

# Enabling High-throughput 3D Cell-based Assays with Commercially-available Sources of Human iPSC-derived Cell Types

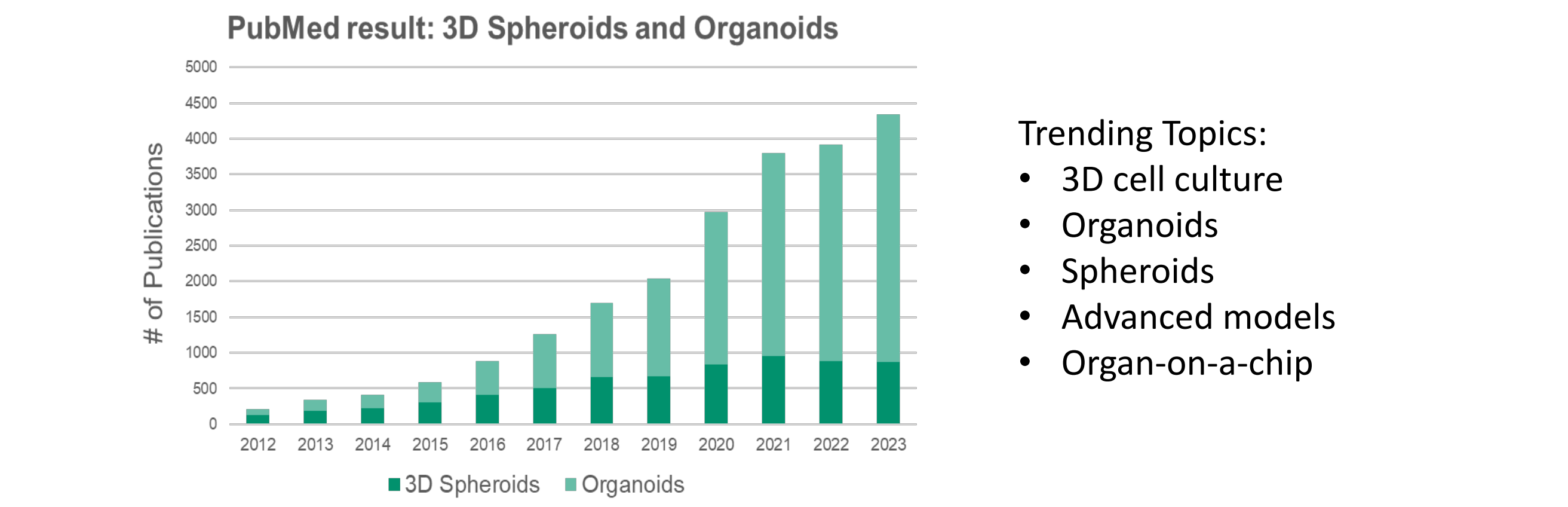
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Poster #1109-B

## Overview

- Increased assay complexity can be achieved with three-dimensional (3D) culture systems.
- Human induced pluripotent stem cell (iPSC) technology has helped to enhance physiological relevance by building a bridge between animal testing and human diseases.
- Like “organoids”, 3D spheroid products can be created by mixing individual cell types at defined numbers and ratios and allowing them to self-assemble in co-culture.
- This approach enables a more flexible method (modular incorporation of defined cell types, including disease-specific lines) while also allowing more control over variability (individual components are well-defined and highly reproducible), both of which are critical to the success of incorporating such technologies into cell-based assay workflows.
- Here we present examples of enabling 3D cell-based assays with human iPSC-derived cell types in 384-well format:
- “Cardiospheres” from cardiomyocytes, cardiac fibroblasts, and endothelial cells show improved myocardial maturity via positive inotropic response (increased  $Ca^{2+}$  waveform amplitude) to compounds like isoproterenol and dobutamine.
- A diverse range of “neurospheres” can be created using healthy or diseased neurons and astrocytes to model neurodegenerative disease, with the option of incorporating microglia to study neuroinflammation.
- Hepatocytes and macrophages together in 3D yield a more complex liver co-culture system
- An isogenic blood-brain barrier (BBB) model system composed of astrocytes, pericytes, and brain microvascular endothelial cells. Importantly, all of these systems described above are isogenic, meaning the cells are derived from the same iPSC donor background.
- These commercially available iPSC-derived cell types from FUJIFILM CDI are manufactured at scale, quality controlled, and cryopreserved, so that they are ready-to-use with confidence at any point in time.
- Implementation of these cells into modular 3D assay workflows is novel approach to complement current organoid research and enhance the biological complexity required in cell-based assays for drug discovery, toxicity screening, and disease modeling.



