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Directed differential behaviors of multipotent adult stem cells from decellularized tissue/organ extracellular matrix bioinks.

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Abstract

The decellularized tissue/organ extracellular matrix (dECM) is a naturally derived biomaterial that inherits various functional components from the native tissue or organ. Recently, various kinds of tissue/organ dECM bioinks capable of encapsulating cells, combined with 3D cell printing, have enabled remarkable progress in tissue engineering and regenerative medicine. However, the way in which the dECM component compositions of each tissue of different origins interact with cells and dictate tissue-specific cell behavior in the 3D microenvironment remains mostly unknown. To address this issue, in-depth differential proteomic analyses of four porcine dECMs were performed. Specifically, the differential variations of matrisome protein composition in each decellularized tissue type were also uncovered, which can play a significant role by affecting the resident cells in specific tissues. Furthermore, microarray analyses of human bone marrow mesenchymal stem cells (hBMMSCs) printed with various dECM bioinks were conducted to reveal the effect of compositional variations in a tissue-specific manner at the cellular level depending on the multipotency of MSCs. Through whole transcriptome analysis, differential expression patterns of genes were observed in a tissue-specific manner, and this research provides strong evidence of the tissue-specific functionalities of dECM bioinks.

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New Insights Into Implementation of Mesenchymal Stem Cells in Cancer Therapy: Prospects for Anti-angiogenesis Treatment.

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Abstract

Tumor microenvironment interacts with tumor cells, establishing an atmosphere to contribute or suppress the tumor development. Among the cells which play a role in the tumor microenvironment, mesenchymal stem cells (MSCs) have been demonstrated to possess the ability to orchestrate the fate of tumor cells, drawing the attention to the field. MSCs have been considered as cells with double-bladed effects, implicating either tumorigenic or anti-tumor activity. On the other side, the promising potential of MSCs in treating human cancer cells has been observed from the clinical studies. Among

the beneficial characteristics of MSCs is the natural tumor-trophic migration ability, providing facility for drug delivery and, therefore, targeted treatment to detach tumor and metastatic cells. Moreover, these cells have been the target of engineering approaches, due to their easily implemented traits, in order to obtain the desired expression of anti-angiogenic, anti-proliferative, and pro-apoptotic properties, according to the tumor type. Tumor angiogenesis is the key characteristic of tumor progression and metastasis. Manipulation of angiogenesis has become an attractive approach for cancer therapy since the introduction of the first angiogenesis inhibitor, namely bevacizumab, for metastatic colorectal cancer therapy. This review tries to conclude the approaches, with focus on anti-angiogenesis approach, in implementing the MSCs to combat against tumor cell progression

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Chondrogenic differentiation of human bone marrow-derived mesenchymal stromal cells in a three-dimensional environment.

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Abstract

Cell therapy combined with biomaterial scaffolds is used to treat cartilage defects. We hypothesized that chondrogenic differentiation bone marrow-derived mesenchymal stem cells (BM-MSCs) in three-dimensional biomaterial scaffolds would initiate cartilaginous matrix deposition and prepare the construct for cartilage regeneration in situ. The chondrogenic capability of human BM-MSCs was first verified in a pellet culture. The BM-MSCs were then either seeded onto a composite scaffold rhCo-PLA combining polylactide and collagen type II (C2) or type III (C3), or commercial collagen type I/III membrane (CG). The BM-MSCs were either cultured in a proliferation medium or chondrogenic culture medium. Adult human chondrocytes (ACs) served as controls. After 3, 14, and 28 days, the constructs were analyzed with quantitative polymerase chain reaction and confocal microscopy and sulfated glycosaminoglycans (GAGs) were measured. The differentiated BM-MSCs entered a hypertrophic state by Day 14 of culture. The ACs showed dedifferentiation with no expression of chondrogenic genes and low amount of GAG. The CG membrane induced the highest expression levels of hypertrophic genes. The two different collagen types in composite scaffolds yielded similar results. Regardless of the biomaterial scaffold, culturing BM-MSCs in chondrogenic differentiation medium resulted in chondrocyte hypertrophy. Thus, caution for cell fate is required when designing cell-biomaterial constructs for cartilage regeneration.

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Intra-articular injection of culture-expanded mesenchymal stem cells with or without addition of platelet-rich plasma

is effective in decreasing pain and symptoms in knee osteoarthritis: a controlled, double-blind clinical trial.

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Abstract

PURPOSE:

To compare the clinical and laboratory outcomes of intra-articular injections of culture-expanded bone-derived mesenchymal stem cells (MSCs) with or without platelet-rich plasma (PRP) to intra-articular corticosteroid injections for the treatment of knee osteoarthritis (OA).

