

Therapeutic Effect of Neural Progenitor cells expanded in the 3D nano-engineered Nichoid substrate in a Parkinson's disease preclinical model

S. Carelli^{1,2}, T. Giallongo¹, F. Rey¹, T. Zandrini³, G. Cerullo³, R. Osellame³, A.M. Di Giulio^{1,2}, M.T. Raimondi⁴

Presenting Author: Stephana Carelli, stephana.carelli@unimi.it

¹Department of Health Sciences, University of Milano, 20142, Milano Italy, ²Pediatric Clinical Research Center Fondazione "Romeo ed Enrica Invernizzi", University of Milan, Milan, Italy. ³Istituto di Fotonica e Nanotecnologie (IFN)-CNR and Department of Physics, Politecnico di Milano, Milano, Italy. ⁴Department of Chemistry, Materials and Chemical Engineering "Giulio Natta", Politecnico di Milano, Milano, Italy.

INTRODUCTION: The use of biomaterials allows to generate active biophysical signals for directing stem cell fate through 3D microcaffolds, such as the one named "Nichoid" [1]. The aim of this study was to investigate: i) the proliferation, differentiation and stemness properties of neural precursor cells (NPCs) [2, 3] following their cultivation in the Nichoid substrate; ii) the therapeutic effect and safety *in vivo* of NPCs cultivated in the Nichoid in preclinical experimental model of Parkinson's Disease (PD).

METHODS: Nichoids were fabricated by 2PP onto circular glass coverslips using a home-made SZ2080 photoresist. NPCs were grown inside the Nichoid for 7 days (1×10^4 cells/cm²), counted and characterized with immunofluorescence, western blot, and Real Time PCR analysis. NPCs were transplanted in a murine experimental model of PD after a 7 days' growth inside the Nichoid. Parkinsonism was induced by the intraperitoneal administration of MPTP in C57/bl mice (Fig.1) [3].

RESULTS: NPCs grown inside the Nichoid create a 3D carpet expanding inside the scaffold. 7 days after plating, cells grown inside the Nichoid show a significantly higher cell viability and proliferation than in normal floating culture conditions. Furthermore, after being re-plated in floating conditions for 7 more days, the cells formed smaller but more abundant neurospheres respect to control. The replated cells, analyzed by immunofluorescence, Real Time-PCR and Western blot, demonstrate an increase in stemness markers. The therapeutic potential and safety of Nichoid-grown NPCs was evaluated by their intrastriatal infusion (7×10^4 cells) in the brain of PD affected mice. Behavioral performances were evaluated with two different tests showing that Nichoid-grown NPCs promoted the recovery of PD

symptoms better than NPCs maintained in normal floating conditions.

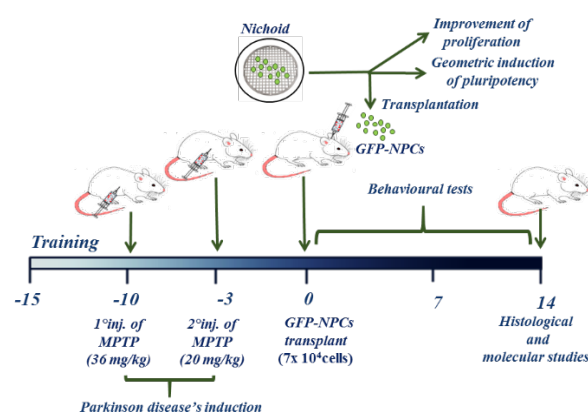


Figure 1: Experimental plan applied for the therapeutic effect evaluation of Nichoid-grown NPCs in a preclinical model of PD.

DISCUSSION & CONCLUSIONS: Stem cells demonstrated an increase in stemness potential when grown inside the Nichoid, showing great promise and strong application in the field of regenerative medicine applied to neurodegenerative disease.

ACKNOWLEDGEMENTS: Financial support was received from "Neurogel-en-Marche" Foundation (France) to SC; Fondazione "Romeo and Enrica Invernizzi" to AMDG. ERC grant NICHOID, G.A. 646990 and NICHUIDS, G.A. 754467.

REFERENCES

- [1] Raimondi et al. Acta Biomater. 2013;9(1):4579-84.
- [2] Carelli et al. Cell Transplant. 2015;24(4):703-19.
- [3] Carelli et al. Neuropharmacol. 2017;119:76-90.