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In Vivo Photoacoustic Tracking of Mesenchymal Stem Cell Viability.

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Abstract

Adult stem cell therapy has demonstrated improved outcomes for treating cardiovascular diseases in preclinical trials. The development of imaging tools may increase our understanding of the mechanisms of stem cell therapy, and a variety of imaging tools have been developed to image transplanted stem cells in vivo; however, they lack the ability to interrogate stem cell function longitudinally. Here, we report the use of a nanoparticle-based contrast agent that can track stem cell viability using photoacoustic imaging. The contrast agent consists of inert gold nanorods coated with IR775c, a reactive oxygen species (ROS) sensitive near-infrared dye. Upon cell death, stem cells produce ROS to degrade the cell. Using this feature of stem cells, the viability can be measured by comparing the IR775c signal to the ROS insensitive gold nanorod signal, which can also be used to track stem cell location. The nanoprobe was successfully loaded into mesenchymal stem cells (MSCs), and then, MSCs were transplanted into the lower limb of a mouse and imaged using combined ultrasound and photoacoustic imaging. MSC viability was assessed using the nanoprobe and displayed significant cell death within 24 h and an estimated 5% viability after 10 days. This nanoparticle system allows for longitudinal tracking of MSC viability in vivo with high spatial and temporal resolution which other imaging modalities currently cannot achieve.

Int J Mol Sci. 2019 Jun 19;20(12). pii: E3002. doi: 10.3390/ijms20123002.

Mesenchymal Stem Cells Empowering Tendon Regenerative Therapies.

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Author information

Abstract

Tendon tissues have limited healing capacity. The incidence of tendon injuries and the unsatisfactory functional outcomes of tendon repair are driving the search for alternative therapeutic approaches envisioning tendon regeneration. Cellular therapies aim at delivering adequate, regeneration-competent cell types to the injured tendon and toward ultimately promoting its reconstruction and recovery of functionality. Mesenchymal stem cells (MSCs) either obtained from tendons or from non-tendon sources, like bone marrow (BM-MSCs) or adipose tissue (ASCs), have been receiving increasing attention over the years toward enhancing tendon healing. Evidences from in vitro and in vivo studies suggest MSCs can contribute to accelerate and improve the quality of tendon healing. Nonetheless, the exact mechanisms underlying these repair events are yet to be fully elucidated. This review provides an overview of the main challenges in the field of cell-based regenerative therapies, discussing the role of

MSCs in boosting tendon regeneration, particularly through their capacity to enhance the tenogenic properties of tendon resident cells.

Transfus Med Hemother. 2019 Feb;46(1):27-34. doi: 10.1159/000496809. Epub 2019 Feb 4.

Clinical Use of Mesenchymal Stromal Cells in the Treatment of Acute Graft-versus-Host Disease.

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Abstract

Acute graft-versus-host disease (aGvHD) continues to impact morbidity and mortality after allogeneic stem cell transplantation (allo-SCT). First-line therapy for aGvHD still remains the use of high-dose corticosteroids. Unfortunately, 40-60% of patients with aGvHD exhibit steroid resistance, which is associated with a very poor prognosis. As no effective second-line therapy existed, in recent decades various treatment options were considered for the treatment of therapy-refractory GvHD. Based on their in vitro immunomodulatory properties, the use of mesenchymal stromal cells (MSCs) in the treatment of aGvHD has been introduced. However, most of the clinical data are generated from uncontrolled trials and case series, showing clinical responses to MSCs. Clinical results are more consistent in children despite the use of MSC preparations of various provenance and manufacturing protocols. While these data support the therapeutic principle, the great variability of outcomes strongly suggests that not all MSC preparations are equal and that the specific manufacturing protocols influence therapeutic success in vivo.

Stem Cell Res Ther. 2019 Jun 25;10(1):187. doi: 10.1186/s13287-019-1296-8.

Labeling of human mesenchymal stem cells with different classes of vital stains: robustness and toxicity.

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Abstract

BACKGROUND:

Mesenchymal stem cell (MSC) transplantation has been explored as a new clinical approach to repair injured tissues. However, in order to evaluate the therapeutic activity of MSC, cell tracking techniques are required to determine the fate of transplanted cells in both preclinical and clinical studies. In these aspects, different vital stains offer the potential for labeling and monitoring of grafted cells in vivo. It is desirable to have tracking agents which have long-term stability, are not toxic to the cells, and do not affect cell function.

METHODS:

Here, we selected three different labels: CellTracker™ Green CMFDA, eGFP-mRNA (genetic pre-tag), and Molday ION Rhodamine B™ (nanoparticle-based fluorescent and magnetic label) and performed extensive analysis of their influence on in vitro expansion of human bone marrow-derived mesenchymal

stem cells (hBM-MSCs), as well as potential of affecting therapeutic activity and the impact on the durability of staining.

RESULTS:

Our study showed that basic hBM-MSC characteristics and functions might be affected by labeling. We observed strong alterations of metabolic activity and morphology after eGFP and CellTracker™ Green CMFDA hBM-MSC staining. Molday ION Rhodamine B™ labeling revealed superior properties relatively to other vital stains. The relative expression level of most of the investigated growth factors remained stable after cell labeling, but we have observed some changes in the case of EGF, GDNF, HGF, and IGF gene expression.

CONCLUSIONS:

Taken together, we suggest performing similar to ours extensive analysis prior to using any cell label to tag MSC in experiments, as it can thoroughly bias results.

Front Immunol. 2019 Jun 4;10:1287. doi: 10.3389/fimmu.2019.01287. eCollection 2019.

