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Directional and asymmetric micro-structured substrates for applications in neuro-pathological models

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In the nervous system, during tissue development or regeneration, neural cells read extracellular stimuli from the micro/nano-environment within which they exist, retrieving essential directionality and wiring information. Controlling and improving neural cell migration and neurite outgrowth are critical elements for tissue engineering applications and for developing artificial neural interfaces. In recent years, nano/micro-structured substrates are emerging as powerful tools for investigating and tailoring these mechnotransduction processes. Neural cells can recognize and interact with directional nano/microtopographies, changing their neural type from multipolar to bipolar with aligned neurites. More specifically, we have demonstrated that nano/micro-gratings (GRs), ranging from ultra-small topographies to boundary guidance regimes, are capable to direct and guide both neuronal and glial cell differentiation, polarization, and migration.
Regenerative medicine is facing new challenges and it is searching for new biocompatible, natural polymer materials. Chitosan is emerging as a promising biopolymer for tissue engineering thanks to its biocompatibility and biodegradability. Remarkably, it is FDA approved for several medical uses. In this framework, the repair of peripheral nerve lesions is a clinical problem where the functional recovery is often far from being satisfactory, although peripheral nerves generally retain good potential for regeneration.
Here, we show that it is possible to obtain, by solvent casting, chitosan thin films with good mechanical properties and to structure them at the microscale and down to the nanoscale level. We developed novel directional micro-geometries, with different levels of axial symmetry: GRs, zigzag patterns composed by isosceles triangles (ISO), and zigzag patterns composed by scalene triangles (SCA). These chitosan membranes were tested *in vitro* with Schwann cells (SCs), which play a primary role during regeneration of injured nerves. The directional patterns were efficient in directing cell growth and migration: the less symmetric topographies (SCA) polarized less efficiently the cell shaping but promoted a faster cell migration of cells, both singularly and collectively. Overall, SCA chitosan membranes showed enhanced healing response.
In conclusion, these results provide new knowledge for the fabrication of new biodegradable scaffolds that have better performances in peripheral nerve regeneration.

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