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Human Synovial MSC Good Manufacturing Practices for Articular Cartilage Regeneration.

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Author information

Abstract

BACKGROUND:

cartilage restoration is a desperately needed bridge for patients with symptomatic cartilage lesions. Chondral lesion is a pathology with high prevalence, reaching as much as 63% of general population and 36% among athletes. Despite Autologous Chondrocyte Implantation (ACI) versatility, it still fails to fully reproduce hyaline articular cartilage characteristics. Mesenchymal stem cells (MSCs) may be isolated from various known tissues, including discarded fragments at arthroscopy such as synovial membrane. Choice of harvesting site is motivated by MSCs abilities to modulate immunologic and inflammatory response via paracrine communication. Synovial MSCs have a greater proliferation and strong chondrogenic potential compared to bone and adipose MSCs and a less hypertrophic differentiation compared to bone MSCs. Good Manufacturing Practice (GMP) laboratory techniques for human clinical trials are still novel. To our knowledge, there are only two clinical trials in humans published since today.

PURPOSE:

therefore, the present work aimed to isolate and characterize synovial MSCs and evaluated their differentiation properties according to GMP standards.

METHODS:

one-gram tissue sample from three patients of synovia was harvested at the beginning of arthroscopy surgery. MSCs were isolated, expanded, and characterized by flow cytometry.

RESULTS:

it was possible to isolate and expand MSCs cultures from synovia, characterize MSCs by flow cytometry using proper monoclonal antibodies, and differentiate MSCs by coloring technique after chondrogenic, adipogenic and osteogenic differentiations. Cartilage treatment may benefit from these tissue-engineering protocols since arthroscopic procedures are routinely performed for different purposes in a previous stage and a favorable chondronegic differentiation cell lineage may be collected and stored in a less invasive way.

CONCLUSION:

laboratory protocols established according to presented GMP were able to isolate and characterize MSCs obtained from synovia.

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Adipose Stem Cell Translational Applications: From Bench-to-Bedside.

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Abstract

During the last five years, there has been a significantly increasing interest in adult adipose stem cells (ASCs) as a suitable tool for translational medicine applications. The abundant and renewable source of ASCs and the relatively simple procedure for cell isolation are only some of the reasons for this success. Here, we document the advances in the biology and in the innovative biotechnological applications of ASCs. We discuss how the multipotential property boosts ASCs toward mesenchymal and non-mesenchymal differentiation cell lineages and how their character is maintained even if they are combined with gene delivery systems and/or biomaterials, both in vitro and in vivo

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Mesenchymal stem cell secretome reduces pain and prevents cartilage damage in a murine osteoarthritis model.

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Abstract

Mesenchymal stem cells (MSCs) represent a promising biological therapeutic option as an osteoarthritis (OA)-modifying treatment. MSCs secrete factors that can counteract inflammatory and catabolic processes and attract endogenous repair cells. The effects of intra-articular injection of MSC secretome on OA-related pain, cartilage damage, subchondral bone alterations and synovial inflammation were studied in a mouse collagenase-induced OA model. The MSC secretome was generated by stimulating human bone-marrow-derived MSCs with interferon gamma (IFNγ) and tumour necrosis factor alpha (TNFα). 54 mice were randomly assigned to injections with i) MSC secretome from 20,000 MSCs, ii) 20,000 MSCs or iii) medium (control). Pain was assessed by hind limb weight distribution. Cartilage damage, subchondral bone volume and synovial inflammation were evaluated by histology. MSC-secretome- and MSC-injected mice showed pain reduction at day 7 when compared to control mice. Cartilage damage was more abundant in the control group as compared to healthy knees, a difference which was not found in knees treated with MSC secretome or MSCs. No effects were observed regarding synovial inflammation, subchondral bone volume or the presence of different macrophage subtypes. Injection of MSC secretome, similarly to injection of MSCs, resulted in early pain reduction and had a protective effect on the development of cartilage damage in a murine OA model. By using the regenerative capacities of the MSC-secreted factors, it will be possible to greatly enhance the standardisation, affordability and clinical translatability of the approach. This way, this biological therapy could evolve towards a true disease-modifying anti-osteoarthritic drug.

Transfus Clin Biol. 2018 Aug 25. pii: S1246-7820(18)30254-4. doi: 10.1016/j.tracli.2018.08.157. [Epub ahead of print]

The majority of cells in so-called "mesenchymal stem cell" population are neither stem cells nor progenitors.

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Abstract

OBJECTIVES:

The first-passage adherent human bone marrow fibroblast-like cell population corresponds, in terms of phenotype and three-lineage differentiation capacity (assayed in bulk culture), to commonly termed "mesenchymal stem cells". Here we determine the proportion of high proliferative capacity multipotent cells present in this population in order to estimate the proportion of cells that can or cannot be considered as stem and progenitor cells.

MATERIAL AND METHODS:

The single-cell cultures were established starting from human bone marrow-derived first-passage fibroblast-like cells and the proliferating clones were either transferred to secondary cultures to evaluate their further clonogenicity, or split into three wells to assess differentiation into each of the three different lineages.

RESULTS:

The analysis of 197 single-cell cultures from three different bone marrow donors shows that only~40% of so-called "mesenchymal stem cells" exhibit multipotency and are capable of sustained clonogenicity in secondary cultures.

CONCLUSION:

Even in the first ex vivo passage under favorable conditions the majority (~60%) of so-called "mesenchymal stem cells" are not multipotent and thus do not represent a stem cell entity.