SAT0055

SIMULATING THE PATHOGENESIS OF ARTHRITIS IN VITRO BY DEVELOPING A HUMAN-BASED MULTICOMPONENT 3D JOINT MODEL

A. Dameu1, T. Gaber1, T. Gaber1, T. Gaber1, T. Gaber1

1Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin Berlin, Berlin, 2ZMB GmbH, Bad Langensalza, Germany

Background: Our ultimate goal is to develop a valid human in vitro 3D joint model to simulate the pathogenesis of arthritis. The in vitro 3D joint model consists of different components including an osteogenic and chondrogenic part, the synovial fluid and the synovial membrane that contains all involved cell types and thus, to allow interactions between cells by cell contacts and signalling molecules.

Methods: For the osteogenic component of the 3D joint model, we populated β-tricalcium phosphate (TCP) mimicking the mineral bony part. For the chondrogenic part, we used mesenchymal stromal cells (hMSC) and coated the particles with an hMSC monolayer cell sheet to get a compact bone-like structure. Survival, adhesion and structural integrity of the cells were evaluated by Scanning Electron Microscopy (SEM). LIVE/DEAD staining and cellular release of LDH. Osteogenic differentiation was analysed by μCT for mineralization and on gene expression level using qRT-PCR.

Results: Modelling the articular cartilage component, we verified its chondrogenic phenotype by hematoxylin and eosin staining and its mineralization by picrosirius staining. Interestingly, co-cultivation of the osteogenic and chondrogenic part for up to 3 weeks demonstrated successful colonisation, connectivity and initial calcification implying a functional transitional bridging structure.

Conclusions: First steps towards the in vitro simulation of an arthritic joint based on a multi-component model confirm good cell vitality and phenotypic stability which indicates successful progression. To finalise the development of healthy joint model, we will combine the established parts to provide a suitable 3D multi-component joint model which enables us to study the efficacy of drug treatment in vitro.

Disclosure of Interest: None declared

SAT0056

OSTEOARTHRITIS SEVERITY IS REDUCED BY INTRA-ARTICULAR ADMINISTRATION OF HYDROGEN SULFIDE

E.F. Burguera1, 2, A. Vela-Anero1, T. Hermida-Gómez1, P. Filgueira-Fernández2, L. Gato-Calvo1, R. Mejide-Falda1, F.J. Blanco1, Rheumatology Research Group, Instituto de Investigación Biomédica de A Coruña, A Coruña, 2CIBER-BBN, Madrid, 3Cell Therapy and Regenerative Medicine Group, Dep. of Medicine, University of A Coruña, A Coruña, Spain

Background: Osteoarthritis (OA) is a chronic inflammatory disease leading to cartilage loss and eventual joint destruction. Exogenous supplementation of hydrogen sulphide (H2S) with synthetic salts in vitro models of OA has been shown to exert anti-inflammatory effects and to result in reduced cartilage degradation

Objectives: To evaluate the effects of administering an H2S-producing compound intra-articularly in an experimental model of OA.

Methods: Experimental OA was induced in Wistar rats by transecting the medial collateral ligament and removing the medial meniscus of the left knee. Right knees were used as control. Animals were randomised into 3 groups (3 rats per group). Group 1 (intra-articular sulphide, IS): A single intra-articular injection of GYY4137 (200 mM in saline, 50 ml) at day 7. Group 2 (intra-articular control, IC): A single intra-articularly injection of saline (50 ml) at day 7. Group 3 (Surgical control, C): No treatment.

Results: All 3 groups showed worse performance in the Rotarod test at day 7 after surgery. Number of falls was significantly increased (except in IC) and time to first st fall was reduced (table 1). At day 40, there was no significant improvement in either of these parameters in group C, while in IC the n# of falls had returned to pre-surgical levels. In IS there were significant improvements with respect to day 0 and both C and IC groups (table 1). Times to 1 st fall were also significantly better in the IS group vs. C and IC both at days 15 and 40. Histology showed no significant differences among groups in the lateral tibial plateau (TP) or femoral condyle (FC) separately or in the compartment as a whole. Conversely, MS in the medial compartment were significantly better in the IS group vs the C group, both when considering TP or FC separately, and for the whole compartment (figure 1). No significant differences were found among groups on the Krenn Scores.

Conclusions: Exogenous H2S administered intra-articularly (200 mM GYY4137 in 50 ml saline) can reduce the severity of cartilage destruction in an in vitro model of OA as compared to no treatment or a vehicle control. H2S also led to a reduction in pain levels as demonstrated by a performance test. Therefore, hydrogen sulphide is a viable pharmacological candidate for OA treatment and should be further tested, including human clinical trials.

Disclosure of Interest: None declared