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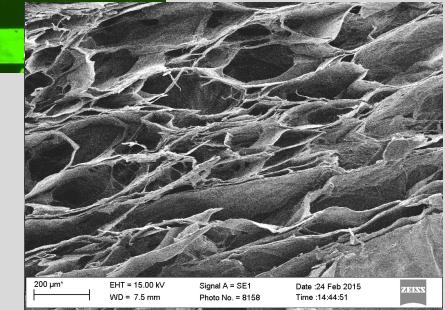
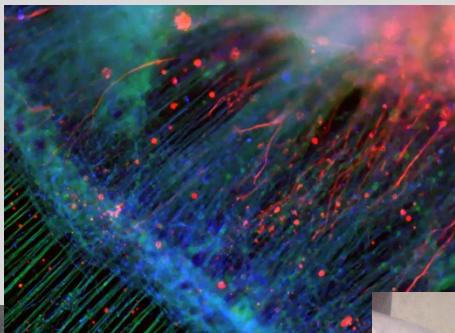
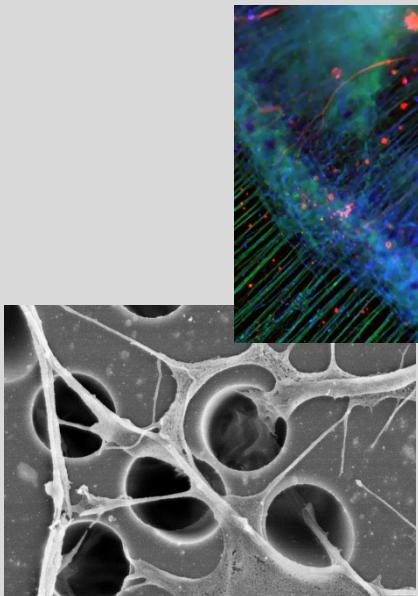
Applying Regenerative Medical Technologies in Cultivated Meat

Speaker

Ashton Choi

Tech Investor & Columnist

*Researcher, Oxford Centre for Tissue Engineering and
Bioprocessing*



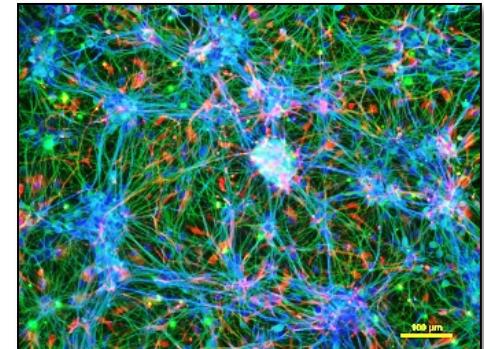
The Oxford Centre for Tissue Engineering and Bioprocessing



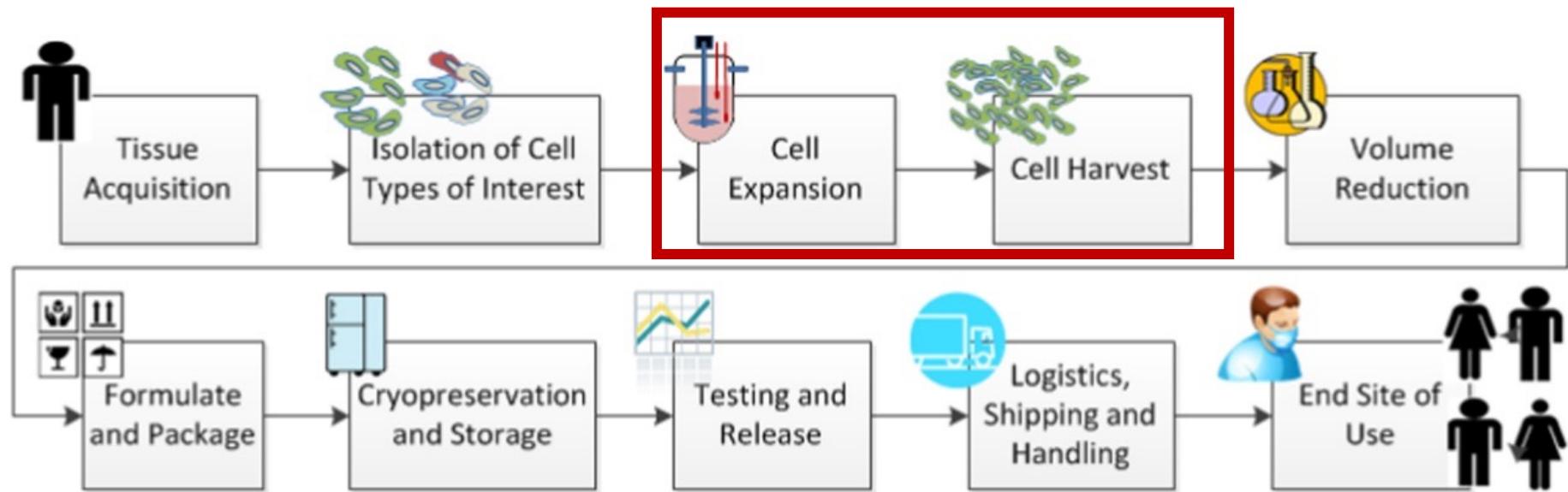
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Main areas of research

- Bioreactor design
 - Large scale cell culture
 - Perfused bioreactor for cell/tissue culture
 - Hollow fibre membrane based bioreactor for generating bulky tissues
- Biomaterial selection, modification and processing
 - Cell culture substrate modification
 - Scaffolds for 3D cell culture
- 3D cell culture and characterisation
 - 3D human neural network
 - In vitro cancer model
 - Co-culture



Manufacturing process flow for cell based allogeneic regenerative medicine therapy



- ❖ Cell expansion step: the most expensive and time consuming step
- ❖ Cell harvesting step: not yet the optimum quality of cell harvesting

