Fabrication of a 3D combinatorial fibrous-porous scaffold for neural tissue engineering applications

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***Abstract*— The ability of tissue engineered scaffolds to modulate the response of neural stem cells (e.g. adhesion, proliferation and differentiation) is boosting the unlocking of advanced therapeutic strategies capable of attenuating the effects of traumatic pathologies like spinal cord injury [1]. From the wide range of reported scaffolding concepts, it has been consistently demonstrated that nanofibrous networks and graphene-based porous systems are proficient for guiding neurite outgrowth and inducing specific differentiation patterns, respectively [2].**

Taking this into account, we propose a scaffold with a combinatorial fibrous-porous architecture with the final goal of recreating *in vitro* a 3D cellular microenvironment suitable to promote a noticeable impact in the viability and differentiation of the cultured embryonic neural progenitor cells (ENPCs). Briefly, electrospinning was used to fabricate biocompatible polycaprolactone-gelatin (PCL-gelatin) nanofibres with diameter of 200 nm. Such electrospun mesh was then accurately cut into small pieces and mixed into a reduced graphene oxide (rGO) aqueous solution with the intent of generating a hydrogel-like structure. Finally, it was possible to accommodate the nanofibres onto the surface of a 3D rGO microporous network after a controlled lyophilization process. Results showed that as the PCL-gelatin nanofibres covered uniformly the surface of the rGO sheets, the mechanical integrity of the scaffold was reinforced without compromising its 3D interconnected porosity and water uptake capability. Additionally, these complementary morphological features were responsible for inducing synergistic functionalities since the ENPCs were able to adhere onto the surface of the scaffold and efficiently differentiate into viable neuronal and glial cell types. In this way, during 14 days in cell culture, the biochemical and topographical cues provided by the fibrous-porous geometry were capable of stimulating neurite outgrowth and elongation through the scaffold, leading, consequently, to the formation of an interconnected neural network.

Taking this into account, the reported scaffolding approach presents potential not only to support therapeutic neural regenerative approaches, but also to contribute to a better understanding of key factors related to the repair of the central nervous system after injury.

Keywords*— *Neural tissue engineering; Fibrous-porous scaffold; electrospinning; polycaprolactone; reduced graphene oxide

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TOPIC

2) a.: Technologies for the Wellbeing – Multiscale Technologies and Devices for Medicine, Environment and Energy.

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