ML 45-18 (07/12/2018)

BMC Res Notes. 2018 Nov 29;11(1):848. doi: 10.1186/s13104-018-3949-6.

Quantitative assessment of mesenchymal stem cells contained in concentrated autologous bone marrow aspirate transplantation for the treatment of osteonecrosis of the femoral head: predictive factors and differences by etiology.

Kumagai H[1], Yoshioka T[2], Sugaya H[1], Tomaru Y[1], Shimizu Y[3], Yamazaki M[1], Mishima H[1].
Author information

Abstract

OBJECTIVE:

We previously established concentrated autologous bone marrow aspirate transplantation as a one-step, lowly invasive, joint-preserving surgical technique for treating osteonecrosis of the femoral head. The objectives of this study were to identify factors that may predict the mesenchymal stem cell (MSC) count in bone marrow aspirate, concentrated using our method, and to clarify etiology related differences in the number of MSCs in concentrated bone marrow aspirate.

RESULTS:

The MSC counts per 10^6 nucleated cells before concentration in the steroid, alcohol, and trauma groups were 2.31 ± 2.96, 2.58 ± 2.30, and 1.95 ± 1.85, respectively. The MSC counts per 10^6 nucleated cells after concentration were 3.23 ± 3.41, 3.30 ± 2.83, and 2.56 ± 1.98 cells, respectively. The MSC concentration rates in the steroid, alcohol, and trauma groups were 7.15 ± 5.62, 5.08 ± 1.96, and 8.23 ± 4.82 times, respectively. None of the differences were significant. Multiple regression analysis revealed that MSC count was related to the total bone marrow aspirated, peripheral blood platelet count, and nucleated cell count in the initial aspiration.

KEYWORDS:

Concentrated autologous bone marrow aspirate transplantation; Joint-preserving surgery; Mesenchymal stem cells; Osteonecrosis of the femoral head

Adv Exp Med Biol. 2018;1103:305-307. doi: 10.1007/978-4-431-56847-6_17.

Clinical Trials of Muse Cells.

Dezawa M[1].

Author information

Abstract

Among many kinds of somatic stem cells, hematopoietic stem cells are the cells that have been successfully applied to treating leukemia patients as forms of bone marrow and cord blood transplantation. Mesenchymal stem cells, collectable from several sources including the bone marrow and adipose tissue, are also widely applied to clinical trials for their easy accessibility and low risks of tumorigenesis, while their outcomes were shown to be not clinically relevant in several target diseases.

The most important issue for the stem cells is whether the cells are safe and effective for curing diseases. In this chapter, the outline of the clinical trial in Muse cells is discussed.

Methods Mol Biol. 2018 Nov 28. doi: 10.1007/7651_2018_197. [Epub ahead of print]

Adipogenic and Osteogenic Differentiation of In Vitro Aged Human Mesenchymal Stem Cells.

Ogando CR[1], Barabino GA[1], Yang YK[2].

Author information

Abstract

Multipotent mesenchymal stem cells (MSCs) are an attractive candidate for regeneration of damaged cells, tissues, and organs. Due to limited availabilities, MSC populations must be rapidly expanded to satisfy clinical needs. However, senescence attributed to extensive in vitro expansion compromises the regenerative and therapeutic potential of MSCs. In this chapter, we describe a step-by-step protocol that aims to induce adipogenic and osteogenic differentiation of in vitro aged human MSCs and highlight noteworthy issues that may arise during the process.

J Biol Eng. 2018 Nov 20;12:26. doi: 10.1186/s13036-018-0119-2. eCollection 2018.

In vitro culture expansion impairs chondrogenic differentiation and the therapeutic effect of mesenchymal stem cells by regulating the unfolded protein response.

Shen C[#1,2], Jiang T[#1,2], Zhu B[#1], Le Y[1,2], Liu J[1], Qin Z[1], Chen H[1], Zhong G[1,2], Zheng L[1], Zhao J[1,2,3], Zhang X[4].