Bioreactor: Fluidized Bed

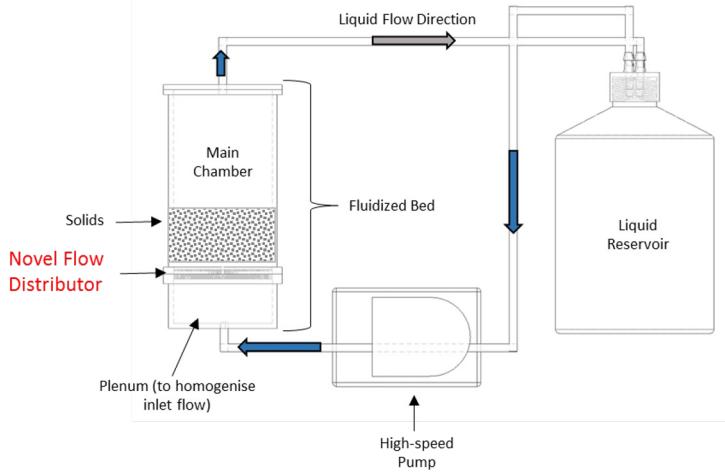
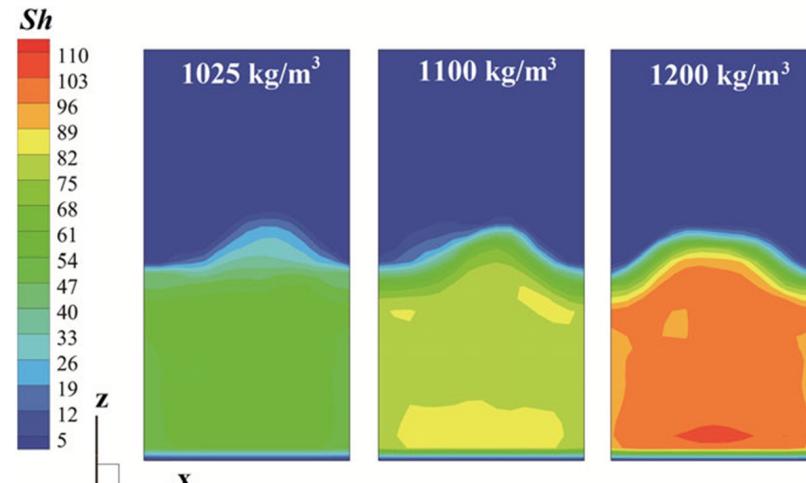
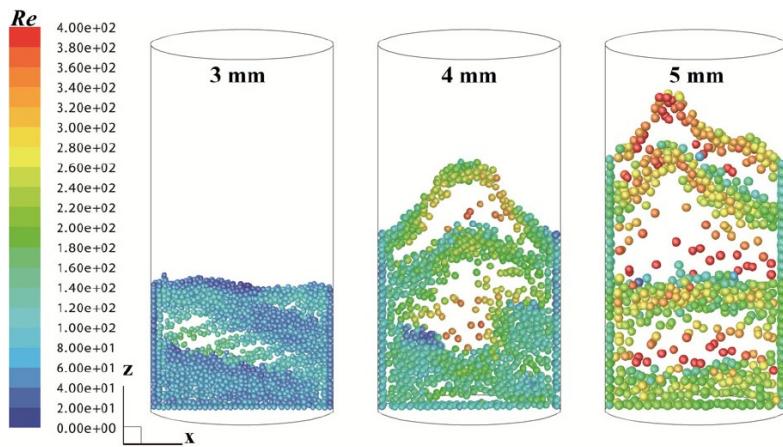
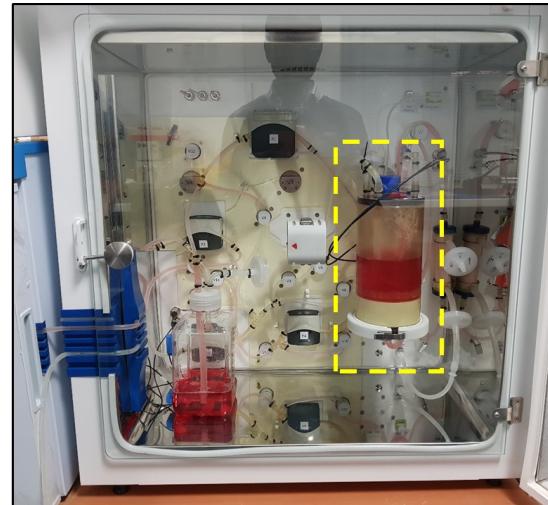


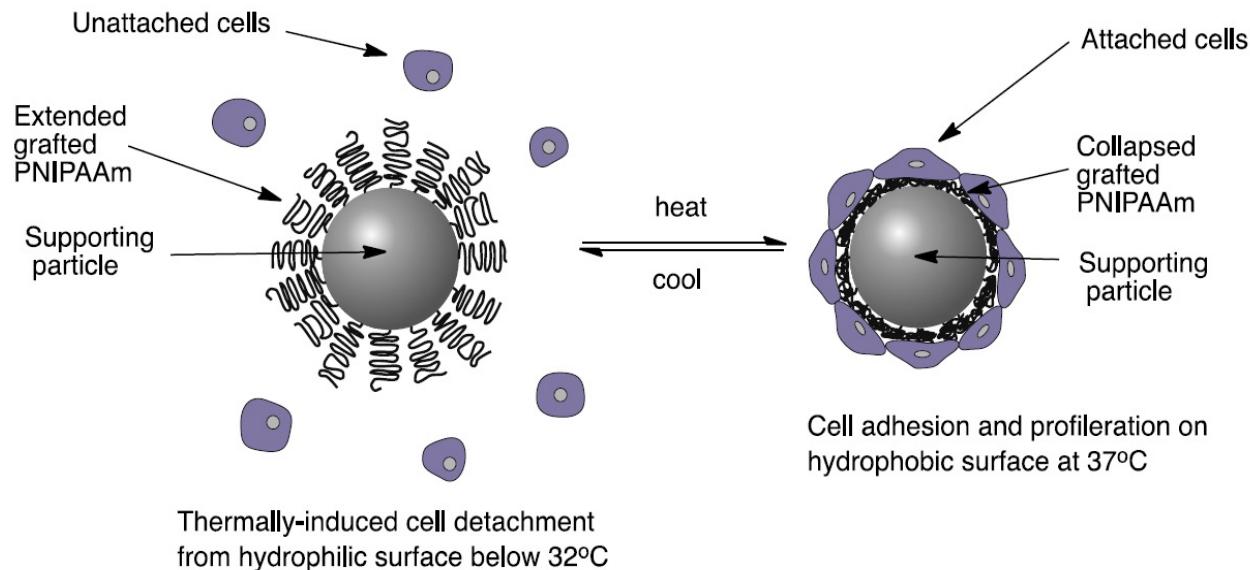
Figure: Liquid-solid fluidized bed experimental set-up



Particle Design: Thermoresponsive Macrocarrriers

A thermo-responsive polymer is able to change its properties in response to changes in temperature.

