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In-vitro analysis of Quantum Molecular Resonance effects on human mesenchymal stromal cells.

Sella S[1], Adami V[2], Amati E[1], Bernardi M[1,3], Chieregato K[1,3], Gatto P[2], Menarin M[1], Pozzato A[4], Pozzato G[4], Astori G[1].
Author information

Abstract

Electromagnetic fields play an essential role in cellular functions interfering with cellular pathways and tissue physiology. In this context, Quantum Molecular Resonance (QMR) produces waves with a specific form at high-frequencies (4-64 MHz) and low intensity through electric fields. We evaluated the effects of QMR stimulation on bone marrow derived mesenchymal stromal cells (MSC). MSC were treated with QMR for 10 minutes for 4 consecutive days for 2 weeks at different nominal powers. Cell morphology, phenotype, multilineage differentiation, viability and proliferation were investigated. QMR effects were further investigated by cDNA microarray validated by real-time PCR. After 1 and 2 weeks of QMR treatment morphology, phenotype and multilineage differentiation were maintained and no alteration of cellular viability and proliferation were observed between treated MSC samples and controls. cDNA microarray analysis evidenced more transcriptional changes on cells treated at 40 nominal power than 80 ones. The main enrichment lists belonged to development processes, regulation of phosphorylation, regulation of cellular pathways including metabolism, kinase activity and cellular organization. Real-time PCR confirmed significant increased expression of MMP1, PLAT and ARHGAP22 genes while A2M gene showed decreased expression in treated cells compared to controls. Interestingly, differentially regulated MMP1, PLAT and A2M genes are involved in the extracellular matrix (ECM) remodelling through the fibrinolytic system that is also implicated in embryogenesis, wound healing and angiogenesis. In our model QMR-treated MSC maintained unaltered cell phenotype, viability, proliferation and the ability to differentiate into bone, cartilage and adipose tissue. Microarray analysis may suggest an involvement of QMR treatment in angiogenesis and in tissue regeneration probably through ECM remodelling.

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Phenotypic and functional characterization of mesenchymal stromal cells isolated from pediatric patients with severe idiopathic nephrotic syndrome.

Starc N[1], Li M[2], Algeri M[1], Conforti A[1], Tomao L[1], Pitisci A[1], Emma F[3], Montini G[4], Messa P[5], Locatelli F[6], Bernardo ME[1], Vivarelli M[7].

Author information

Abstract

BACKGROUND:

Idiopathic nephrotic syndrome (INS) is one of the most common renal diseases in the pediatric population; considering the role of the immune system in its pathogenesis, corticosteroids are used as first-line immunosuppressive treatment. Due to its chronic nature and tendency to relapse, a significant proportion of children experience co-morbidity due to prolonged exposure to corticosteroids and concomitant immunosuppression with second-line, steroid-sparing agents. Mesenchymal stromal cells (MSCs) are multipotent cells that represent a key component of the bone marrow (BM) microenvironment; given their unique immunoregulatory properties, their clinical use may be exploited as an alternative therapeutic approach in INS treatment.

METHODS:

In view of the possibility of exploiting their immunoregulatory properties, we performed a phenotypical and functional characterization of MSCs isolated from BM of five INS patients (INS-MSCs; median age, 13 years; range, 11-16 years) in comparison with MSCs isolated from eight healthy donors (HD-MSCs). MSCs were expanded ex vivo and then analyzed for their properties.

RESULTS:

Morphology, proliferative capacity, immunophenotype and differentiation potential did not differ between INS-MSCs and HD-MSCs. In an allogeneic setting, INS-MSCs were able to prevent both T- and B-cell proliferation and plasma-cell differentiation. In an in-vitro model of experimental damage to podocytes, co-culture with INS-MSCs appeared to be protective.

DISCUSSION:

Our results demonstrate that INS-MSCs maintain the main biological and functional properties typical of HD-MSCs; these data suggest that MSCs may be used in autologous cellular therapy approaches for INS treatment.

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Therapy-educated mesenchymal stem cells enrich for tumor initiating cells.