## Methods

► **Induced Pluripotent Stem Cell Technology**

► **Application Protocol to make 3D cardiac tri-culture spheroids**

Legend:

- iCell Cardiomyocytes, 01434
- iCell Cardiac Fibroblasts, 01434
- iCell Endothelial Cells, 01434

Media: iCMM (100 mL), iCell Supplement (25 mL)

► **Ultra Low Attachment (ULA) 3D Cell Culture Spheroid Plates**

Corning ULA      faCellitate BIOFLOAT      InSphero Akura      Sbio Primesurface

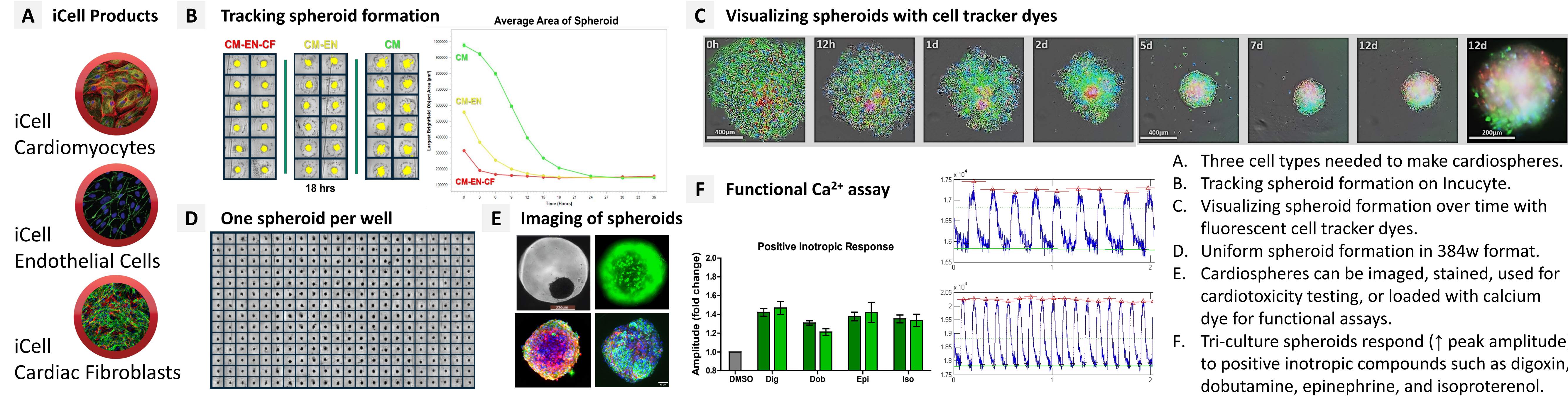
► **Platform Technologies to Monitor, Image, Characterize 3D Spheroids**

