MICROFABRICATION OF A 3D NICHOID WITH SPECIFIC GEOMETRY FOR THE EXPANSION OF HUMAN MESENCHYMAL STEM CELLS

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Introduction

In the body, stem cells (SCs) reside in a specialized niche, characterized by a unique combination of biophysical and biochemical properties. Together, these features allow the maintenance of stemness. Recently, biomaterials have been used to create 3D scaffolds, which mimic the biomechanical characteristics of SCs niches. Raimondi and colleagues applied two-photon polymerization (2PP) technique to fabricate a 3D micro-scaffold, called Nichoid [1], in order to promote cellular proliferation and maintain stemness capabilities without adding any exogenous additive. The Nichoid has the ability to maintain stemness in several stem cells types, to induce the expression of pluripotency genes and potentiate the therapeutic potential of neural SCs [2,3]. Adipose-Derived Stem Cells (ADSCs) represent a promising source for cell therapies because their availability is less invasive compared to the one from other organs or tissue. Indeed, the aim of this study was to investigate the proliferation and stemness properties of human ADSCs expanded in engineered niches with a specific configuration to guarantee isotropic stimuli.

Materials and Methods

Nichoids were fabricated by 2PP using a hybrid organic-inorganic photoresist. The laser source presented in this work is a commercial femtosecond laser with a wave-length of 1042 nm and 1 MHz repetition rate [4]. hADSCs were isolated from lipoaspiarate adipose tissue and elective liposuction procedures were performed in voluntary patients after having received their informed consent.

The validation of the new cubic pore configuration of the scaffold was started by expanding $6x10^3$ hADSCs for 7 days. Then, cells expanded inside the cubic Nichoid have been characterized by viability assay, Real Time PCR and immunofluorescence analysis. Furthermore, neural differentiation was also investigated (Figure 1).

Results

The expansion inside the 3D micro-scaffold permits the potentiation of stemness features by upregulating the expression of pluripotency genes. These observations are in line with the nuclear measurements, confirming the cubic pore Nichoid's ability to induce isotropic cytoskeletal tension which resulted in a roundish nucleus. Furthermore, with this structure of the Nichoid, hADSCs can be efficiently detached and collected in order to be transplanted.

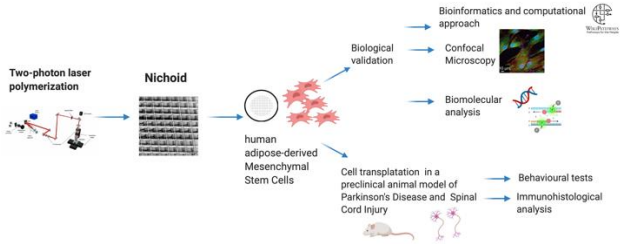

Figure 1: experimental set up of hADSCs expanded inside the cubic pore Nichoid

Discussion

These results represent an incredible improvement needed to reach the biological and clinical demands. Moreover, this approach can be applied also to fabricate any kind of porous Nichoid with different geometries, suitable for different stem cells. In particular, our findings represent a great promise for the Nichoid's application in the field of regenerative medicine, in particular in neurodegenerative diseases as Parkinson's disease and Spinal Cord Injury.

References

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Acknowledgements

European Research Council (ERC projects NICHOID, G.A. 646990, NICHOIDS, G.A. 754467, and MOAB, G.A. 825159); European Commission (FET-OPEN project IN2SIGHT, G.A. 964481); European Space Agency (ESA project NICHOID-ET, G.A. 4000133244/20/NL/GLC); National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs projects MOAB, G.A. NC/C01903/1 and NC/C019201/1); Italian Ministry of University and Research (MIUR-FARE project BEYOND, G.A. R16ZNN2R9K); Fondazione Social Venture Giordano Dell'Amore, Cariplo Factory, Politecnico di Milano, Fondazione Bassetti and Fondazione Triulza (S2P project EGGS&BEACON) and Fondazione Romeo ed Enrica Invernizzi.