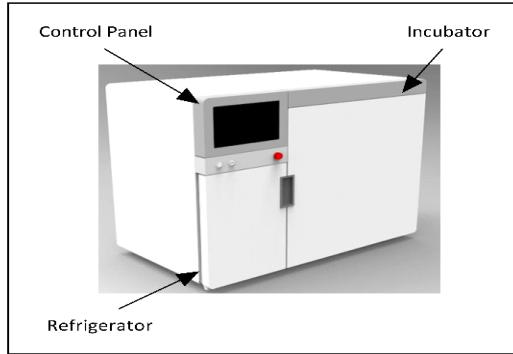
Poly(N-isopropyl acrylamide) – PNIPAAm or PIPAAm



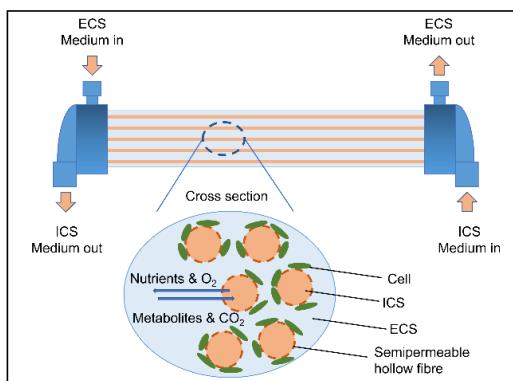
European Polymer Journal 67 (2015) 346–364

An Automated, High-throughput, Hollow Fibre Bioreactor System for MSC-sEV Production

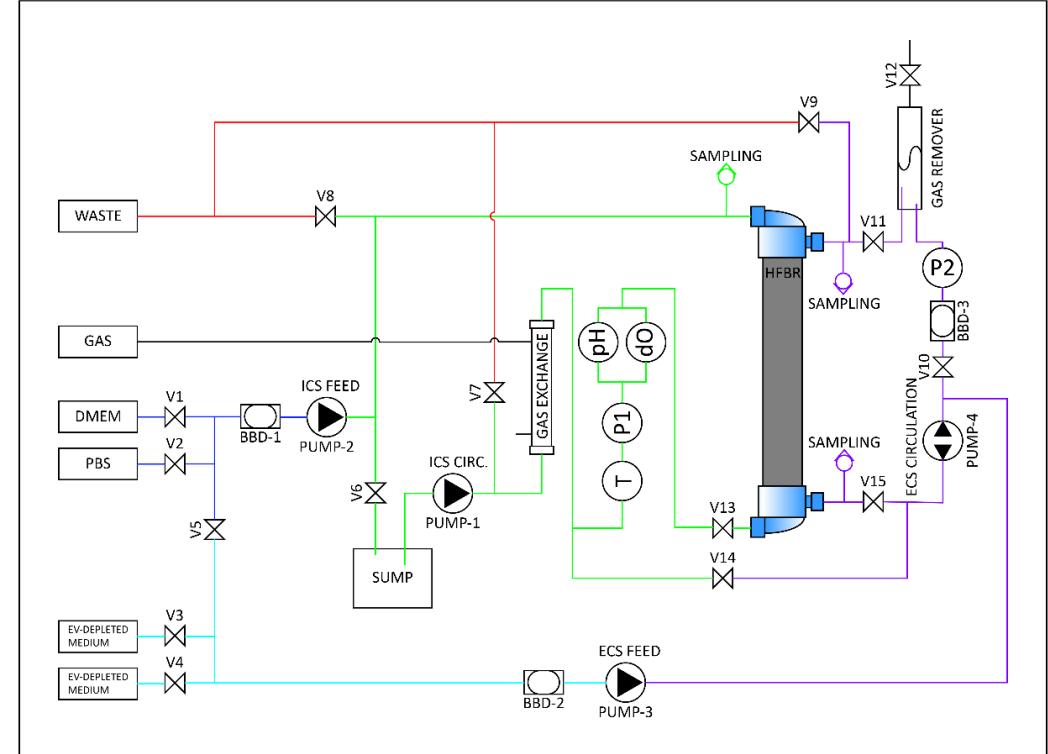
a



b



c



Cell Expansion System. (a) The outside appearance of the CES. (b) Schematic diagram and working principle of the HFBR cartridge. (c) Process flow diagram of the CES. BBD – bubble detector, V – valve, T – temperature sensor, P – pressure sensor, pH – pH sensor, dO – oxygen sensor.

What **if** we could grow meat just like a plant?



