

towards improvement in designing hydrogel platforms suitable for clinical uses.

634

EFFICACY AND SAFETY OF UMBILICAL CORD-MESENCHYMAL STEM CELLS TRANSPLANTATION FOR TREATING OSTEOARTHRITIS

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Purpose: To investigate the efficacy and safety of UC-MSC (umbilical cord mesenchymal stem cells, UC-MSC) transplantation for osteoarthritis.

Methods: Three patients with knee osteoarthritis, admitted by our hospital from May 2016 to July 2016, were received UC-MSC transplantation once with total cellular number of UC-MSC was $5\sim 7 \times 10^7$ by intra-articular injection. These patients were followed up regularly for 3 months after transplantation. The clinical situation and recovery of knee joint function were observed.

Results: After transplantation the joint pain relieve significantly, the recovery of the ability of daily activities of the three patients improved obviously. No significant difference was observed when compared post-treatment with pre-treatment of biochemical parameters, which contains blood routine, hepatic function, renal function.

Conclusions: The intra-articular injection of UC-MSC transplantation could ameliorate clinical manifestations and delay progression of osteoarthritis. It may be safe and effective in the treatment of osteoarthritis, but further observation was still required to evaluate its long term efficacy.

635

MESENCHYMAL STEM CELL ANTIGENICITY IS SUPPRESSED IN AN INFLAMED JOINT ENVIRONMENT

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Purpose: Osteoarthritis (OA) is one of the leading causes of decreased athletic performance in people and horses. Treatment with autologous mesenchymal stem cells (MSCs) has been shown to be beneficial, but is subject to individual variability. Allogeneic MSCs would provide a more consistent and available product, that is not subject to age and patient variability as is seen with autologous MSCs. MSCs were traditionally considered immunoprivileged, and MHC class II negative. However, recently it has been shown that MSCs express varying levels of MHC class II, and that expression is upregulated when exposed to IFN- γ . This suggests that MSCs could acquire antigenicity, particularly in an inflammatory environment. It is unknown whether other pro-inflammatory mediators, such as those encountered in an inflamed joint, could upregulate MHC class II expression and trigger an immune reaction. The aim of this study was to determine if MHC class II expression in equine MSCs would be altered when exposed to a pro-inflammatory environment similar to that in an osteoarthritic joint. The hypothesis was that MHC class II expression in equine MSCs would increase upon exposure to inflammatory cytokines (IL-1 β , TNF- α) present in acute joint disease.

Methods: To verify that qRT-PCR can be used as a surrogate measure of MHC class II cell surface expression, equine MSCs were stimulated with IFN- γ . MSCs from 4 horses were stimulated with IFN- γ (100 ng/ml). Cells were collected at 24, 48, and 96 hours, and MHC class I and II expression were analyzed using flow cytometry and qRT-PCR. To create conditioned media designed to mimic the environment in an inflamed joint, cartilage and synovium were collected from the femoropatellar, femorotibial, and scapulohumeral joints of one horse. Co-cultures were established with a synoviocyte monolayer and cartilage explants were suspended in a transwell. Samples were treated with IL-1 β (10 ng/ml), or standard media, for 24 hours. Media was replaced with standard MSC media, incubated for 48 hours, then collected and frozen. Control and IL-1 β conditioned media were tested on chondrocytes to confirm function activity by measuring MMP-13 expression using qRT-PCR. To determine if MHC class II expression was upregulated in response to pro-inflammatory cytokines, MSCs were plated and exposed to six different treatment medias: 1) standard MSC media, 2) control conditioned media, 3) IL-1 β conditioned media, 4) MSC media with IL-1 β (10 ng/ml), 5) MSC media with TNF- α (10 ng/ml), or 6) MSC media with IFN- γ (100 ng/ml). Cells were incubated with the selected media for 96 hours and qRT-PCR was performed to quantify changes in MHC class I and II expression along with other pro-inflammatory MSC cytokines and chemokines (IL-6, IL-8, CCL2, CXCL10). Differences in gene expression relative to control

were determined by using the $\log(2^{-\Delta\Delta CT})$ values and performing a linear mixed effects model with the horse as a random effect followed by a Tukey HSD test to control for multiple comparisons.

Results: Stimulation of MSCs with IFN- γ resulted in significantly increased expression of MHC class II on both flow cytometry (13-fold) and qRT-PCR (6,000-fold) in all horses by 96 hours. Incubation of chondrocytes with IL-1 β conditioned media resulted in an 11-fold increase in MMP-13 expression compared to control, confirming pro-inflammatory conditioned media was generated. MHC class II gene expression in MSCs was significantly decreased after exposure to IL-1 β conditioned media or media with IL-1 β , and was significantly not increased after exposure to IFN- γ . Neither control conditioned media nor TNF- α caused a change in MHC class II expression. There was variable expression of the cytokines and chemokines in response to the different media.

Conclusions: This study demonstrates that equine MSC MHC class II expression varies depending on the environment to which the cells are exposed. Cytokines known to be present in acute joint disease decrease MHC class II expression, and therefore, an inflamed joint may not increase the risk of developing an immune reaction to allogeneic MSCs.

636

A BIBLIOMETRIC ANALYSIS OF THE TOP 50 MOST CITED PAPERS IN CARTILAGE REGENERATION

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Purpose: The number of times an article has been cited has been used as a marker of its influence in a medical or surgical specialty. Regenerative Orthopaedics is widely becoming recognized as a new sub-specialty within Orthopaedic surgery. The top 50 most cited papers involving cartilage regeneration represent the most quoted level of evidence amongst this new sub-specialty. This study aimed to identify and analyze the 50 most cited articles in cartilage regeneration.

Methods: The Web of Science™ citation indexing service was utilized to determine the most frequently cited articles published after 1956 containing “cartilage regeneration” in the title. The 50 most frequently cited articles were selected. Articles were evaluated for several characteristics including number of citations, publication year, country of origin, institution, journal, publication type of article and authorship.

Results: The most frequently cited article received 576 citations and the least frequently cited article received 50 citations, with a mean of 113.36 citations per article. These citation classics were published in 34 high-impact journals, led by Biomaterials (9 articles). Of the 50 articles, 6 were clinical observational studies, 34 concerned basic science and 10 were review articles. The articles originated from 13 countries, with the United States contributing 17 articles, followed by Japan with 8 articles.

Conclusions: The most cited articles involving cartilage regeneration are detected in both experimental and clinical research fields. The high ratio of basic science to clinical articles reflects the infancy of this relatively new specialty and that further clinical research is required in this area.

Rehabilitation

637

GOOD LIFE WITH OSTEOARTHRITIS IN DENMARK (GLA:D™): A NATIONWIDE IMPLEMENTATION OF CLINICAL RECOMMENDATIONS OF EDUCATION AND SUPERVISED EXERCISE IN KNEE AND HIP OSTEOARTHRITIS

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Purpose: Substantial evidence highlights exercise and education as part of first line treatment. However, implementation in clinical practice is suboptimal with a minority of OA patients receiving appropriate care according to guidelines. Good Life with osteoArthritis in Denmark (GLA:D) was launched in 2013 with the overall aim of implementing the evidence-based recommendations of exercise and education in clinical practice thereby facilitating high quality care of people with OA. We here report the effects of GLA:D from 2013 to 2015 by using data from the national GLA:D registry.

Methods: GLA:D consists of three mandatory elements: 1) a 2-day course for physical therapists in private and public care held at the University of