Reconstructing 3D neural tissue with biocompatible nanofiber scaffolds and hydrogels

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Damage to neural tissue is typically permanent and causes lasting disability in patients, but a new approach has recently been discovered that holds incredible potential to reconstruct neural tissue at high resolution in three dimensions. Research recently published in the Journal of Neural Engineering demonstrated a method for embedding scaffolding of patterned nanofibers within three-dimensional (3D) hydrogel structures, and it was shown that neurite outgrowth from neurons in the hydrogel followed the nanofiber scaffolding by tracking directly along the nanofibers, particularly when the nanofibers were coated with a type of cell adhesion molecule called laminin. It was also shown that the coated nanofibers significantly enhanced the length of growing neurites, and that the type of hydrogel could significantly affect the extent to which the neurites tracked the nanofibers.

"Neural stem cells hold incredible potential for restoring damaged cells in the nervous system, and 3D reconstruction of neural tissue is essential for replicating the complex anatomical structure and function of the brain and spinal cord," said Dr. McMurtrey, author of the study and director of the research institute that led this work. "So it was thought that the combination of induced neuronal cells with micropatterned biomaterials might enable unique advantages in 3D cultures, and this research showed that not only can neuronal cells be cultured in 3D conformations, but the direction and pattern of neurite outgrowth can be guided and controlled using relatively simple combinations of structural cues and biochemical signaling factors."

The next step will be replicating more complex structures using a patient's own induced stem cells to reconstruct damaged or diseased sites in the nervous system. These 3D reconstructions can then be used to implant into the damaged areas of neural tissue to help reconstruct specific neuroanatomical structures and integrate with the proper neural circuitry in order to restore function. Successful restoration of function would require training of the new neural circuitry over time, but by selecting the proper neurons and forming them into native architecture, implanted neural stem cells would have a much higher chance of providing successful outcomes. The scaffolding and hydrogel materials are biocompatible and biodegradable, and the hydrogels can also help to maintain the microstructure of implanted cells and prevent them from washing away in the cerebrospinal fluid that surrounds the brain and spinal cord.

McMurtrey also noted that by making these site-specific reconstructions of neural tissue, not only can neural architecture be rebuilt, but researchers can also make models for studying disease mechanisms and developmental processes just by using skin cells that are induced into pluripotent stem cells and into neurons from patients with a variety of diseases and conditions. "The 3D constructs enable a realistic replication of the innate cellular environment and also enable study of diseased human neurons without needing to biopsy neurons from affected patients and without needing to make animal models that can fail to replicate the full array of features seen in humans," said McMurtrey.

The ability to engineer neural tissue from stem cells and biomaterials holds great potential for regenerative medicine. The combination of stem cells, functionalized hydrogel architecture, and patterned and functionalized nanofiber scaffolding enables the formation of unique 3D tissue constructs, and these engineered constructs offer important applications in brain and spinal cord tissue that has been damaged by trauma, stroke, or degeneration. In particular, this work may one day help in the restoration of functional neuroanatomical pathways and structures at sites of spinal cord injury, traumatic brain injury, tumor resection, stroke, or neurodegenerative diseases of Parkinson's, Huntington's, Alzheimer's, or amyotrophic lateral sclerosis.

More information: McMurtrey RJ. Patterned and Functionalized Nanofiber Scaffolds in 3-Dimensional Hydrogel Constructs Enhance Neurite Outgrowth and Directional Control. J. Neural Eng. 11 (2014) 066009 DOI: 10.1088/1741-2560/11/6/066009 PMID: 25358624

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