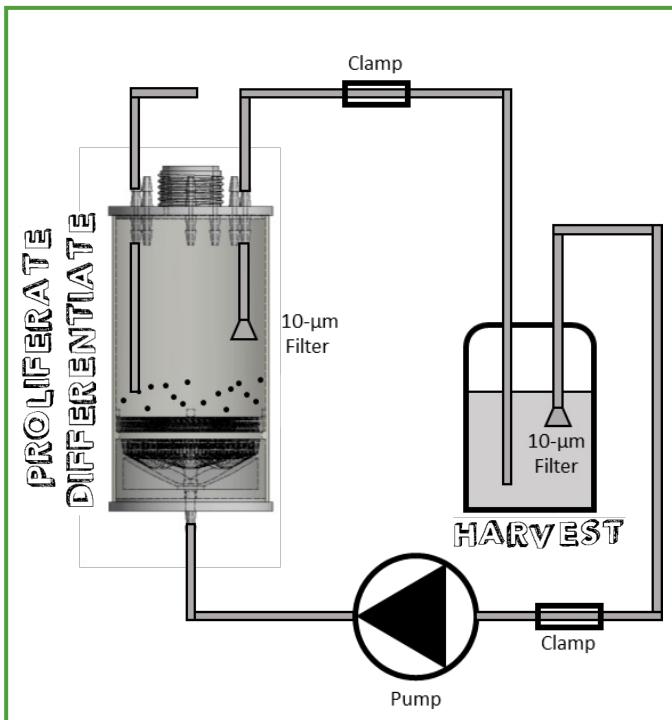
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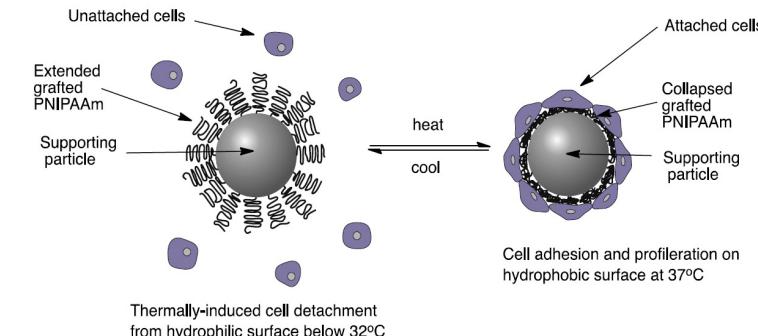


Ivy Farm Technologies: a spin-off company established in 2019

Bioreactor schematic



Exclusive license of patented thermo-responsive macrocarrier technology



- **Lower cost vs. others** (fewer steps in the process, fewer additives)
- Animal-free (alternative is trypsin, an animal-derived enzyme)
- No cytotoxicity
- No adverse effects on cell morphology/physiology
- Cell phenotype remains unaltered
- Predicted regulatory-friendly methodology

Commercial access to advanced bioreactor design

- Angled inlets to increase axial and vertical velocity of mixture
- Encourages mixing leading to better cell quality and higher growth rate
- Defined approach to automation established





sustainable
meat co.

Ivy Farm Operates the Largest Culture Meat Pilot Plant in Europe in its 18,000 Sqft Campus in Oxford, UK



Our R&D center in Oxford has a low-rent space that is capable of hosting over 120 employees, while currently we have only 50. We are thus ready to expand for the upcoming stage of development



I cannot tell the difference between traditional farmed beef and Ivy Farm cultivated beef... Its absolutely delicious" – Tom Heap

January, 29, 2024



"We combine just the best bits of meat – pure muscle and pure fat – to create a product that is better for the environment." – Rich Dillon

November 4, 2022



"Ivy Farm is developing a healthier alternative to traditional and existing plant-based meat products, which is a key value proposition." – Hiral Patel

January 26, 2022



"It's really good, and it's a real hot dog! Wow." – Poppy O'Toole

November 25, 2021



First cultured burger

In 2013, this beef burger was made at the cost of eye-watering \$300k



More companies are doing it



At much lower cost

cnbc.com/2020/12/18/singapore-restaurant-first-ever-to-serve-eat-just-lab-grown-chicken.html

lamda Mail - 14JYong@microsoft.com Dashboard - MCS S... Microsoft Teams

makeit SUCCESS MONEY WORK LIFE VIDEO

This restaurant will be the first ever to serve lab-grown chicken (for \$23)

Published Fri, Dec 18 2020 2:30 PM EST • Updated Wed, Dec 23 2020 9:40 AM EST

Jade Scipioni @JADESCIPIONI

SHARE f t in e



1880's crispy maple waffle with GOOD cultured chicken Credit: Eat Just and 1880

Trending Now

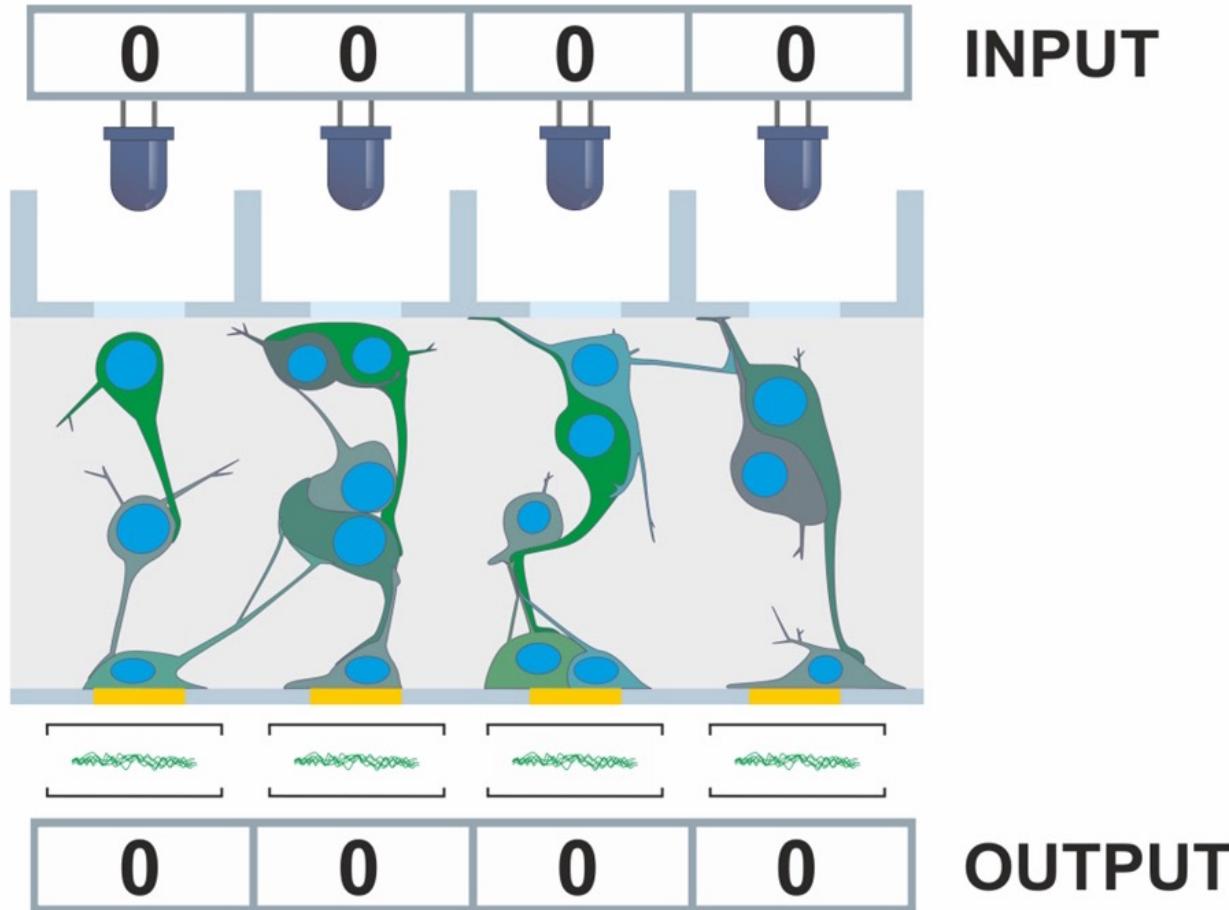
- 1 Dogecoin up 12,000%—here's how much money you'd have if you invested \$1,000 at the beginning of 2021
- 2 Bill and Melinda Gates just announced their divorce — here's a breakdown of the billionaire's wealth
- 3 This 42-year-old made over \$366,000 from her side hustle turned full-time job
- 4 Dogecoin millionaire invested his savings in the meme

