NeuraPillar Myelination Explorer

A biomimetic assay designed for fast-tracking exploration of drug candidates for neurodegenerative diseases with micropillar arrays

Category
Research Tools, Bioanalytics & Assays

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Background

Neurological disorders are a global burden and a public health challenge. Among them, demyelinating diseases of the central nervous system (CNS) are characterised by any condition that leads to damage of the insulating and protective myelin sheathing surrounding neuronal axons in the brain and spinal cord. Multiple Sclerosis (MS) is the most common demyelinating disorder, and there are an estimated 2.8 million people living with MS. Moreover, recent studies suggest that myelin dysfunction is an upstream risk factor for Alzheimer's Disease (Depp et al., Nature., 2023), a neurodegenerative disease expected to affect 138 million people by 2050.

To date, there are no approved remyelinating therapies for such conditions. This is mostly attributable to the lack of reliable myelination models. 96% of drugs that have shown successful outcomes in animal models (mostly rodents are used to model neurological disorders) fail when they are tested on humans. Current in vitro cell culture technologies remain limited in their ability to support robust functional modelling of myelination.

Technology Overview

A biomimetic assay designed for fast-tracking exploration of drug candidates for neurodegenerative diseases with micropillar arrays that recapitulate the main biophysical, biomechanical and biochemical cues of the Central nervous System (CNS), making this model the state-of-the-art for myelination studies (Figure 1).

This novel custom-made micropillar assay with unique geometrical and bio-material/mechanical features has led to effective myelination of micropillars by Oligodendrocytes exhibiting clear dense myelin-wraps (Figure 2). In vitro generation of such densely packed myelin sheaths around artificial axon-like structures gives a state-of-the-art platform for axon modelling.

Benefits

State-of-the-art human nerve replication, to allow discrimination between OL drugs, showing multiple concentric myelination growth to give a faster drug discovery pathway, with more accurate feedback and reduced cost:

• Pillar dimension control - mimic diameter nerves below 5?m and large aspect ratios allowing realistic 3D growth

• Soft Polyacrylamide hydrogel – benchmark and realistic mimic of soft brain and spinal material

• Array dimensions allow cross section of myelination analysis to be quantified and rated

• Address human disease directly - Controlled functionalisation of micropillars with extracellular matrix (ECM) proteins, such as laminin and fibronectin and human cells.

• Facile and scalable assay gives rapid efficient screening of myelination therapeutics

Applications

This platform can give rise to three potential commercialisation aspects:

• A service for biotech companies, biopharma, or academics to test hypotheses and/or candidate molecules on myelination.

• Licence a Contract Research Organization (CRO) providing neuroscience-related services for scaling 96-well plates, or to offer the service of performing the myelination bioassay themselves to test a hypothesis or molecule for a biotech or biopharma company or academics.

• Partner with the industry utilising the platform to answer biological questions in-house that would generate more potential patentable discoveries:

o The high-throughput screening platform can be used to screen molecules affecting myelination in MS or neurodegenerative diseases. Any new molecules or repurposed drugs can generate a patent or more industrial partnerships to move into clinical trials.

o The platform can be used to identify biomarkers of the myelination status that would then be tested in rodent models of diseases and human fluids for diagnosis or to monitor response to treatment. Importantly, the Alzheimer's Disease biomarkers market was $825.2 million in 2021 and is estimated to reach $1.7 billion by 2031.

o Develop further the use of the platform beyond myelination.

Opportunity

UCLB are looking for industrial partnership/investment to develop the platform and its spectrum of applicability (Alzheimer and Parkinson diseases, MS, aging) as well as potential other applications of the 3D platform beyond myelination (T cell activation, adipocyte browning, stem cell differentiation for cell therapy, …).

Patents

Patent application number for Biomimetic device: 2314005.6. Filed Sep 2023.

Seeking

Commercial partner, Licensing, Seeking investment

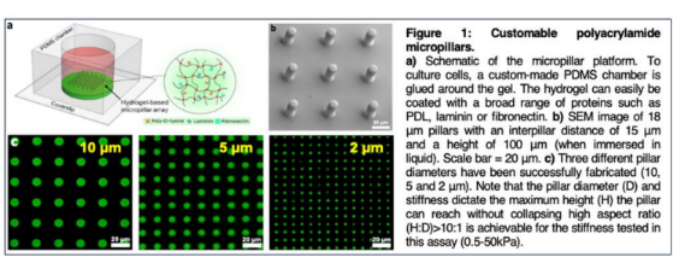

Figure 1: Customable polyacrylamide micropillars.
a) Schematic of the micropillar platform. To culture cells, a custom-made PDMS chamber is glued around the gel. The hydrogel can easily be coated with a broad range of proteins such as PDL, laminin or fibronectin. **b)** SEM image of 18 µm pillars with an interpillar distance of 15 µm and a height of 100 µm (when immersed in liquid). Scale bar = 20 µm. **c)** Three different pillar diameters have been successfully fabricated (10, 5 and 2 µm). Note that the pillar diameter (D) and stiffness dictate the maximum height (H) the pillar can reach without collapsing high aspect ratio (H:D)>10:1 is achievable for the stiffness tested in this assay (0.5-50kPa).

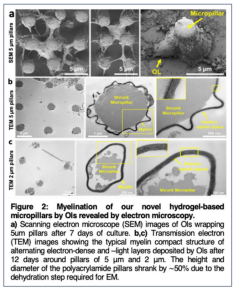

Figure 2: Myelination of our novel hydrogel-based micropillars by OLs revealed by electron microscopy.
a) Scanning electron microscope (SEM) images of OLs wrapping 5um pillars after 7 days of culture. **b,c)** Transmission electron (TEM) images showing the typical myelin compact structure of alternating electron-dense and –light layers deposited by OLs after 12 days around pillars of 5 µm and 2 µm. The height and diameter of the polyacrylamide pillars shrank by ~50% due to the dehydration step required for EM.