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Clinical Application of Bone Marrow Mesenchymal Stem/Stromal Cells to Repair Skeletal Tissue

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Abstract

There has been an escalation in reports over the last decade examining the efficacy of bone marrow derived mesenchymal stem/stromal cells (BMSC) in bone tissue engineering and regenerative medicine-based applications. The multipotent differentiation potential, myelosupportive capacity, anti-inflammatory and immune-modulatory properties of BMSC underpins their versatile nature as therapeutic agents. This review addresses the current limitations and challenges of exogenous autologous and allogeneic BMSC based regenerative skeletal therapies in combination with bioactive molecules, cellular derivatives, genetic manipulation, biocompatible hydrogels, solid and composite scaffolds. The review highlights the current approaches and recent developments in utilizing endogenous BMSC activation or exogenous BMSC for the repair of long bone and vertebrae fractures due to osteoporosis or trauma. Current advances employing BMSC based therapies for bone regeneration of craniofacial defects is also discussed. Moreover, this review discusses the latest developments utilizing BMSC therapies in the preclinical

and clinical settings, including the treatment of bone related diseases such as Osteogenesis Imperfecta

Tomography
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Enhancement of Radiotherapy with Human Mesenchymal Stem Cells Containing Gold Nanoparticles

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Abstract

Radiotherapy is a common approach for the treatment of a wide variety of cancer types. Available data indicate that nanoparticles can enhance the effect of radiotherapy. We report the use of human mesenchymal stem cells to selectively deliver gold nanoparticles (GNPs) to MDA-MB-231 breast tumor xenografts in mice for the purpose of enhancing the effect of radiation therapy. Targeted delivery of GNPs to the tumor site, followed by irradiation of the tumor, enabled control of tumor growth. The results indicate that tumor-selective GNP delivery by human mesenchymal stem cells may represent a viable way to enhance the effectiveness of radiotherapy.

Front Immunol
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Tolerance to Bone Marrow Transplantation: Do Mesenchymal Stromal Cells Still Have a Future for Acute or Chronic GvHD?

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Abstract

Mesenchymal Stromal Cells (MSCs) are fibroblast-like cells of mesodermal origin present in many tissues and which have the potential to differentiate to osteoblasts, adipocytes and chondroblasts. They also have a clear immunosuppressive and tissue regeneration potential. Indeed, the initial classification of MSCs as pluripotent stem cells, has turned into their identification as stromal progenitors. Due to the relatively simple procedures available to expand *in vitro* large numbers of GMP grade MSCs from a variety of different tissues, many clinical trials have tested their therapeutic potential *in vivo*. One pathological condition where MSCs have been quite extensively tested is steroid resistant (SR) graft versus host disease (GvHD), a devastating condition that may occur in acute or chronic form following allogeneic hematopoietic stem cell transplantation. The clinical and experimental results obtained have outlined a possible efficacy of MSCs, but unfortunately statistical significance in clinical studies has only rarely been reached and effects have been relatively limited in most cases. Nonetheless, the extremely complex pathogenetic mechanisms at the basis of GvHD, the fact that studies have been conducted often in patients who had been previously treated with multiple lines of therapy, the variable MSC doses and schedules administered in different trials, the lack of validated potency assays and clear biomarkers, the difference in MSC sources and production methods may have been major factors for this lack of clear efficacy *in vivo*. The heterogeneity of MSCs and their different stromal differentiation potential and biological activity may be better

understood through more refined single cell sequencing and proteomic studies, where either an "anti-inflammatory" or a more "immunosuppressive" profile can be identified. We summarize the pathogenic mechanisms of acute and chronic GvHD and the role for MSCs. We suggest that systematic controlled clinical trials still need to be conducted in the most promising clinical settings, using better characterized cells and measuring efficacy with specific biomarkers, before strong conclusions can be drawn about the therapeutic potential of these cells in this context. The same analysis should be applied to other inflammatory, immune or degenerative diseases where MSCs may have a therapeutic potential.