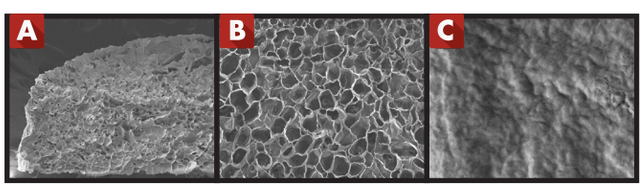
3D CelluSponge

InvitroCue

NOVEL *IN VITRO* PLATFORM TECHNOLOGY

3D CelluSponge is a range of innovative *in vitro* platforms for 3D cell culture. It is fabricated from inert hydroxypropyl cellulose (HPC), has a uniform macroporosity of 80 - 150 µm and each disk is 1 mm thick. The controlled macroporosity allows the formation of uniformly sized spheroids thereby preventing necrosis in the spheroid core via access to nutrients without mass transfer limitations. The constrained spheroids have shown excellent maintenance of 3D cell morphology, viability, cell-cell interaction, cell polarity, synthetic and metabolic functions. The 3D CelluSponge exhibits minimal drug absorption and offers new possibilities for *in vitro* drug safety testing.

This innovative technology has been developed by Professor Hanry Yu in the Laboratory of Cellular and Tissue Engineering of the National University of Singapore and validated through collaboration with leading pharmaceutical companies.



SEM images of 3D CelluSponge:
A) cross-sectional view (scale bar 100 µm),
B) top view (scale bar 100 µm),
C) surface nano-roughness (scale bar 1 µm).

Institute of Bioengineering and Nanotechnology
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NUS National University of Singapore

Benefits

- Simulates complex cell microenvironment *in vitro*
- Promotes enhanced cell-cell contact
- Long term maintenance of differentiated hepatocellular function
- Supports HCV entry and replication
- Supports accelerated differentiation of HepaRG progenitor cells with higher yield of mature HepaRG™ cells
- Easy to use

Features

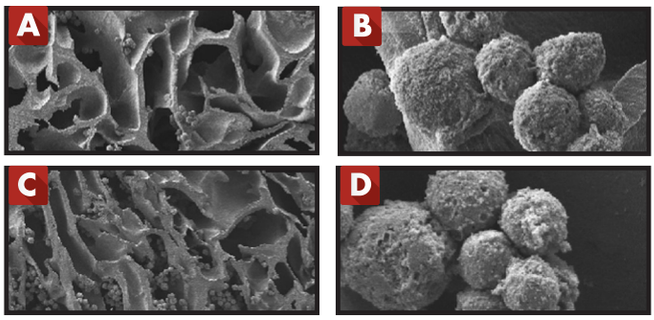
- Macroporous
- Homogenous distribution of spheroids in pores
- Controlled and well-defined spheroid size thus preventing necrosis of the spheroid core
- Similar mechanical properties as the *in vivo* liver
- Works with primary rat, human and monkey hepatocytes as well as HepG2 and HepaRG™ cells
- Compatible with multi-well plates
- Suitable with routine downstream analytical techniques
- Easily scalable

3D CelluSponge Series

3D CelluSponge

√ HPC scaffold with no bioligand conjugation

- Human breast cancer cells (MCF-7)
- Mouse embryonic fibroblasts (NIH-3T3)
- Human foreskin fibroblast (HFF)



A) and B): SEM images of NIH-3T3 cultured on day 1 at low (scale bar 100 µm) and high magnification (scale bar 10 µm), respectively.
C) and D): SEM images on day 5 at low (scale bar 100 µm) and high magnification (scale bar 10 µm), respectively.

3D CelluSponge-GAL

√ Galactose conjugated HPC scaffold

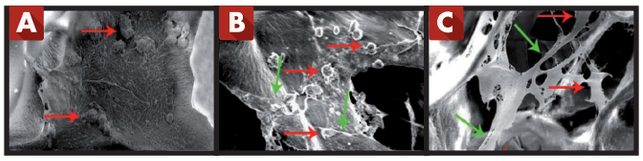
- Primary hepatocytes (rat, human and monkey)
- Hepatic cell lines (Huh 7, Huh 7.5, HepG2 and hepatic progenitor)

SEM images of primary rat hepatocyte spheroids formed in 3D CelluSponge-GAL.

3D CelluSponge-COL

√ Collagen conjugated HPC scaffold

- Embryonic stem cells
- Human mesenchymal stem cells
- iPS derived cardiomyocytes
- Neuronal cells



SEM images of neural differentiation of human mesenchymal stem cells on 3D CelluSponge-COL at different time points of differentiation. The time points are as follows: A) 2 days B) 7 days and C) 14 days. The red arrow indicates the cell body, while the green arrows indicate the neurite. Scale bar 30 µm.

Applications

- 3D cell culture
- *In vitro* drug metabolism and pharmacokinetics (DMPK) assays
- *In vitro* toxicology
- Stem-cell differentiation and maturation
- Pathogen infection and hit identification
- Regenerative medicine

Technical Specifications

- Fabricated from hydroxypropyl cellulose (HPC), an FDA approved biocompatible material
- Diameter of 3D CelluSponge: 9 mm (24-well plate), 6 mm (48-well plate and 96-well plate)
- Thickness of 3D CelluSponge: 1 mm
- Pore size: 80 – 150 µm

Patents

- U.S. patent 8283028 B2
- U.S. patent application 20140080214 A1

Publications

1. Z. Yue et al. 2010. Preparation of three-dimensional interconnected macroporous cellulosic hydrogels for soft tissue engineering. Biomaterials 31(32), 8141-8152
2. H. Gu et al. 2010. Control of *in vitro* neural differentiation of mesenchymal stem cells in 3D macroporous, cellulosic hydrogels. Regenerative Medicine 5(2), 245-253
3. B. Nugraha et al. 2011. Galactosylated cellulosic sponge for multi-well drug safety testing. Biomaterials 32(29), 6982-6994
4. A. Ananthanarayanan et al. 2014. Scalable spheroid model of human hepatocytes for hepatitis C infection and replication. Molecular Pharmaceutics 11(7), 2106-14

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