Mesenchymal Stromal Cells for Transplant Tolerance.

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Abstract

In solid organ transplantation lifelong immunosuppression exposes transplant recipients to life-threatening complications, such as infections and malignancies, and to severe side effects. Cellular therapy with mesenchymal stromal cells (MSC) has recently emerged as a promising strategy to regulate anti-donor immune responses, allowing immunosuppressive drug minimization and tolerance induction. In this review we summarize preclinical data on MSC in solid organ transplant models, focusing on potential mechanisms of action of MSC, including down-regulation of effector T-cell response and activation of regulatory pathways. We will also provide an overview of available data on safety and feasibility of MSC therapy in solid organ transplant patients, highlighting the issues that still need to be addressed before establishing MSC as a safe and effective tolerogenic cell therapy in transplantation.

Biochemistry (Mosc). 2019 Mar;84(3):250-262. doi: 10.1134/S0006297919030076.

Clonal Composition of Human Multipotent Mesenchymal Stromal Cells: Application of Genetic Barcodes in Research.

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Abstract

Clonal composition of human multipotent mesenchymal stromal cells (MMSCs) labeled with lentiviral vectors carrying genetic barcodes was studied. MMSCs were transduced with a cloned library of self-inactivating lentiviral vectors carrying 667 unique barcodes. At each cell culture passage, 120 cells

were plated one cell per well in 96-well plates. The efficiency of cloning and labeling of the clonogenic cells was determined. DNA was extracted from the cell-derived colonies, and the barcodes were identified by Sanger sequencing. Also, DNA was extracted from the total MMSC population at each passage to analyze the diversity and representation of barcodes by deep sequencing using the Illumina platform. It was shown that the portion of MMSCs labeled with the lentiviral vectors remained stable in the passaged cells. Because of the high multiplicity of infection, the labeling procedure could decrease the proliferative potential of MMSCs. Identification of barcodes in individual cell clones confirmed the polyclonal character of the MMSC population. Clonal composition of MMSCs changed significantly with the passages due to the depletion of proliferative potential of most cells. Large clones were found at the first passage; at later passages, many small clones with a limited proliferative potential were detected in the population. The results of deep sequencing confirmed changes in the clonal composition of MMSCs. The polyclonal MMSC population contained only a small number of cells with a high proliferative potential, some of which could be stem cells. MMSCs with a high proliferative potential were detected more often in the earliest passages. In this regard, we would recommend to use MMSCs of early passages for regenerative medicine applications based on cell proliferation.

Biomed Res Int. 2019 May 8;2019:2820853. doi: 10.1155/2019/2820853. eCollection 2019.

Mesenchymal Stem Cells and Cancer: Clinical Challenges and Opportunities.

Lin W[1,2], Huang L[1], Li Y[1], Fang B[1], Li G[2,3], Chen L[1], Xu L[1,4].
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Abstract

Stem cell-based therapies exhibit profound therapeutic potential for treating various human diseases, including cancer. Among the cell types that can be used for this purpose, mesenchymal stem cells (MSCs) are considered as promising source of stem cells in personalized cell-based therapies. The inherent tumor-tropic property of MSCs can be used to target cancer cells. Although the impacts of MSCs on tumor progression remain elusive, they have been genetically modified or engineered as targeted anticancer agents which could inhibit tumor growth by blocking different processes of tumor. In addition, there are close interactions between MSCs and cancer stem cells (CSCs). MSCs can regulate the growth of CSCs through paracrine mechanisms. This review aims to focus on the current knowledge about MSCs-based tumor therapies, the opportunities and challenges, as well as the prospective of its further clinical implications.

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Human colorectal cancer derived-MSCs promote tumor cells escape from senescence via P53/P21 pathway.

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Abstract

PURPOSE:

The purpose of this study was to evaluate effect of MSCs on CRC cell.

METHODS:

in this study the MSC was isolated from CRC tissue, its effect on CRC cells was investigated in vivo and vitro, and the underlying mechanism was investigated.

RESULTS:

In this study we found that MSC-CM could promote colorectal cancer cells escape from senescence both in vitro and in vivo. Further research we demonstrated that MSC-CM acted in colorectal cancer cells senescence through P53/P21 pathway. Next we found that MSC-CM regulate P53 via posttranscription method.

CONCLUSION:

Collectively, these results reveal that MSCs can help colorectal cancer cells defend against senescence through P53/P21 pathway, which may be a new strategy for colorectal cancer therapy.

Mol Ther Methods Clin Dev. 2019 May 17;14:1-15. doi: 10.1016/j.omtm.2019.05.004. eCollection 2019 Sep 13.

Dissecting the Pharmacodynamics and Pharmacokinetics of MSCs to Overcome Limitations in Their Clinical Translation.

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Abstract

Recently, mesenchymal stromal stem cells (MSCs) have been proposed as therapeutic agents because of their promising preclinical features and good safety profile. However, their introduction into clinical practice has been associated with a suboptimal therapeutic profile. In this review, we address the biodistribution of MSCs in preclinical studies with a focus on the current understanding of the pharmacodynamics (PD) and pharmacokinetics (PK) of MSCs as key aspects to overcome unsatisfactory clinical benefits of MSC application. Beginning with evidence of MSC biodistribution and highlighting PK and PD factors, a new PK-PD model is also proposed. According to this theory, MSCs and their released factors are key players in PK, and the efficacy biomarkers are considered relevant for PD in more predictive preclinical investigations. Accounting for the PK-PD relationship in MSC translational research and proposing new models combined with better biodistribution studies could allow realization of the promise of more robust MSC clinical translation.