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Evaluating the right source of Mesenchymal Stem cells for Clinical application in osteoarthritis and bone defects

Mesenchymal stem cells (MSCs) are primordial cells of mesodermal origin and are involved in formation of connective tissues throughout the body. Their inherent ability to differentiate into cells of chondrogenic and osteogenic lineage have made them emerge as a candidate cell type with great potential for cell-based articular cartilage repair technologies. MSCs can be isolated from a variety of adult tissues, readily culture-expanded without losing their multilineage differentiation potential, and have been induced to undergo chondrogenic and osteogenic differentiation in vitro and in vivo. Cellular therapy or cell based repair strategies are proposed to be the next generation medicine for osteoarthritis and cartilage repair. Chondrocytes were primarlily considered to be the first choice of cellular treatment as they are involved in the pathology of the disease. Chondrocytes , although have shown clinical efficiency in clinical applications, the destructive harvest protocol, poor proliferation and time-delay associated with autologous expansion before use, have set a limiting barrier. Evidence suggests that cell aging is important and a crucial factor in the pathogenesis of osteoarthritis. In addition to severe changes that occur in the extracellular matrix, the chondrocytes have also shown to display abnormalities during degeneration which include inappropriate activation of anabolic and catabolic activities, and alterations in cell numbers. The transplanted chondrocytes might still suffer the same fate as that of the native chondrocytes due to the diseased milieu present.

Not only OA chondrocytes, even autologous mesenchymal stem cells from patients with osteoarthritis show differential gene expression pattern. This could be due to their prolonged endurance in the diseased milieu. There are evidences to suggest the decline in potency of the autologous mesenchymal stem cells from OA patients attributable to age and senescence of the cells. These data warrants the characterization of autologous MSCs and chondrocytes before usage on individual basis before taking them to the clinical application.

Considering the above mentioned points, the most viable method could be to use an allogeneic source that provides non-affected, highly efficient and differentiation-capable cells. In a study, therapeutic efficacies between MSCs from cord blood (CB-MSCs) and bone marrow (BM-MSCs) on OA treatment was evaluated. The CB-MSCs showed a markedly higher chondrogenic potential and relatively lower osteogenic and adipogenic capacities than BM-MSCs. During chondrogenesis, the committed CB-MSCs also showed significant increases in cell proliferation, adhesion molecules, signaling molecules, and chondrogenic-specific gene expressions. This data demonstrates that CB-MSCs possess specific advantages in cartilage regeneration over BM-MSCs. The CB-MSCs showed a better therapeutic potential that can contribute to advanced cell-based transplantation for clinical OA therapy. Other sources like Adipose derived MSCs, need to be run through a detailed evaluation for their efficiency in ortho-indications.

Although there were numerous studies supporting the need for allogeneic source of stem cells to substitute the age-related malfunctioning of endogenous MSCs, there were also a few studies that suggest there are no such inverse relationship between age and MSC number. Given the efficacy of UC/ CB -MSCs which is in par with autologous MSCs, if not superior, would be the most feasible and efficient source of “Off-the-Shelf” cellular product for orthopaedic- indications.

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