Bio Focus

Silk-collagen scaffolds engineered to create cortical brain tissue model

What if we could reconstruct the neuronal network of a human brain? An interdisciplinary bioengineering approach, silk protein processing, has now been used to develop a novel compartmentalized cortical brain tissue model with biomaterials resembling neuron-rich gray matter and axon-rich white matter.

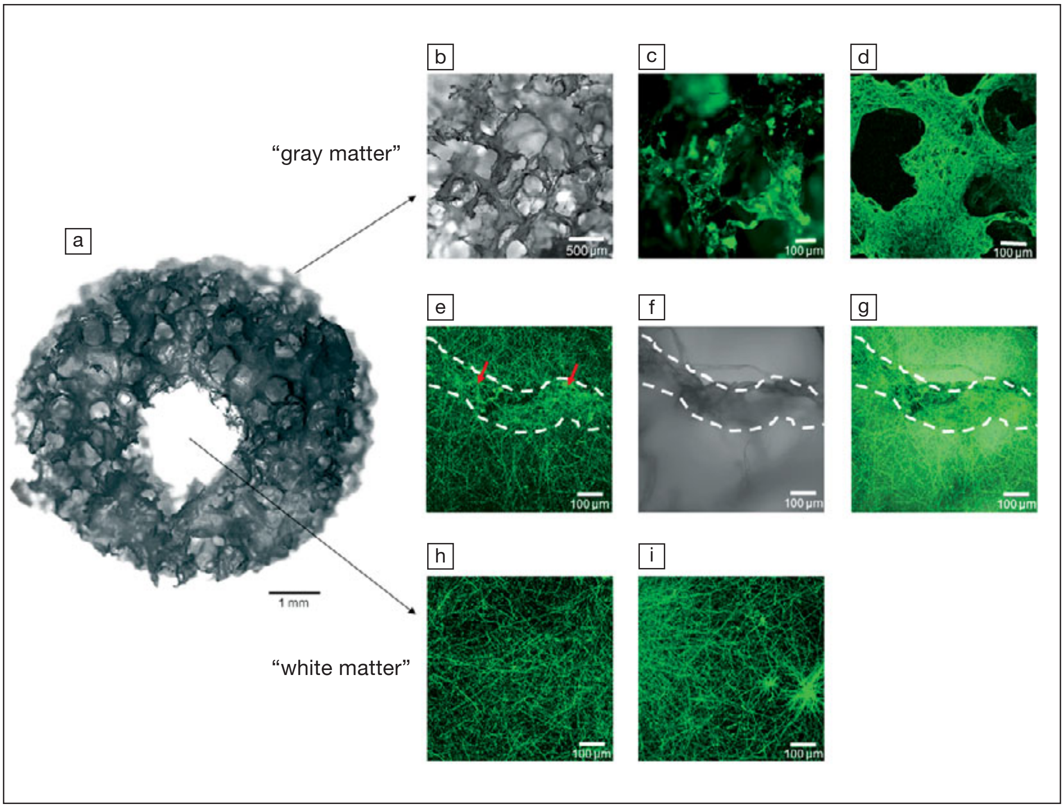
This silk-collagen scaffold provides a three-dimensional (3D) model with structural and functional complexity of native brain tissue, which could serve as a research platform for studies in disease phenotype, pharmaceutical testing, and genetic engineering. "To a certain degree, the model can also substitute [for] animal research to study neuronal network formation and cell–cell interaction in 3D," says Karolina Chwalek, the lead author of this work recently published in *Nature Protocols* (DOI:10.1038/NPROT.2015.091).

A research team led by David L. Kaplan in the Biomedical Engineering Department at Tufts University described the optimized conditions and processes of developing an artificial neuronal network with emphasis on materials, procedures, and troubleshooting advices. "The silk-collagen scaffolds, which are the basis of the model, are architectonically designed in a novel way to create two compartments," added Chwalek. "[The] outer one is a highly porous silk sponge of specific pore size, which creates a large area to house the neurons. The inner compartment is a semitransparent collagen hydrogel, which creates the 3D environment for neuronal network formation."

The design was inspired by the anatomical structure of the brain cortex. The resulting model is highly reproducible, user-friendly with consistent properties, and has a short processing time compared to other previously published methods using organoids, neurospheroids, or hydrogels. The porous scaffold architecture provides mechanical stability to support collagen gel in the center, and adequate physiological conditions to the neuronal network by allowing free diffusion of metabolic nutrients.

"Exploring the integration of signals in brain tissue during normal and pathological processes is a significant challenge, particularly in live organisms and explants," says Kilian Kristopher, an assistant professor in the Department of Materials Science and Engineering at the University of Illinois at Urbana-Champaign, with expertise in the field of biomaterials. "The work by Kaplan and colleagues demonstrates an innovative model architecture of silk-collagen scaffolding that effectively recapitulates cortical brain tissue. This advance provides a flexible and tunable approach to create functional neuronal tissue, with the promise of generating patient-specific models of disease for fundamental studies and therapeutic development."

YuHao Liu



(a) Three-dimensional bioengineered brain tissue model where (b) the silk sponge shows the high porosity of the scaffold, and (c) cell distribution is shown upon attachment to the scaffold on day 1 of culture. On day 7, (d) the lack of collagen in the scaffold will result in no network formation; (e) neurons grow neurites into the surrounding collagen gel; the white dashed lines are the silk scaffold on which cell bodies are present (red arrows); (f) the silk scaffold; (g) overlay image of neuronal projections and silk in (e) and (f); (h) neuronal network in the central collagen window; and (i) neuronal network with cell foci in the sample with insufficient washing steps before collagen embedding. Credit: *Nature Protocols*.

https://doi.org/10.1557/mrs.2016.8 Published online by Cambridge University Press