Scan Type: Standard, Image Lock, Whole Well, Dilution Cloning, Spheroid

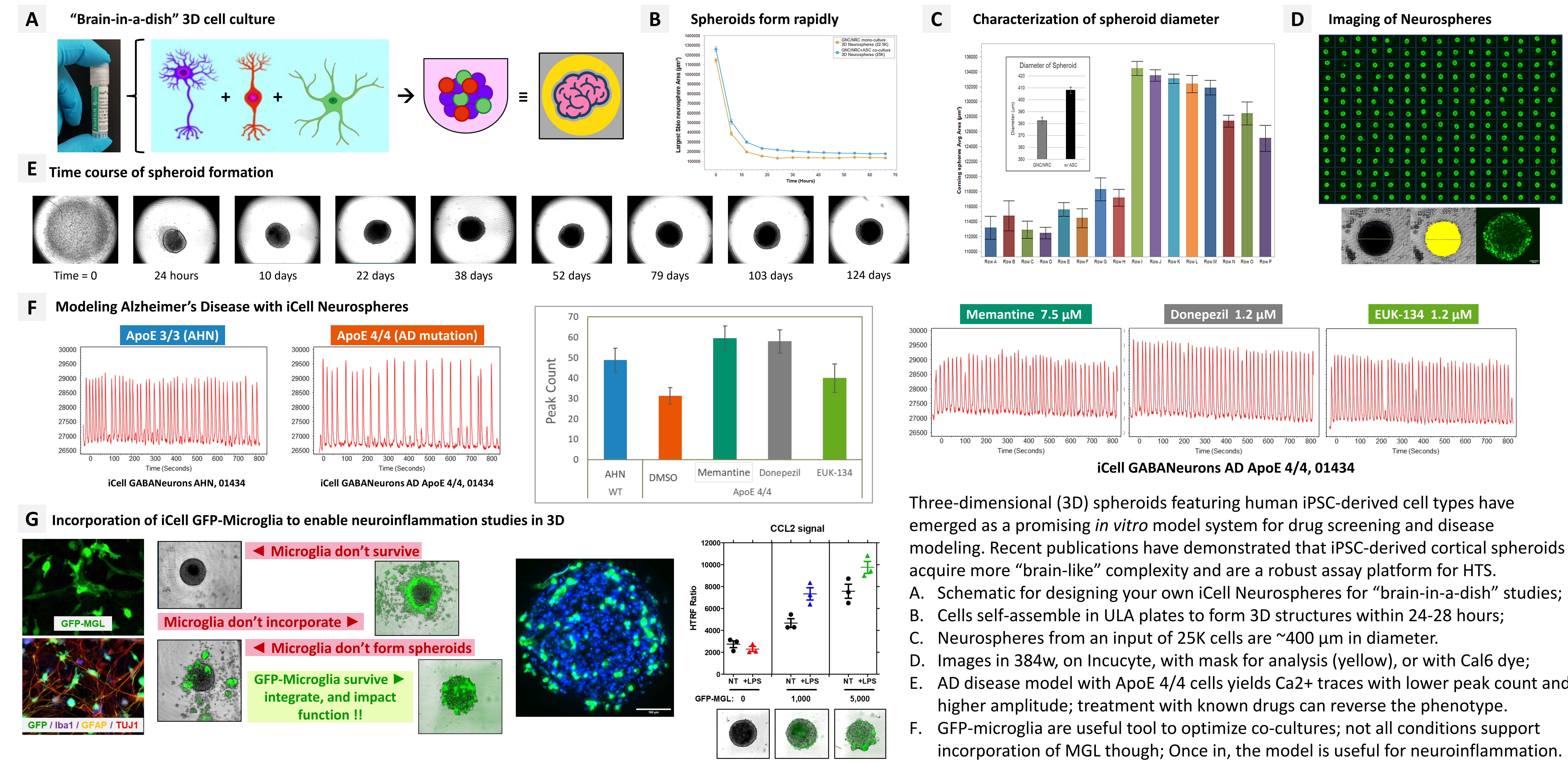
MaxTwo Multi-Well

MaxOne Single-Well

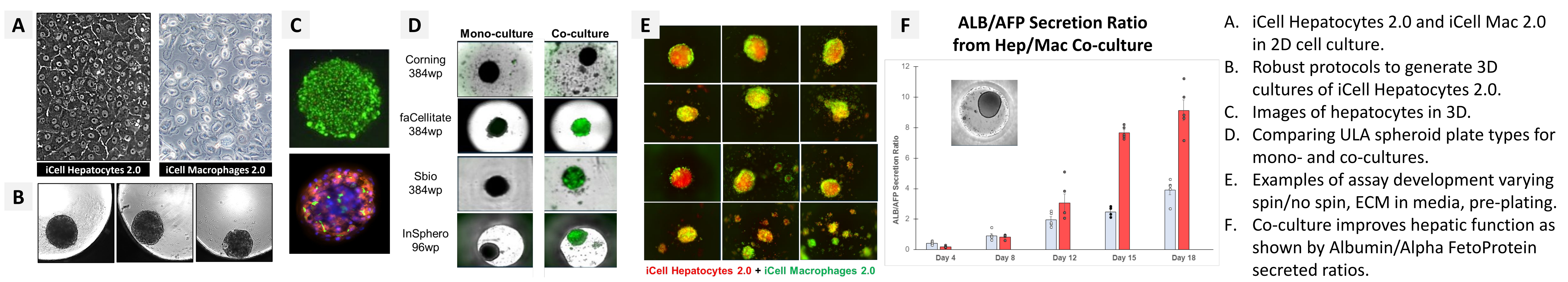
## iCell Cardiospheres: human, isogenic, tri-culture microtissues for advanced cardiac assays



