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Similarities and differences between mesenchymal stem/progenitor cells derived from various human tissues.

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Abstract

BACKGROUND:

Mesenchymal stromal/stem cells (MSCs) constitute a promising tool in regenerative medicine and can be isolated from different human tissues. However, their biological properties are still not fully characterized. Whereas MSCs from different tissue exhibit many common characteristics, their biological activity and some markers are different and depend on their tissue of origin. Understanding the factors that underlie MSC biology should constitute important points for consideration for researchers interested in clinical MSC application.

AIM:

To characterize the biological activity of MSCs during longterm culture isolated from: bone marrow (BM-MSCs), adipose tissue (AT-MSCs), skeletal muscles (SM-MSCs), and skin (SK-MSCs).

METHODS:

MSCs were isolated from the tissues, cultured for 10 passages, and assessed for: phenotype with immunofluorescence and flow cytometry, multipotency with differentiation capacity for osteo-, chondro-, and adipogenesis, stemness markers with qPCR for mRNA for Sox2 and Oct4, and genetic stability for p53 and c-Myc; 27 bioactive factors were screened using the multiplex ELISA array, and spontaneous fusion involving a co-culture of SM-MSCs with BM-MSCs or AT-MSCs stained with PKH26 (red) or PKH67 (green) was performed.

RESULTS:

All MSCs showed the basic MSC phenotype; however, their expression decreased during the follow-up period, as confirmed by fluorescence intensity. The examined MSCs express CD146 marker associated with proangiogenic properties; however their expression decreased in AT-MSCs and SM-MSCs, but was maintained in BM-MSCs. In contrast, in SK-MSCs CD146 expression increased in late passages. All MSCs, except BM-MSCs, expressed PW1, a marker associated with differentiation capacity and apoptosis. BM-MSCs and AT-MSCs expressed stemness markers Sox2 and Oct4 in long-term culture. All MSCs showed a stable p53 and c-Myc expression. BM-MSCs and AT-MSCs maintained their differentiation capacity during the follow-up period. In contrast, SK-MSCs and SM-MSCs had a limited ability to differentiate into adipocytes. BM-MSCs and AT-MSCs revealed similarities in phenotype maintenance, capacity for multilineage differentiation, and secretion of bioactive factors. Because AT-MSCs fused with SM-MSCs as effectively as BM-MSCs, AT-MSCs may constitute an alternative source for BM-MSCs.

CONCLUSION:

Long-term culture affects the biological activity of MSCs obtained from various tissues. The source of MSCs and number of passages are important considerations in regenerative medicine.

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Bovine pericardium membrane as new tool for mesenchymal stem cells commitment.

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Abstract

Acellular matrices are widespread biomaterials used in surgical practice as tissue reinforcement and anatomical support to favor tissue regeneration. It is clear that a fundamental role in the regeneration of tissue is played by cell-material interaction. In this work, the interaction between a bovine pericardium membrane and human adult stem cells was investigated by microscopy analysis and gene expression analysis. Parallel cell cultures were prepared on the pericardium membrane or tissue culture plate. They were incubated in basal growth medium or in adipogenic differentiation medium to perform experiments on the seventh and the fourteenth day of culture. Results demonstrated that the membrane allows cell viability, adhesion, and proliferation of human stem cells. During adipogenic commitment on the membrane, the accumulation of cytoplasmatic lipid droplets and the expression of adipogenic gene PPARG, CEBPA, GLUT4, FABP4 and ADIPOQ were detected. Concurrently, a downregulation of mesenchymal stem cell gene CD29, CD90 and CD105 was detected. In basal medium, the adipogenic gene expression was up regulated while the mesenchymal markers were indifferently expressed. These findings suggest that the bovine pericardium membrane is a biocompatible matrix, and that their rough surface allows cell adhesion, spreading and proliferation. The surface morphology activates mechanochemical signals that stimulate the adipogenic commitment of stem cells in basal medium, and potentiate their commitment in adipogenic differentiation medium.

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Mesenchymal stromal cells confer chemoresistance to myeloid leukemia blasts through Side Population functionality and ABC transporter activation.

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Abstract

Targeting chemoresistant malignant cells is one of the current major challenges in oncology. Therefore, it is mandatory to refine the characteristics of these cells to monitor their survival and develop adapted therapies. This is particularly of interest for acute myeloid leukemia for which 5-year survival rate reach only 30% for all prognosis. The role of microenvironment is increasingly reported to be a key regulator

for blast survival. In this context, we demonstrate that contact with mesenchymal stromal cells promote a better survival of blasts in culture in presence of anthracycline through the activation of ABC transporters. Stroma-dependent ABC transporter activation leads to the induction of a side population phenotype in a subpopulation of primary leukemia blasts through Alpha4 engagement. The stroma-promoting effect is reversible and is observed with stromal cells isolated from either healthy donors or leukemia patients. Blasts expressing a side population phenotype are mostly quiescent and are chemoresistant in vitro and in vivo in patient-derived xenograft mouse models. At the transcriptomic level, blats from the side population are specifically enriched in drug metabolism program. This detoxification signature engaged in contact with mesenchymal stromal cells represents promising ways to target stroma-induced chemoresistance of acute myeloid leukemia cells.

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Concise Review: Mesenchymal Stromal Cells Anno 2019: Dawn of the Therapeutic Era?

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Abstract

2018 was the year of the first marketing authorization of an allogeneic stem cell therapy by the European Medicines Agency. The authorization concerns the use of allogeneic adipose tissue derived mesenchymal stromal cells (MSCs) for treatment of complex perianal fistulas in Crohn's disease. This is a breakthrough in the field of MSC therapy. The last few years have furthermore seen some breakthroughs in the investigations to the mechanisms of action of MSC therapy. Although the therapeutic effects of MSCs have largely been attributed to their secretion of immunomodulatory and regenerative factors, it has now become clear that some of the effects are mediated through host phagocytic cells that clear administered MSCs and in the process adapt an immunoregulatory and regeneration supporting function. The increased interest in therapeutic use of MSCs and the ongoing elucidation of the mechanisms of action of MSCs are promising indicators that 2019 may be the dawn of the therapeutic era of MSCs and that there will be revived interest in research to more efficient, practical, and sustainable MSC-based therapies