising tool for use in various clinical settings. As an example, we investigated the bone regeneration potential of HFF-iMSCs (iPSCs derived from human fetal foreskin fibroblasts) combined with calcium phosphate granules (CPG) in critical-size defects in the proximal tibias of mini-pigs in the early phase of bone healing compared to treatment with a composite made of either a combination of autologous bonemarrow-derived MSC and CPG or CPG alone. Transplanted iMSCs survived at the site of injury. As confirmed by radiology and histo-morphometry, HFF-iMSC + CPG transplantation resulted in significantly better osseous consolidation than the transplantation of CPG alone and produced no significantly different outcomes compared to the transplantation of autologous MSCs + CPG after 6 weeks. The results of this translational study imply that iMSCs represent a valuable future treatment option for load-bearing bone defects in human.

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