Scale up challenge

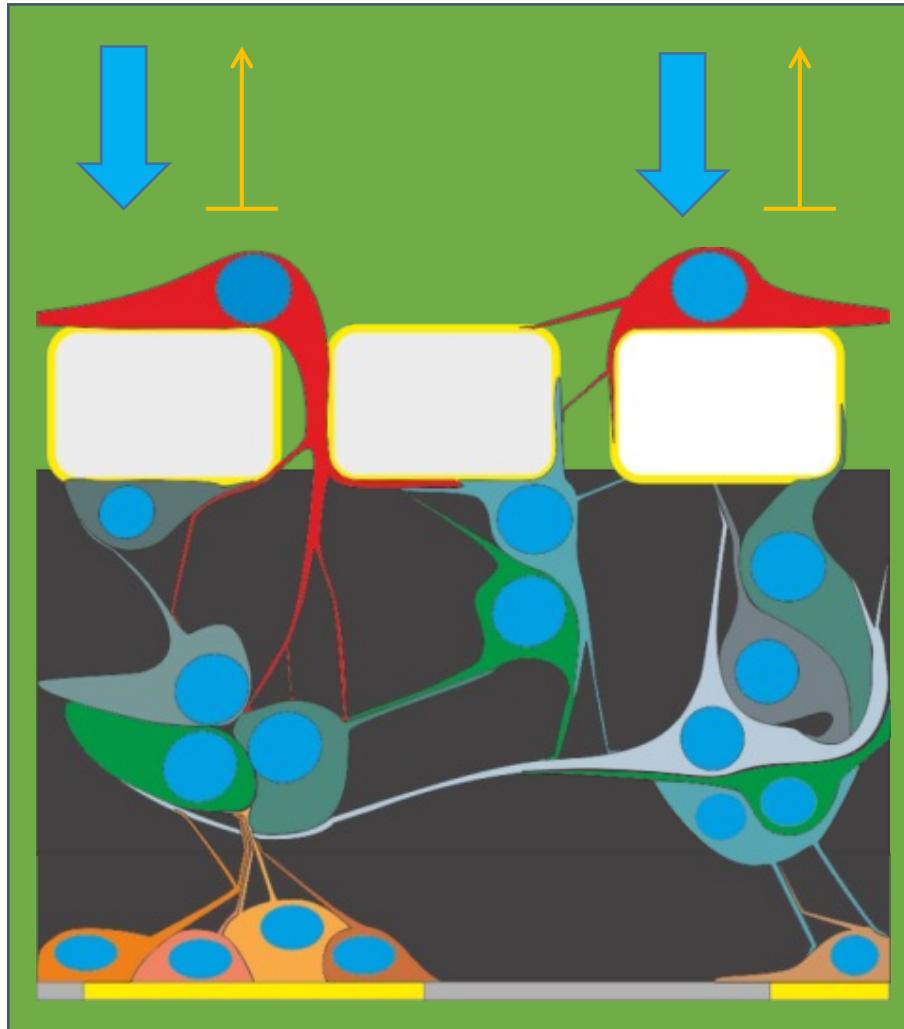
- There are \sim 100 billion cells in a kg of meat
- World meat consumption: 300 billion kg/year
- If cultured meat is to supply only 10% of the world meat consumption, i.e. 30 billion kg/year, we need to produce $30 \text{ billion} \times 100 \text{ billion cells}$ ($3 \times 10^{21} \text{ cells /year}$)
- Even with high density cell culture in bioreactors, we would need at least $2 \times 10^6 \text{ m}^3$ bioreactor volume (corresponding to \sim 200,000 of 10,000 litre bioreactors).
- Currently, there aren't even enough amount of stainless steel materials
- Innovation is needed:
 - Bioreactor design
 - Reduce waste
 - Regulation



