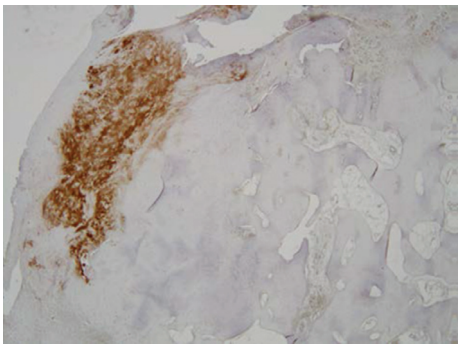
focally in degenerated cartilage and differentially in FJ with active bone marrow infiltrates. TrkA was primarily found in all bone marrows and capsular tissues but not in cartilage. TrkA expression colocalized with osteocalcin in subchondral bone, indicating an association with new bone formation. SP strongly positive cells were found in the bone marrow, cartilage and synovial tissue of all FJ.



Abstract AB0100 – Figure 1

Conclusions: Here we define for the first time tissue compartments of the NGF axis in human FOA. The findings indicate that neurogenic inflammation is prevalent in different compartments of FOA. Based on these data NGFi might be efficient by targeting inflamed joint capsule or subchondral bone marrow as a source of pain. NGFi may thus have an impact on bone remodelling. Further studies are needed to more precisely examine this mechanism.

REFERENCES:

[1] Seidel MF, Herguijuela M, Forkert R, Otten U. Nerve growth factor in rheumatic diseases. Semin Arthritis Rheum. 2010;40(2):109–26.
[2] Netzer C, Urech K, Hügle T, Benz RM, Geurts J, Schären S. Characterization of subchondral bone histopathology of facet joint osteoarthritis in lumbar spinal stenosis. J Orthop Res. 2016;34(8):1475–80.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.4157

AB0101 MESENCHYMAL STEM CELLS DERIVED FROM BONE MARROW, UMBILICAL CORD AND ADIPOSE TISSUE DO NOT HAVE THE SAME EFFECT ON HUMAN OSTEOARTHRITIC CARTILAGE

N. Alaaeddoine[1], N. saliba[2], M. moussa[3], G. hilal[3], C. khalil[3], G. haykal[3].
[1]CRCHUM, Lab of Cellular and Molecular Immunology, Montreal, Canada; *[2]Regenerative and Inflammation lab, Hotel Dieu de France*; *[3]Regenerative and Inflammation Lab, Laboratory of Regenerative Medicine, Faculty of Medicine, St. Joseph University, Beirut, Lebanon*

Background: Osteoarthritis is a chronic debilitating disease characterised by degeneration of cartilage, synovitis and osteophytes formation.[1] This disease does not only affect aged people but it afflicts also young athletes where until today no medications has proven efficacy in stopping the progression of the disease and/or regenerate the loss of cartilage.[2] Recently cell therapy has attracted attention in many medical fields and especially in rheumatology and orthopaedic specialty. Stem cells due to their differentiation capacity, trophic and paracrine effects have been shown to serve as promising new modality in treating osteoarthritis.[3,4]
Objectives: Our objective in this study is to investigate the effect and mechanism of action of the three sources of stem cells; bone marrow derived stem cells (B-MSC), adipose derived stem cells (A-MSC) and umbilical cord stem cells (U-MSC) on osteoarthritic chondrocytes.
Methods: Mesenchymal stem cells were isolated from bone marrow, adipose tissue and umbilical cord from 5 different donors respectively and cocultured with human osteoarthritic chondrocytes obtained from 5 patients undergoing total knee arthroplasty. The effect autophagy was determined using flow cytometry analysis. Quantitative polymerase chain reaction (qPCR) and ELISA were used to measure the changes in the major factors playing a role in OA such as(a disintegrin and metalloproteinase with thrombospondin motifs-5(ADAMDTS-5), Metalloproteinases (MMP-3, MMP13), tissue inhibitor of metalloproteinases (TIMP-1–2–3), Collagen, Cox-2, Il-6, the regulators of autophahy FOXO1, FOXO3, and LC3II and Beclin I in the tissues and cocultured media.
Results: In our study we found that the three stem cells sources increased significantly the proliferation of chondrocytes, and increased autophagy via increasing Beclin 1 and LC3II, along with its regulators FOXO1, FOXO3 in human osteoarthritic chondrocytes with $p<0.05$. Furthermore, the three sources of stem cells caused a dose dependent significant decrease in MMP-3, MMP-13, ADAMTS-5, IL-6, CCL20 and COX-2 with $p<0.05$. Aggregan, collagen, TIMPs were also significantly increased by the co-culture of A-MSC, B-MSC, U-MSC.
Conclusions: These results suggest that stem cells could be a promising therapeutic target for the treatment of osteoarthritis.

REFERENCES:

[1] Soler R, et al. Final results of a phase I-II trial using ex vivo expanded autologous mesenchymal stromal cells for the treatment of osteoarthritis of the knee confirming safety and suggesting cartilage regeneration. Knee 2016;23(4):647–6541.
[2] Lagorce T, Buxeraud J, Guillot X. Comprendre l'arthrose. Actual Pharm 2016 Apr;55(555):18–22.
[3] Martel-Pelletier J, Wildi LM, Pelletier J-P. Future therapeutics for osteoarthritis. Bone 2012 Aug;51(2):297–311.
[4] Orozco L, Munar A, Soler R, Alberca M, Soler F, Huguet M, et al. Treatment of knee osteoarthritis with autologous mesenchymal stem cells: A pilot study. Transplantation 2013 Jun 27;95(12):1535–41.
[5] Soler R, et al. Final results of a phase I-II trial using ex vivo expanded autologous mesenchymal stromal cells for the treatment of osteoarthritis of the knee confirming safety and suggesting cartilage regeneration. Knee 2016;23(4):647–654.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.1747

AB0102 THE GINGER DERIVATIVE 6-SHOGAOL AS A TREATMENT IN OSTEOARTHRITIS.MODULATION OF CHONDROCYTE HYPERTROPHY AND MATRIX CALCIFICATION

P. Gratal, A. Lamuedra, A. Mediero, G. Herrero-Beaumont, R. Largo. *IIS-Fundación Jiménez Díaz UAM, Madrid, Spain*

Background: Osteoarthritis (OA) is a complex joint disease characterised by a progressive lost of articular cartilage (AC), synovial inflammation and subchondral bone alterations. The latest theories of OA pathogenesis implicate the interplay between mechanical damage and chronic inflammation that has been associated to the activation of the innate immune system, intricately involved in the development of this low-grade inflammation. During the course of OA, Toll like receptor (TLR) activation has been related to the release of cytokines and inflammatory mediators, which further aggravate synovitis and AC damage.[1] In this scenario, hyaline chondrocytes seem to acquire a hypertrophic-like phenotype associated to AC degradation. 6-shogaol (6S), an effective anti-inflammatory Ginger derivative, is able to inhibit TLR4-mediated innate immune responses.[2]
Objectives: Our aim was to study the therapeutic benefit of 6-shogaol studying its anti-inflammatory effects in an OA mice model, and in the modulation of hypertrophic markers in chondrocyte cultures.
Methods: C57BL/6 male mice were randomly assigned to two groups: control (n=7) and OA (n=17). OA was induced by transection of the medial menisco-tibial ligament. Nine OA mice started receiving 6S (15 mg/kg/day; OA +6S) since surgery. After 8 weeks, animals were euthanized and joints were collected. Chondrogenic differentiation was induced *in vitro* in the pre-chondrogenic cell line ATDC5 in presence or absence of 5 × 10–6M 6S. Gene expression of hypertrophic markers, as well as mineralization and proteoglycan synthesis were determined.
Results: Both synovial inflammation and AC damage were more severe in OA animals (Control: 0.1±0.1; OA: 3.0±0; $p<0.005$, and Control: 0.5±0.2, OA: 5.4 ±0.6; $p<0.005$, respectively) with a significant reduction in OA+6S animals (2.4 ±0.2; $p<0.05$ and 2.6±0.5 $p<0.01$ vs. OA, respectively). Collagen X and MMP13 immunohistochemistry showed an increase in the AC of OA and OA-6S mice, while a significant reduction was found in 6S-treated mice (ColX: Control: 0.13 ±0.03, OA: 0.93±0.1; OA-6S: 0.43±0.1; $p<0.05$ and MMP13: Control: 0.35±0.1, OA: 0.68±0.1, OA-6S: 0.28±0.07, $p<0.05$). Similar results were found in the synovium and meniscus for these two markers. 6S was able to significantly inhibit the expression of Collagen X, Ihh and MMP13 in ITS-stimulated cells after 14 and 21 days of culture. Furthermore, 6S prevented the increase in mineralization and proteoglycan synthesis in ITS-stimulated ATDC5 cells after 14 days of culture ($p<0.05$), as seen by Alizarin red and Alcian blue staining, respectively.
Conclusions: Our results showed that 6S significantly prevented cartilage degradation and synovial inflammation, in parallel to a reduction in the presence of hypertrophic markers in the cartilage of OA mice. *In vitro*, 6S inhibited the chondrogenic differentiation of ATDC5 cells. These results suggest that 6S could work as a good treatment in OA both inhibiting differentiation markers and reducing the severity of joint damage in an OA murine model.

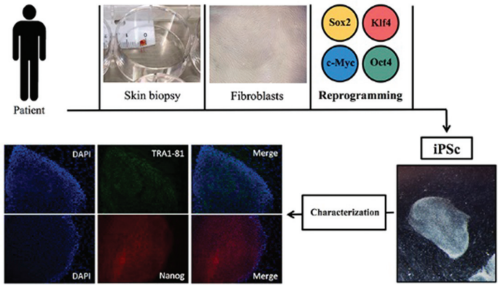
REFERENCES:
[1] Gómez R, et al. Nat Rev Rheumatol 2015.
[2] Villalvilla A, et al. J Mol Nutr Food Res 2013.

Disclosure of Interest: P. Gratal: None declared, A. Lamuedra: None declared, A. Mediero Grant/research support from: CP15/00053 PI16/00991, G. Herrero-Beaumont Grant/research support from: PI16/00065, R. Largo Grant/research support from: PI15/00340
DOI: 10.1136/annrheumdis-2018-eular.4689

AB0103 ESTABLISHMENT OF A HUMAN INDUCED PLURIPOTENT STEM CELL-LINE FROM PATIENTS WITH HAND OSTHEOARTHRITIS

R. Castro-Viñuelas[1], C. Sanjurjo-Rodríguez[1], M. Piñeiro-Ramil[1], T. Hermida-Gómez[2], I.M. Fuentes-Boquete[1], F.J. De Toro-Santos[1], F.J. Blanco-García[3], S. M. Díaz-Prado[1]. *[1]Biomedical Sciences, Medicine and Physiotherapy, University of A Coruña*; *[2]Unidad de Bioingeniería Tisular y Terapia Celular (GBTTC-CHUAC). Grupo de Investigación en Reumatología*; *[3]Grupo de investigación en Reumatología., Instituto de Investigación Biomédica de A Coruña, A Coruña, Spain*

Background: To date, there is no drug able cure such a prevalent disorder as it is hand osteoarthritis (OA). Cell therapies using stem cells have emerged as a promising strategy to explore and develop new treatments. Specifically, induced pluripotent stem cells (iPSc) are considered ideal tools not only for this purpose, but also for modelling the disease. The advantages of using an established iPSc line are unlimited cell source with regeneration capacity and chondrogenic differentiation potential. However, there are not many studies published generating iPSc from patients with hand OA.
Objectives: The aim of this study has been to generate an iPSc-line from human fibroblasts obtained from patients with radiographic hand OA, which can be useful for drug discovery, disease modelling and regenerative medicine applications.
Methods: Patients with radiographic hand OA and a healthy control were selected for the study. Using the explant culture technique, fibroblasts from 3 mm skin biopsies of these patients were isolated. These cells were histologically characterised and positivity for fibroblast markers was quantified. These cells were also karyotyped in order to confirm that chromosomal abnormalities did not exist before reprogramming. Four transcriptional factors were used for the reprogramming process: Oct4, Sox2, Klf4 and c-Myc. These were delivered using a non-integrative methodology that involves the use of Sendai virus. Cell lines obtained were clonally expanded over 20 passages and characterised for pluripotency markers by immunohistochemistry and RT-PCR, before and after reprogramming (figure 1). The best two clones of each one of the patients were selected according to the expression of the pluripotency markers to establish the cell-line.
Results: Cells were isolated from skin biopsies of two patients with radiographic hand OA and one healthy donor. Histological and immunohistochemical analyses showed that the 85%–95% of cells in the culture were fibroblasts, which presented a normal karyotype: 46, XX. Three weeks after reprogramming, embryonic stem cell-like colonies emerged in culture. These cells were positivity stained for alkaline phosphatase activity and the pluripotency markers Tra1–81 and Nanog. Alkaline phosphatase staining shows in blue the colonies correctly reprogrammed. Molecular analyses showed high relative expression levels of the endogenous pluripotency associated genes OCT4, SOX2, KLF4, NANOG and CRIPTO in the iPSc, but not in the no-reprogrammed fibroblasts. No presence of Sendai Virus-related genes was detected.



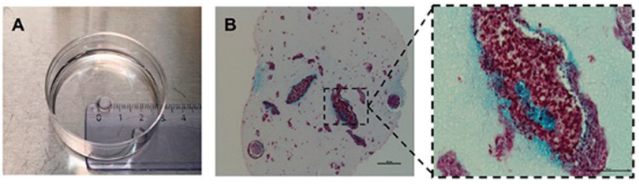
Abstract AB0103 – Figure 1

Conclusions: Fibroblasts were successfully isolated from all the patients. The reprogramming process using Sendai virus enabled us to generate iPSc from two patients with radiographic hand OA and one healthy donor.
Acknowledgements: Fundación Española de Reumatología; CIBER-BBN; REDICENT; GPC (Xunta de Galicia); Diputación da Coruña; Xunta de Galicia y Fondo Social Europeo, Servicio de genética del Hospital Teresa Herrera; Servicio de Radiofísica del Centro Oncológico de Galicia, Universidade da Coruña.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.4585

AB0104 CARTILAGE-LIKE TISSUE GENERATION BY 3D-BIOPRINTING OF INDUCED PLURIPOTENT STEM CELLSIN A MODIFIED NANOCELLULOSE/ALGINATE BIOINK

R. Castro-Viñuelas[1], A. Forsman[2], E. Karabulut[3], E. Romberg[3], C. Brantsing[2], M. Brittberg[4], A. Lindahl[2], P. Gatenholm[3], S. Simonsson[2]. *[1]Biomedical Sciences, Medicine and Physiotherapy, University of a Coruña, A Coruña, Spain*; *[2]Clinical Chemistry and Transfusion Medicine, Institute of Biomedicine at Sahlgrenska Academy. University of Gothenburg*; *[3]Chemistry and Chemical Engineering, 3D Bioprinting Center. Chalmers University of Technology, Gothenburg*; *[4]Cartilage Repair Unit, University of Gothenburg, Region Halland Orthopaedics, Kungsbacka Hospital, Kungsbacka, Sweden*

Background: Today, several hundreds of million people all over the world are suffering from different joint disorders; like osteoarthritis (OA). Further, traumatic cartilage lesions can develop into OA. Recent studies indicate that human-derived induced pluripotent stem cells (iPSCs) can be 3D bioprinted and directed to form cartilage-like tissue, thus offering new approaches to treat cartilage lessions.[N-guyen *et al.* 2017] The advantages of using an established iPSC line are unlimited cell source with regeneration capacity and chondrogenic differentiation potential.
Objectives: The aim of this study was to improve the generation of cartilage-like tissue when 3D bioprinting of iPSCs by using molecularly modified nanocelullose/alginate bioink to resemble natural environment found in the tissue.
Methods: In this study the chondrocyte-derived iPSC line "A2B" was used (Borestrom *et al.* 2014). These cells were bioprinted in combination with a modified nanocellulose and alginate bioink. Constructs obtained after the 3D bioprinting were cultured in chondrogenic medium in order to stimulate chondrogenic differentiation. Cell number and viability inside the prints was studied and histological analyses of the 3D printed constructs were performed. Furthermore, expression of pluripotency and chondrogenic specific genes was assessed by Taqman qPCR before and after differentiation.
Results: After 3D bioprinting high cell viability was found inside the constructs. 3D printed constructs were positively stained for alcian blue van gieson (AB-vG) staining, showing proteoglycans presence inside the prints (figure 1B). Molecular analyses showed high relative expression levels of the pluripotency-related gene Oct4 before starting the differentiation protocol. Cells inside the constructs express chondrogenic specific genes, such as collagen type 2 and Sox9 after 6 weeks of differentiation. Moreover, 3D printed constructs showed cartilage-resembles (figure 1A).



Abstract AB0104 – Figure 1

Conclusions: The 3D printing of the iPSc and the *in vitro* generation of cartilage-like tissue was successfully achieved using the modified nanocellulose/alginate bioink. This approach could be use in the future to model OA disease and to perform screenings of different therapeutic compounds.

REFERENCES:
[1] Nguyen D, et al. Cartilage Tissue Engineering by the 3D Bioprinting of iPS Cells in a Nanocellulose/Alginate Bioink. Sci Rep 2017;7(1):658.
[2] Borestrom C, et al. Footprint-free human induced pluripotent stem cells from articular cartilage with redifferentiation capacity: a first step toward a clinical-grade cell source. Stem Cells Transl Med 2014;3;433–447.

Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.4724