Magnetic Manipulations for Controlling Neuronal Engineering and Regeneration

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Abstract

Controlling cell navigation, organization and growth has great importance in tissue engineering and regeneration, for a wide range of tissues. In this talk I will present our recent studies of magnetic-based manipulations for nerve regeneration and for controlled drug delivery.

Neurons rely on physical topographical cues. Techniques to control cell growth include bio-mimetic scaffolds, nano-fibrous constructs, structured gels, etc., offering a mechanical guide to the regenerating cells. We have developed a novel approach of injectable hydrogels combined with magnetic nanoparticles (MNPs), to be incorporated directly into the injured site. We show that gel fiber structure can be aligned in situ dynamically and remotely in response to an external magnetic field. Neurons embedded within the aligned gel demonstrated polarized growth pattern. We show a directed and effective neuronal regeneration for neurons embedded in the aligned gels in vitro and ex-vivo. This platform is now examined as a novel method to direct neuronal growth and to bridge gaps efficiently post trauma.

In addition, we functionalized the MNPs by coating them with nerve growth factor, presenting a 'smart' delivery system of biomolecules, together with integral guidance cues. The enrichment of the gel platform with biomolecules conjugated MNPs promoted differentiation and elongation.

As physical mechanical forces play a key role in neuronal morphogenesis, we used magnetic nanoparticles (MNPs) as mediators to apply forces locally on neurons throughout their migration and organization. Following incubation, the MNPs accumulated in the cells, turning the cells sensitive to magnetic stimulation. Applying magnetic fields with controlled magnetic flux densities led to pre-designed cellular movement and to organized networks. Growing neurons loaded with MNPs under magnetic fields has affected the pattern of dendritic trees. With this method we could control drug distribution and delivery as well. Our study presents an emerging magneto-chemical approach for promoting tissue regeneration.

References

[1] Antman-Passig et al., Tissue Eng., 2017 page (Arial 10) Indicate references with sequential numbers within [square brackets].
[2] Antman-Passig and Shefi, Nano Letters, 2016Journal, Issue (Year) page (Arial Narrow 11)
[3] Marcus et al., J NanoBioTech., 2016Authors, Journal, Issue (Year) page (Arial Narrow 11)
[4] Alon et al., Lab on Chip, 2015 Authors, Journal, Issue (Year) page (Arial Narrow 11)

Figures

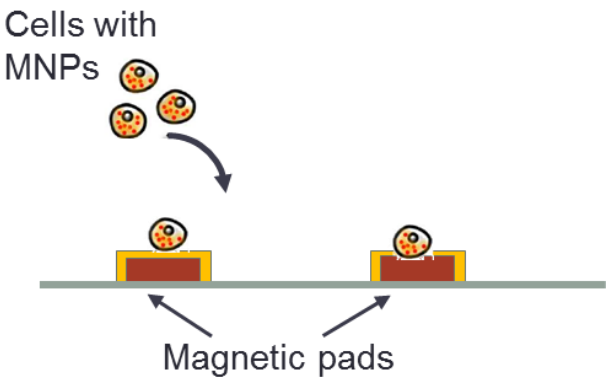

Figure 1. Organizing neural networks by controlled magnetic fluxes. Cells are uploaded with MNPs turned into magnetic elements.

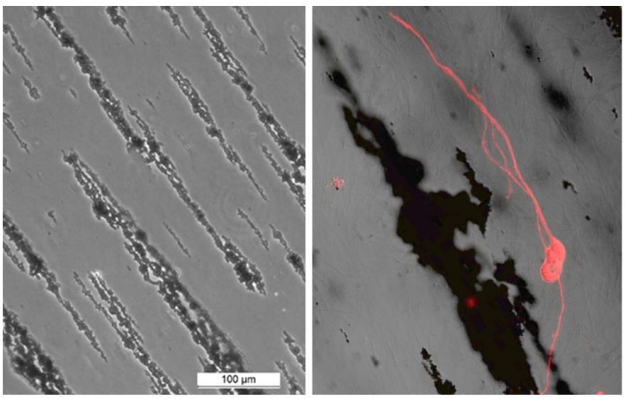

Figure 2. Collagen gel embedded with aligned aggregates of MNPs (Left). PC12 cell (red) is polarized within the magnetically aligned gel (Right).