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Culture of Primary Cortical Neurons on Hydrophobic Nanofibers Induces the Formation of Organoid-Like Structures

Authors : Nick Weir, Robert Stevens, Alan Hargreaves, Martin McGinnity, Chris Tinsley

Abstract : Hydrophobic materials have previously demonstrated the ability to elevate cell-cell interactions and promote the formation of neural networks whilst aligned nanofibers demonstrate the ability to induce extensive neurite outgrowth in an aligned manner. Hydrophobic materials typically elicit an immune response upon implantation and thus materials used for implantation are typically hydrophilic. Poly-L-lactic acid (PLLA) is a hydrophobic, non-immunogenic, FDA approved material that can be electrospun to form aligned nanofibers. Primary rat cortical neurons cultured for 10 days on aligned PLLA nanofibers formed 3D cell clusters, approximately 800 microns in diameter. Neurites that extended from these clusters were highly aligned due to the alignment of the nanofibers they were cultured upon and fasciculation was also evident. Plasma treatment of the PLLA nanofibers prior to seeding of cells significantly reduced the hydrophobicity and abolished the cluster formation and neurite fasciculation, whilst reducing the extent and directionality of neurite outgrowth; it is proposed that hydrophobicity induces the changes to cellular behaviors. Aligned PLLA nanofibers induced the formation of a structure that mimics the grey-white matter compartmentalization that is observed in vivo and thus represents a step forward in generating organoids or biomaterial-based implants. Upon implantation into the brain, the biomaterial architectures described here may provide a useful platform for both brain repair and brain remodeling initiatives.

Keywords : hydrophobicity, nanofibers, neurite fasciculation, neurite outgrowth, PLLA
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