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Nanofibrillar cellulose for 2D and 3D culturing of human adipose derived mesenchymal stromal/stem cells

INTRODUCTION:

For wound healing, cell transplantation provides a potential therapeutic strategy. However, cell survival and retention in the wound is a challenge to be overcome. A supporting material acting as a scaffold for the cell seeding and the subsequent transplantation into the body could increase the potential of a cell transplant.

AIM:

To characterize human adipose derived mesenchymal stromal/stem cells (hASCs) during 2D and 3D culturing on wood derived nanofibrillar cellulose (NFC) based wound dressing or when embedded in NFC GrowDex® hydrogel, respectively, in order to develop efficacious cell transplantation method for wound treatment.

MATERIALS AND METHODS:

NFC dressing and hydrogel (GrowDex®) were obtained from UPM Kymmene, Finland. hASCs from ATCC and patient origin hASCs were used for 2D assays. Patient cell isolation and use is approved by the Ethics Committee (Pirkanmaa Hospital District, Tampere, Finland, N:o R15161). hASCs from Lonza were used for 3D culturing. Cells were cultured in DMEM or MEM α nucleosides medium supplemented with 6% human serum, 2D cells on sterile reinforced 50% NFC (Type 3) dressing. For 3D culture, cells were embedded in 0,125% NFC-hydrogel (diluted from GrowDex®). Control cells were seeded on plastic culture dishes. Cell viability was measured using alamarBlue® and cytotoxicity using Pierce LDH Cytotoxicity Assay. Cytokine secretion was measured by ELISA. Vimentin staining was performed using antibody sc-6260 (Santa Cruz) diluted 1:150.

RESULTS:

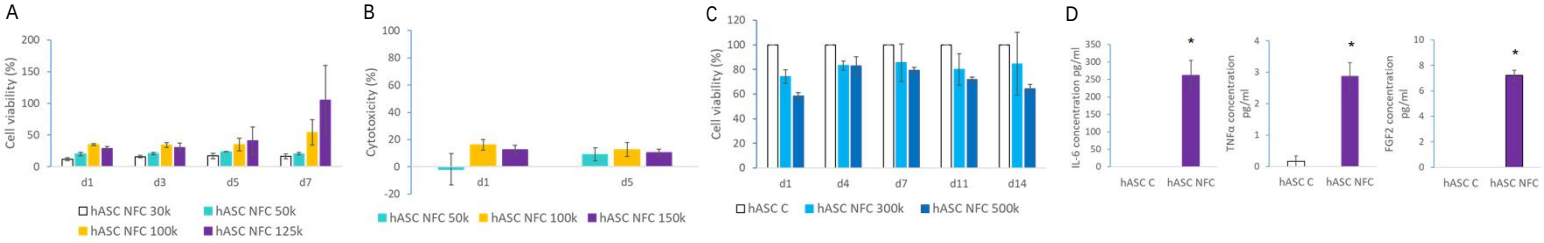

Figure 1. 2D culturing of hASCs on NFC dressing. A) Cell viability of hASCs at different cell densities. Low cell viability is observed with densities 30k (30 000 cells/cm2)-125k. B) Cytotoxic effect of NFC on hASCs. Culturing of hASCs on NFC dressing does not induce remarkable cytotoxicity. C) Cell viability of hASCs at higher cell densities (300k, 500k. High cell viability is observed for 14 days especially at density 300k. D) Cytokine secretion of IL-6, TNF-α and FGF2 is increased in hASCs (10k) cultured on NFC dressing compared to control cells (hASC C). Values are mean (±SEM), n=2-4.*p<0.05.

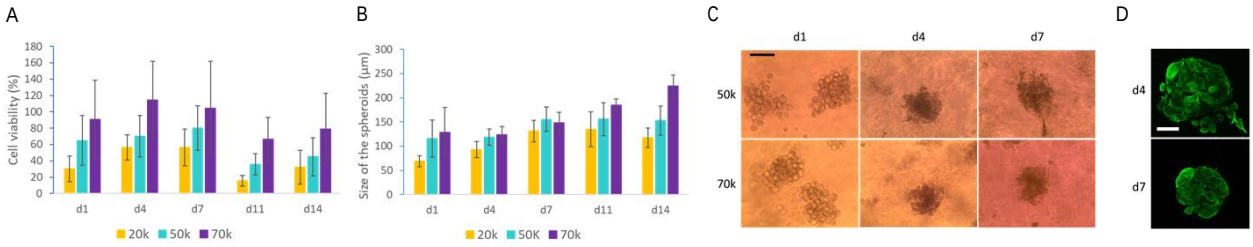

Figure 2. 3D cultures of hASCs in 0.125% NFC GrowDex® hydrogel. A) Cell viability of hASCs at different cell densities. High cell viability is observed with density of 70k for 7 days. B) Size of the hASC spheroids remains mainly between 100-200 µm with densities of 50k and 70k. C) Light microscopy images of the spheroids on days 1, 4 and 7 with densities of 50k and 70k. D) Immunocytochemistry of the spheroids with Vimentin antibody on days 4 and 7. Scale bars 100 µm. Values are mean (±SEM), n=2-4.

CONCLUSIONS:

- NFC dressing offers efficient culture conditions for hASCs without any cell adhesion coatings
- Culturing hASCs on NFC dressing may increase hASCs' potential to enhance wound healing process
- Encapsulation of hASCs in NFC GrowDex® hydrogel supports the formation and growth of cell spheroids that maintain their expression of mesenchymal marker vimentin
- NFC may prove to be a successful cell scaffold for cell transplantation but better understanding of cell-biomaterial interactions are still required

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