Nanosurfaces Scaffold and Magnetic Nanoparticles to Direct the Neuronal Growth Process: Future Strategies for Peripheral Nerve Regeneration.

Peripheral nerves injuries are common lesions than often cause loss of function and poor outcome. Current strategies to nerve repair take advantage by microsurgical suture. In case of severe nerve gap (>50mm), the gold standard remains the autologous graft. The limits of this technique are: functional damage at the donor site, double surgical access and the lack of large amounts of grafts.

In response to injury, Schwann cells (SC) take advantage to extracellular matrix (ECM) connection, proliferate in organized structures (bands of Büngner) and guiding axons during regeneration offering mechanical support and growth factors.

Recently, researchers focused on two main areas of investigation: the role of the interaction between cells with the extracellular membrane (ECM) and the forces acting during axonal elongation.

Both phenomena are strictly dependent on the mechanical cell guidance mediated via the focal adhesion (FA) connection complexes. The trans-membrane receptors (integrin) are the starter of cell adhesion with the contact to extracellular proteins; later, in the inner part of cell, initial linkage to actin fibres of the cytoskeleton forming mature FAs complexes. Therefore, new protrusions are extending only from regions with successful FAs formation focusing the direction of cell motion in that direction. The set of these processes results in a change of cell morphology, migration speed and orientation.

Regarding the contact between cells (nervous and glial) and physical stimuli arising from the ECM, the tissue engineering build artificial surfaces than reproduce the topographical signals of the ECM (Micro and Nano size spur): curved surfaces, single steps, planes angle, vertical obstacles, depressions, pores, cylinders, spheres, ridges and grooves. The most studied surfaces are the “anisotropic signals” whose characteristics depend on the direction of use .

The influence of micro and nano-topography on the behaviour of cells is explored both in vitro and in vivo. The ability to bias cell growth depends on the dimensions of the topographical signals and the cell type.

Interestingly is the behaviour of SC put in contact with anisotropic substrates. SC grown on smooth surfaces and on ridge and groove surfaces presents a different motility, alignment and speed of cell movement.

SC quit on the anisotropic substrate aligning preferably along the axis of the topographical signal, while cells cultured on flat surfaces show a random orientation. Beside, the cell's motility occurred preferentially in parallel to the topography design[2].

Therefore, influencing focal adhesion formation allows control of cell shape and guidance of neurite outgrowth.

In reference to the forces acting during axonal elongation, in 1984 Bray demonstrated in vitro that the application of a mechanical tension by micro-needles of glass inserted in the growing cones helped the axon's elongation without reducing the diameter[3].

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Recently, Riggio et al proposed to use nervous rat pheochromocytoma PC12 cells cultured in vitro with magnetisable nanoparticles (MNPs) (1-100 μgml-1), "assimilated" by cells by endocytosis. Subsequently, an external magnetic field was applied. The association of the nanoparticles and an external magnetic field, generates a tension force in order of pN, virtually able to guide axonal growing and orienting cells along the direction of the magnetic force[4].

The author investigated the early step of in vivo application of this technique and used an experimental model of the median nerve injury in rats (personal communication). The data show that did not hinder with the nerve regeneration (one week after injury, it is evident the presence of Schwann cells migrated from the proximal to the distal stump). The MNPs were endocited by Schwann cells, but also within the same nerve fibres.

Finally, in case of severe nerve gap the gold standard remains the autologous nerve graft. However, the technique could be overcomed in the future by different and alternative solutions.

Artificial anisotropic scaffolds with a specific topography could be able to shape the motility, alignment and speed of nervous and glial cells. Tissue engineering techniques provide methods for building aligned cellular biocompatible that recreates the aligned cellular and extracellular matrix architecture like nerve grafts and conduits with anisotropic surfaces could direct neuronal growth. On the other hand, the cells after the magnetic nanoparticles internalization could be guided under external magnetic field effect to develop tension forces able to stimulate and direct axon growing.

Regards,

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