Timaner M[1], Letko-Khait N[2], Kotsofruk R[1], Benguigui M[1], Beyar-Katz O[1], Rachman-Tzemach C[1], Raviv Z[3], Bronshtein T[2], Machluf M[4], Shaked Y[5].
Author information

Abstract

Stromal cells residing in the tumor microenvironment contribute to the development of therapy resistance. Here we show that chemotherapy-educated mesenchymal stem cells (MSCs) promote therapy resistance via crosstalk with tumor-initiating cells (TICs), a resistant tumor cell subset that initiates tumorigenesis and metastasis. In response to gemcitabine chemotherapy, MSCs colonized pancreatic adenocarcinomas in large numbers and resided in close proximity to TICs. Furthermore, gemcitabine-educated MSCs promoted the enrichment of TICs in vitro and enhance tumor growth in vivo. These effects were dependent on the secretion of CXCL10 by gemcitabine-educated MSCs and

subsequent activation of the CXCL10-CXCR3 axis in TICs. In an orthotopic pancreatic tumor model, targeting TICs using nano-vesicles (called nano-ghosts) derived from MSC membranes and loaded with a CXCR3 antagonist enhanced therapy outcome and delayed tumor re-growth when administered in combination with gemcitabine. Overall, our results establish a mechanism through which MSCs promote chemoresistance, and propose a novel drug delivery system to target TICs and overcome this resistance.

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Runx2 overexpression compromises bone quality in acromegalic patients.

Valenti MT[1], Mottes M[2], Cheri S[3], Deiana M[4], Micheletti V[5], Cosaro E[6], Davì MV[7], Francia G[8], Dalle Carbonare L[9].
Author information

Abstract

Acromegalic patients, characterized by excessive secretion of GH and IGF-1, show a high fracture risk but Bone Mineral Density is a poor predictor for bone fractures in these patients. The effects of an excess of GH/IGF1 on skeleton as well as on osteogenic progenitors, i.e. mesenchymal stem cells, have not been investigated in these patients. We aimed to elucidate the skeletal conditions of acromegalic patients by means of bone microarchitecture analysis and evaluation of MSCs osteogenic commitment. In particular, we performed histomorphometric analyses and we quantified the expression levels of the osteogenic transcription factor RUNX2 in circulating MSCs. Our results showed an abnormal microarchitecture and demonstrated that bone impairment in APs is associated with the upregulation of RUNX2 expression. Furthermore, osteoblastic activity was significantly reduced in patients under pharmacological treatment, compared to untreated patients. In conclusion, this study demonstrates the key role of RUNX2 gene overexpression in causing bone impairment in acromegalic patients. It also suggests a therapeutic approach for the improvement of bone quality, focused on the osteoblastic lineage rather than the inhibition of osteoclastic activity.

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Stem cell therapy in early post-traumatic talus osteonecrosis.

Hernigou P[1], Dubory A[2], Flouzat Lachaniette CH[2], Khaled I[2], Chevallier N[2], Rouard H[2].

Author information

Abstract

PURPOSE:

Avascular necrosis of the talus is one of the most notable complications associated with talar neck fractures with frequent evolution of the osteonecrosis into a difficult arthrodesis. We tested whether the injection of bone marrow mesenchymal stem cells (MSCs) could improve the repair process of the osteonecrosis.

MATERIAL AND METHODS:

Forty-five early (without collapse) post-traumatic talus osteonecroses (group 1; study group) were treated between 1995 and 2012 with percutaneous injection of progenitor cells (autologous bone marrow concentrate from the iliac crest). The number of MSCs transplanted in each ankle of group 1 was 124 × 103 cells (range 101 × 10^3 to 164 × 10^3 cells). The evolution of these osteonecroses treated with autologous bone marrow implantation was compared with the evolution of a control group of 34 talar osteonecroses without collapse and treated with only core decompression (group 2; control group) between 1985 and 1995. The outcome was determined by progression in radiographic stages to collapse, by the need of arthrodesis, and by the time to successfully achieve fusion for patients who needed arthrodesis.

RESULTS:

For the 45 ankles with autologous concentrate bone marrow grafting, collapse frequency was lower (27%, 12 among 45 versus 71%, 24 among 34; odds ratio 0.1515, 95% CI 0.0563-0.4079; P = 0.0002) and follow-up showed longer duration of survival before collapse or arthrodesis, compared to 34 ankles of the control patients with core decompression alone. Furthermore, the time to successfully achieve fusion after arthrodesis was significantly shorter in patients treated with bone marrow progenitors as compared with the other ankles, which had core decompression alone.

CONCLUSION:

In our study the early conservative surgical treatment with autologous bone marrow grafting improved the natural course of the disease as compared with core decompression alone