Building a brain slice in a dish



The physical model



Stimuli - light

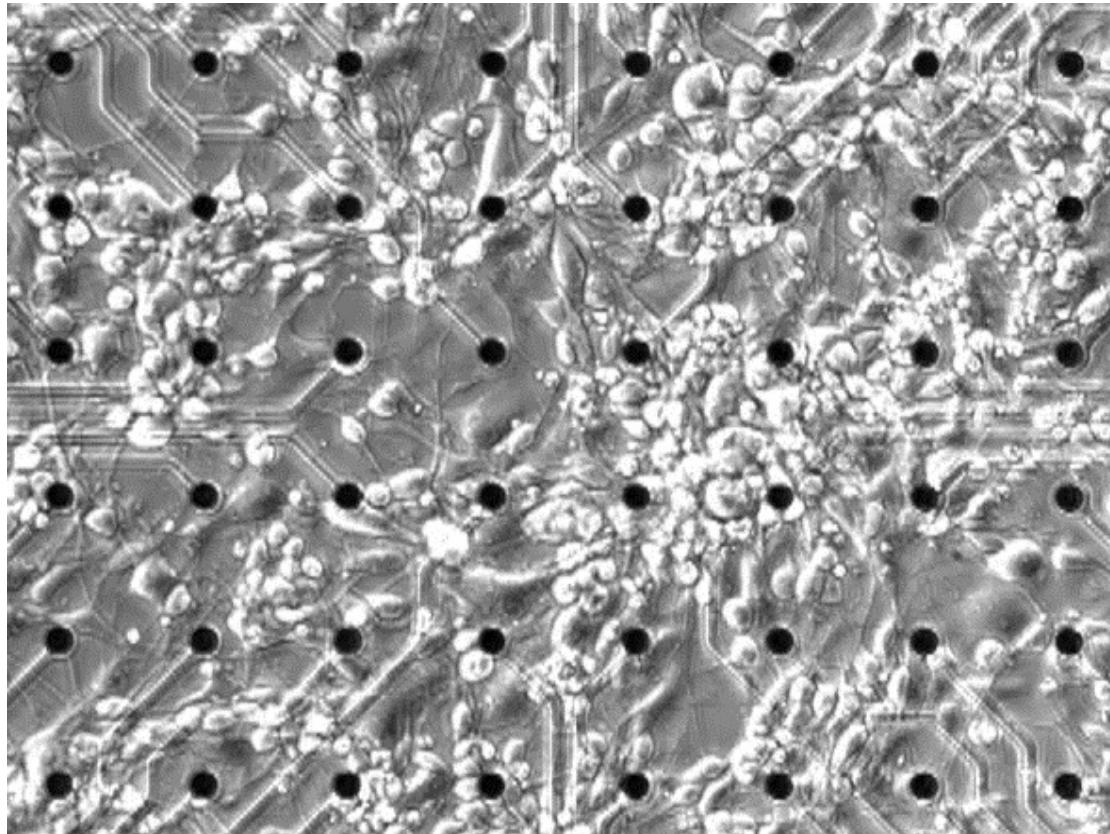
Light sensitive neurons

Porous membrane

3D Model neural network

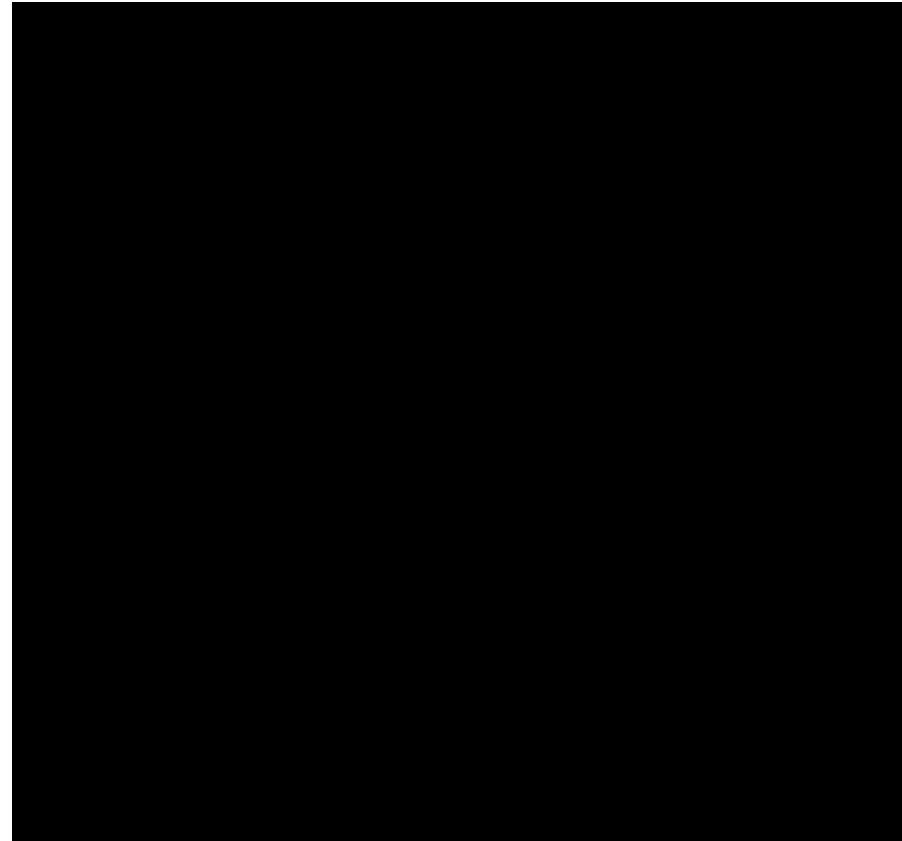
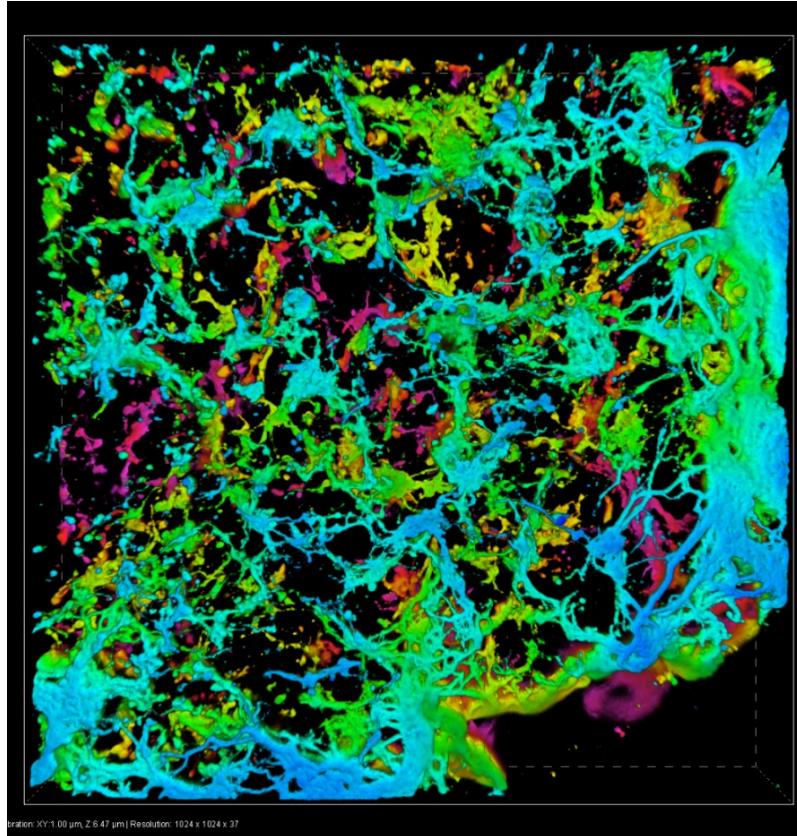
Neurons patterned on MEA

