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BIOMATERIALS

Blazing trails

“A functional neural circuit was developed in this platform, and neural connectivity was augmented in directionally aligned gels”

A fibrous structure enables the growth of nerve cells, facilitating the development of artificial tissue mimicking brain neural networks, reports Nakwon Choi, Eun-Mi Hur and colleagues in *Nature Communications*.

Tissues within the human body are highly organised, and recapitulating this structure in the laboratory has proven very complex. In particular, the complexity of the brain and the neural networks of the hippocampus, which are essential for spatial navigation and memory, have been investigated widely. In this context, the development of matrices that can mimic the alignment and structure of hippocampal neural networks has been of great interest in the field of neuroscience.

So far, research has shown that several strategies can enable the development of anisotropic structures using external forces, such as magnetic- and microfluidic-induced techniques, although the majority cannot confer sufficient alignment in three dimensions. To overcome these limitations, the researchers have developed a method that relies on anisotropic strain to produce collagen fibres with homogenous alignment.

On placing collagen gels within a pre-strained mould and subsequently releasing the strain, the researchers observed self-assembly of collagen into an aligned matrix. This approach was used for the development of a hippocampal circuit using a multichannel chip that contains a collagen gel cultured with two populations of hippocampal neurons in adjacent channels. Microfluidic channels have been widely used in numerous applications, including complex biomaterials. For example, “we have previously developed engineered tissue-on-a-chip including biomaterials with control over the spatial distribution of specific biochemicals,” explains Choi.

The use of pre-strained chips that contain neurons led to axonal growth along the length of the aligned collagen fibres. The researchers also observed that dendritic structures from the neurons grew along the aligned collagen fibres and were comparable in length and number to those obtained from native hippocampal neurons. When the neurons were electrically stimulated, they were capable of responding biochemically by the release of calcium, which is a characteristic of neurons during impulse propagation. Interestingly, the researchers also observed the development of functional synapses in the cultured neurons, which enabled the transmission of signals from one population of neurons to another. “A functional neural circuit was developed in this platform, and neural connectivity was augmented in directionally aligned gels,” states Hur.

Moving forward, the ability of such a platform for use in other applications was also demonstrated by culturing other cell types from other tissues, including muscle. Preliminary results demonstrated that the platform was able to support alignment of the cells, thus highlighting the importance of such contact guidance. As a result of their findings, the researchers intend to use such a platform to develop engineered tissues that can be used to elucidate the structure of neural circuits as well as understanding numerous disorders. “We plan to reconstruct normal and diseased neural circuits to gain insights towards understanding the dysfunction of neural circuits that may underlie a wide range of brain disorders,” conclude Choi and Hur.

Jose A. Bernat Bacete/Getty Images

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