METHODS:

Forty-seven patients with radiographic and symptomatic knee OA were randomized into three groups for intra-articular injections: autologous bone marrow-derived culture-expanded MSCs (n = 16); autologous bone marrow-derived culture-expanded MSCs + PRP (n = 14); and corticosteroid (n = 17). The outcomes were assessed by the Knee Injury and Osteoarthritis Outcome Score (KOOS) and range of motion (ROM) at baseline, 1, 2, 3, 6, 9 and 12 months and intra-articular cytokines analysis at baseline, 6 and 12 months postoperatively.

RESULTS:

The three groups showed significant improvement in most KOOS domains and global score at 1st month and all domains and global score at 12-month follow-up ($p < 0.05$). At the 1st month, only the MSCs group showed significant differences in KOOS symptoms domain ($p = 0.003$). The MSCs and MSCs + PRP groups showed the highest percentage of improvement in most KOOS domains and global score compared to the corticosteroid group. All three groups showed a significant reduction in intra-articular levels of human interleukin-10 cytokine, from baseline to 12 months ($p < 0.05$).

CONCLUSION:

An intra-articular injection of bone marrow-derived culture-expanded MSCs with or without the addiction of PRP is effective in improving the function and decreasing symptoms caused by knee OA at 12-month follow-up.

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The Tumor-Immune Response Is Not Compromised by Mesenchymal Stromal Cells in Humanized Mice.

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Abstract

Therapeutic uses of mesenchymal stromal cells (MSCs) have emerged over the past decade. Yet, their effect on tumor growth remains highly debated, particularly in an immune competent environment. In this study, we wanted to investigate the impact of human umbilical cord-derived MSCs (hUC-MSCs) on

tumor growth in humanized mice generated by the human adoptive transfer of PBMCs or the cotransplantation of hematopoietic stem cells and human thymic tissue (human BLT [Hu-BLT]). Our results showed that the growth and immune rejection of engineered human fibroblastic tumors was not altered by the injection of hUC-MSCs in immune-deficient or humanized mice, respectively. This was observed whether tumor cells were injected s.c. or i.v. and independently of the injection route of the hUC-MSCs. Moreover, only in Hu-BLT mice did hUC-MSCs have some effects on the tumor-immune infiltrate, yet without altering tumor growth. These results demonstrate that hUC-MSCs do not promote fibroblastic tumor growth and neither do they prevent tumor infiltration and rejection by immune cells in humanized mice.

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The potential role of stromal cell-derived factor-1α/CXCR4/CXCR7 axis in adipose-derived mesenchymal stem cells.

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Abstract

To investigate the potential role of stromal cell-derived factor-1α (SDF-1α)/CXCR4/CXCR7 axis in adipose-derived mesenchymal stem cells (ADSCs), quantitative reverse transcription-polymerase chain reaction (qRT-PCR) was employed to screen the effective small interfering RNA against CXCR4 and CXCR7 in ADSCs. The messenger RNA (mRNA) and proteins abundances of AKT (p-AKT), ERK (p-ERK), JNK (p-JNK), and p38 (p-p38) in different groups were identified by qRT-PCR, western blot, and immunofluorescence staining method. Meanwhile, cell migration and cell proliferation with SDF-1 treated were examined by a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay and transwell permeable assay, respectively. Moreover, the interaction between CXCR4 and CXCR7 was examined by a GST pull-down assay. CXCR4 small interfering RNA3 (siRNA3) and CXCR7 siRNA3 have been proved to the most effective tools for knockdown CXCR4 and CXCR7 expressions. mRNA abundance of JNK and p38 could be affected by SDF-1α/CXCR4/CXCR7 axis. However, western blot analysis of p-AKT, p-ERK, p-JNK, and p-p38 in CXCR43-treated ADSCs was significantly higher than that in the control group. Moreover, the immunofluorescence staining analysis revealed that the expressions of p-ATK and p-JNK proteins were significantly higher in NC- and SDF-1-treated subgroups than that in the CXCR4 and CXCR7 groups. p-ATK and p-JNK proteins in CXCR4 group were similar to that in CXCR7 group. Cell migration analysis of CXCR4-treated ADSCs suggested that knockdown CXCR4 could effectively promote cell migration ($p < .05$). Moreover, CXCR4 could interact with CXCR7. The results in this study could provide a better understanding of SDF-1α/CXCR4/CXCR7 axis during ADSCs development.