Neurons like to form clusters

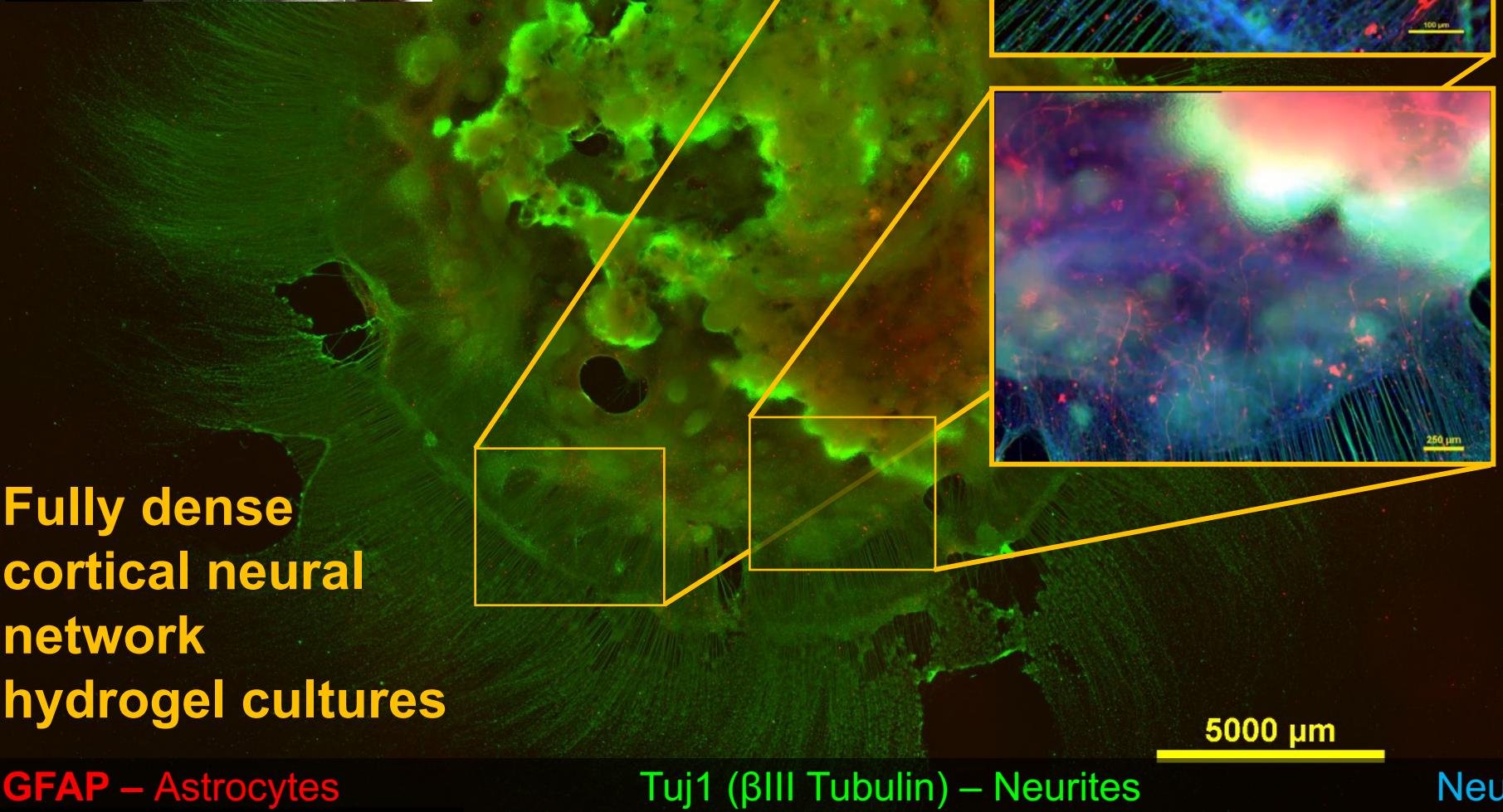
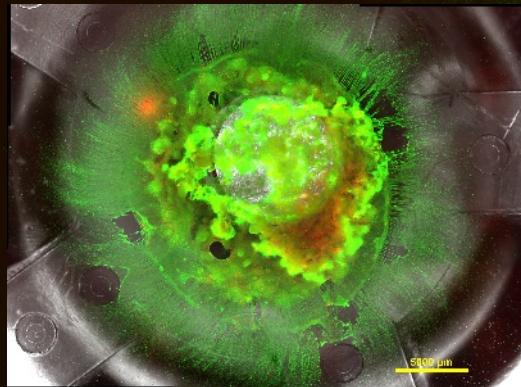


Seeding of human iPSC derived neurons on a Laminin coated MEA (720x, 4hr time-lapse)

Neurons form networks throughout gel



4-week culture of human iPSC derived neurons in granular HyStem hydrogel + Laminin