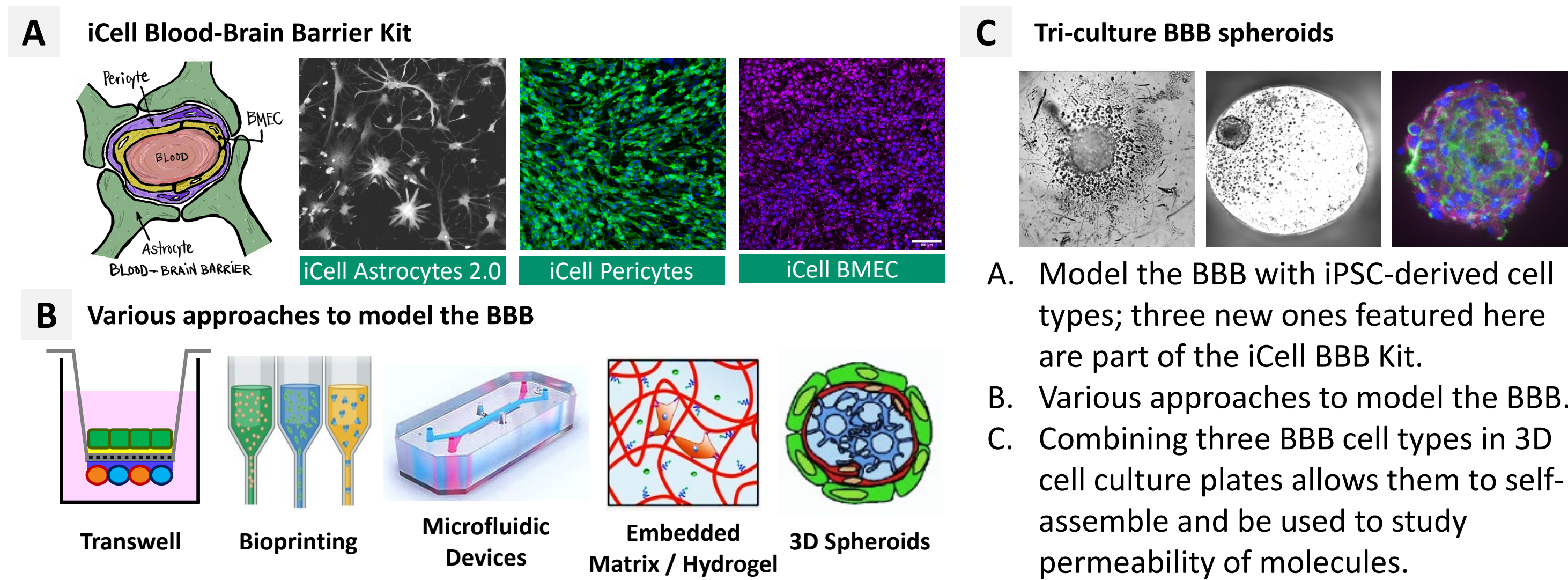
## iCell Neurospheres



## Combine iCell Hepatocytes 2.0 + iCell Macrophages 2.0 to model Hepato/Immuno Interactions in vitro



## Blood-Brain Barrier: 3D spheroid model for permeability studies



## Summary and Future Directions

There is a great deal of excitement and promise around 3D cell culture. Research with iPSC-based organoids and spheroids is focused on creating a more complex and biologically relevant model system to bridge the translational gap, better our understanding of human disease, and facilitate the discovery of new drugs. The advantage of the modular approach presented here with commercially available, cryopreserved, ready-to-use cells is that you can vary cell type numbers and ratios to have exquisite control over the spheroid size and composition. Importantly, this method further enables disease modeling studies and the incorporation of iPSC-derived microglia into neurospheres, for example, is something that is not easily accomplished with organoids. FUJIFILM CDI will continue to develop new applications with iCell products and establish advanced co-culture systems that are amenable to standard workflows.