Author information

Abstract

In vitro expansion of mesenchymal stem cells (MSCs) has been implicated in loss of multipotency, leading to impaired chondrogenic potential and an eventual therapeutic effect, as reported in our previous study. However, the precise regulatory mechanism is still unclear. Here, we demonstrate that endoplasmic reticulum (ER) stress and the unfolded protein response (UPR) were involved in transformation of MSCs induced by in vitro culture based on the comparative profiling of in vitro cultured bone marrow MSCs at passage 3 (P3 BMSCs) vs. fresh P0 BMSCs by microarray analysis. Indeed, RT-PCR and Western blot analysis showed significantly lower expression levels of three key UPR-related molecules, ATF4, ATF6 and XBP1, in P3 BMSCs than P0 BMSCs. Further, we found that UPR suppression by 4-phenylbutyrate (4-PBA) reduced the chondrogenic potential of P0 BMSCs and further cartilage regeneration. Conversely, UPR induction by tunicamycin (TM) enhanced the chondrogenic differentiation of P3 BMSCs and the therapeutic effect on cartilage repair. Thus, the decline in the chondrogenic potential of stem cells after in vitro culture and expansion may be due to changes in ER stress and the UPR pathway.

Prostate. 2018 Nov 28. doi: 10.1002/pros.23738. [Epub ahead of print]

Tumor-infiltrating mesenchymal stem cells: Drivers of the immunosuppressive tumor microenvironment in prostate cancer?

Krueger TE[1], Thorek DLJ[2,3], Meeker AK[4,5,6], Isaacs JT[4,5], Brennen WN[4].

Author information

Abstract

BACKGROUND:

Prostate cancer is characterized by T-cell exclusion, which is consistent with their poor responses to immunotherapy. In addition, T-cells restricted to the adjacent stroma and benign areas are characterized by anergic and immunosuppressive phenotypes. In order for immunotherapies to produce robust anti-tumor responses in prostate cancer, this exclusion barrier and immunosuppressive microenvironment must first be overcome. We have previously identified mesenchymal stem cells (MSCs) in primary and metastatic human prostate cancer tissue.

METHODS:

An Opal Multiplex immunofluorescence assay based on CD73, CD90, and CD105 staining was used to identify triple-labeled MSCs in human prostate cancer tissue. T-cell suppression assays and flow cytometry were used to demonstrate the immunosuppressive potential of primary MSCs expanded from human bone marrow and prostate cancer tissue from independent donors.

RESULTS:

Endogenous MSCs were confirmed to be present at sites of human prostate cancer. These prostate cancer-infiltrating MSCs suppress T-cell proliferation in a dose-dependent manner similar to their bone marrow-derived counterparts. Also similar to bone marrow-derived MSCs, prostate cancer-infiltrating MSCs upregulate expression of PD-L1 and PD-L2 on their cell surface in the presence of IFNγ and TNFα.

CONCLUSION:

Prostate cancer-infiltrating MSCs suppress T-cell proliferation similar to canonical bone marrow-derived MSCs, which have well-documented immunosuppressive properties with numerous effects on both innate and adaptive immune system function. Thus, we hypothesize that selective depletion of MSCs infiltrating sites of prostate cancer should restore immunologic recognition and elimination of malignant cells via broad re-activation of cytotoxic pro-inflammatory pathways.

Methods Mol Biol. 2018 Nov 30. doi: 10.1007/7651_2018_199. [Epub ahead of print]

Human Synovium-Derived Mesenchymal Stem Cells: Ex Vivo Analysis.

Zupan J[1].

Author information

Abstract

Synovium-derived mesenchymal stem/stromal cells (MSCs) have been shown to have superior features in comparison with MSCs from other tissue sources. As they are far less recognised compared to bone marrow- or adipose tissue-derived MSCs, I provide here a detailed procedure on how to isolate MSCs from human synovium. This includes determination of the proportions of viable cells in ex vivo isolated fractions before the seeding of the cells and a description of how to carry out colony-forming fibroblast assays to quantify the clonogenicity of these cells.
KEYWORDS: