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

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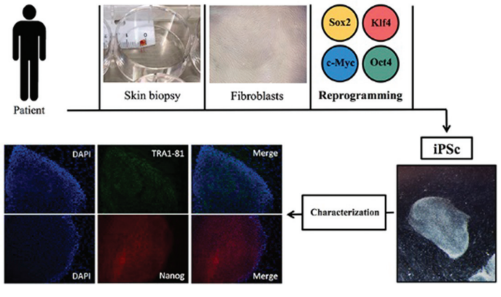
Background: To date, there is no drug able cure such a prevalent disorder as it is hand osteoarthritis (OA). Cell therapies using stem cells have emerged as a promising strategy to explore and develop new treatments. Specifically, induced pluripotent stem cells (iPSc) are considered ideal tools not only 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.
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AB0104 CARTILAGE-LIKE TISSUE GENERATION BY 3D-BIOPRINTING OF INDUCED PLURIPOTENT STEM CELLSIN A MODIFIED NANOCELLULOSE/ALGINATE BIOINK

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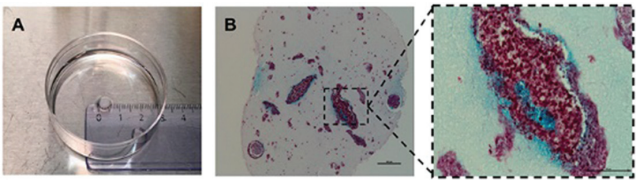
Background: Today, several hundreds of million people all over the world are suffering from different joint disorders; like osteoarthritis (OA). Further, traumatic cartilage lesions can develop into OA. Recent studies indicate that human-derived induced pluripotent stem cells (iPSCs) can be 3D bioprinted 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.

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