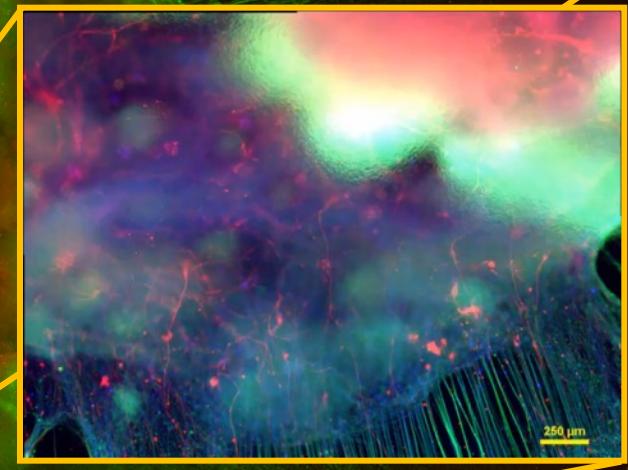
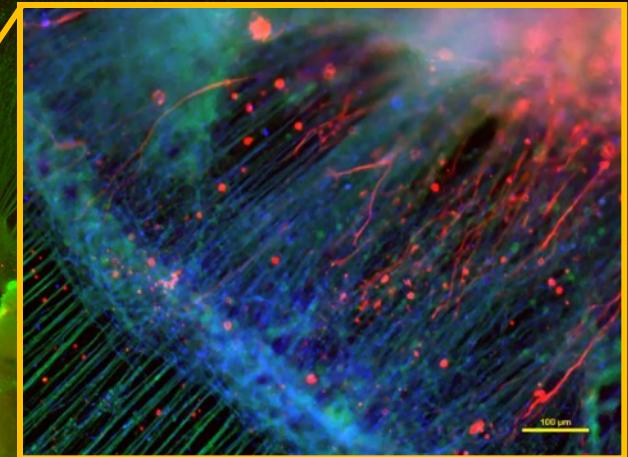
**Fully dense
cortical neural
network
hydrogel cultures**

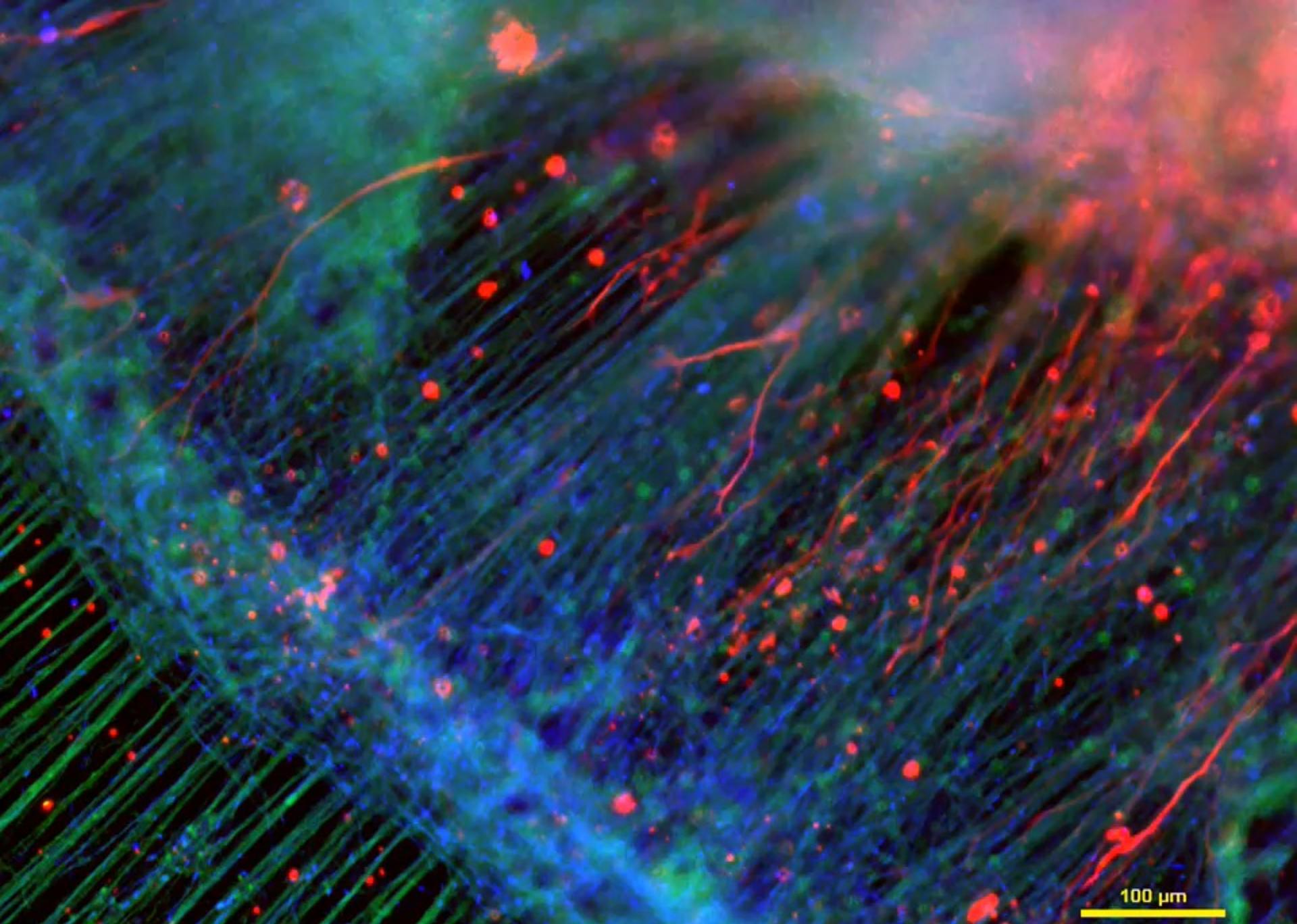
GFAP – Astrocytes

Tuj1 (βIII Tubulin) – Neurites

5000 μm

Neuro





GFAP – Astrocytes

Tuj1 (βIII Tubulin) – Neurites

Neurofilament – Axons