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HUMAN INDUCED PLURIPOTENT STEM CELL-DERIVED MESCENCHYMAL STEM CELLS ARE SUPERIOR TO ADULT BONE MARROW-DERIVED MESCENCHYMAL STEM CELLS IN THE TREATMENT OF LIMB ISCHEMIA

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Background: Aging and aging-related disorders impair the survival and differentiation potential of bone marrow mesenchymal stem cells(BM-MSCs) and limit their therapeutic efficacy. Induced pluripotent stem cells(iPSCs) may provide an alternative source of functional MSCs for tissue repair. This study aimed to generate and characterize human iPSC-derived MSC and to investigate their biological function for the treatment of limb ischemia.
Methods and Results: Human iPSCs were induced to MSC differentiation using a clinically compliant protocol. Three monoclonal, karyotypically stable and functional MSC-like cultures were successfully isolated using a combination of CD24- and CD105+ sorting. They did not express pluripotent-associated markers, but displayed MSC surface antigens and differentiated into adipocytes, osteocytes and chondrocytes. Transplanting iPSC-MSCs into mice significantly attenuated severe hind-limb ischemia and promoted vascular and muscle regeneration. The benefits of iPSC-MSCs on limb ischemia were superior to those of adult BM-MSCs. The greater potential of iPSC-MSCs may be attributable to their superior survival and engraftment following transplantation to induce vascular and muscle regeneration via direct de-novo differentiation and paracrine mechanisms.
Conclusion: Functional MSCs can be clonally generated, beginning at a single cell level, from human iPSCs. Compared to adult bone marrow derived MSCs, transplanting iPSC-MSCs into mice achieved a better beneficial effect in attenuation of severe limb ischemia. Our study provides a proof-of-concept that functional MSCs can be generated from human iPSC and used to treat ischemic disease in a patient-specific, cost-effective and batch-to-batch consistent manner.