# Decellularized extracellular matrix-based 3D nanofibrous scaffolds functionalized with polydopamine-reduced graphene oxide for neural tissue engineering

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One of the exciting prospects of using decellularized extracellular matrices (ECM) lies in their biochemical profile of preserved components, many of which are regeneration permissive. Herein, a decellularized ECM from adipose tissue (adECM) was explored to design a scaffolding strategy for neural tissue engineering. Targeting the recreation of the nano-scaled architecture of native ECM, adECM was first processed into nanofibers by electrospinning to produce bidimensional platforms. These were further shaped into three-dimensional nanofibrous constructs by gas foaming. The conversion into a 3D microenvironment of nanofibrous walls was assisted by blending the adECM with lactide-caprolactone copolymers, which allow to fine tune the 3D nanofibrous constructs, that exhibit structural stability, adequate microporosity and mechanical compliance with soft neural tissues.

In culture, neural stem cells (NSCs) responded differently depending on the adECM-based architecture: nanofibrous 2D or nanofibrous 3D design. Although broadly exploited, 2D membranes are hardly effective platforms to test neural stem cells response in a physiological-like environment. Gas foaming emerges as a straightforward technique to produce 3D nanofibrous constructs, so that when testing novel biomaterials, it readily provides a 3D microenvironment, that reveals biomaterial-induced effects which otherwise could remain unperceived. Indeed, the 3D spatial arrangement of the adECM-based nanofibers – induced by gas foaming – exhibited a remarkable effect on NSCs' phenotype determination and neurite formation, thereby reinforcing the critical importance of engineering scaffolds with multiple length-scale architecture.

In view of boosting their performance to guide neural stem cell fate, adECM-based platforms were doped with a bioinspired surface modification relying on polydopamine-functionalized reduced graphene oxide (PDA-rGO), which significantly promoted neuronal differentiation and neuritogenesis.

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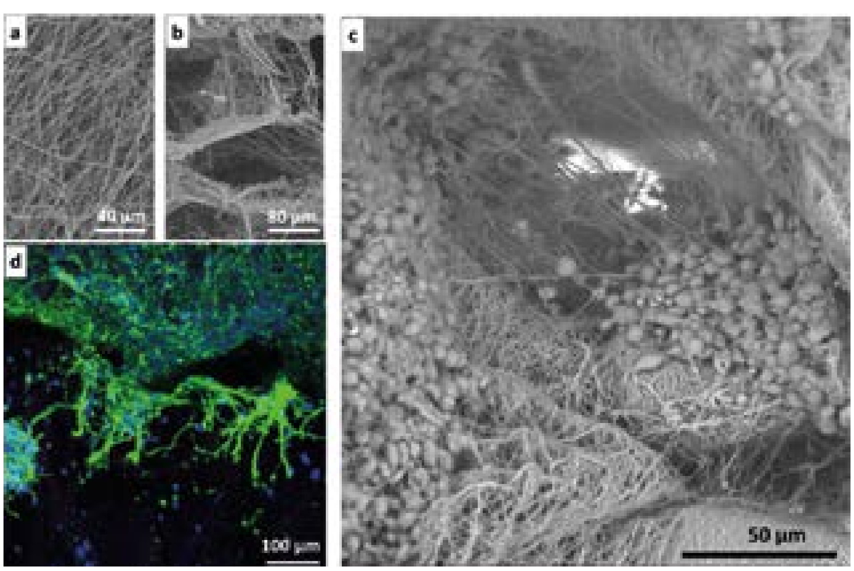


FIGURE 1
a) SEM of 2D nanofibrous adECM-based membrane; b) SEM of 3D nanofibrous construct; c) SEM showing NSC migration and growth within the 3D constructs; and d) confocal imaging of neuronal differentiation.