MINI REVIEW: PGmatrix™ Enables 3D hiPSC Maintenance, Expansion, and Bioprinting

Overview

Human induced pluripotent stem cells (hiPSCs) are fundamental to regenerative medicine, drug discovery, and disease modeling. Conventional 2D culture systems fail to replicate the physiological microenvironment necessary to maintain pluripotency, leading to reduced differentiation potential. This case study highlights PepGel's PGmatrix™ system, a well-defined, xeno-free peptide hydrogel that provides a physiologically authentic 3D microenvironment to support long-term hiPSC maintenance, expansion, and directed differentiation.

Key Features and Findings

- Supports natural formation of uniform 3D hiPSC luminal cyst spheroids (60–100 µm) (**Figure 1a**).
- Achieves 15–25× expansion rate within 4-5 days at optimal seeding density (i.e., 2×10^5 cells/mL) and viability >95%.
- Maintains pluripotency markers (OCT4, SOX2, NANOG, UTF1, hTERT) over 37 passages, with elevated UTF1 and hTERT expression compared to 2D cultures, indicating minimal or no spontaneous differentiations (**Figure 1c**).
- Demonstrates stable karyotype and full pluripotency across three germ layers.
- Enables 3D bioprinting of large sheet constructs (1-3 mm thick) without chemical or photo-crosslinking, preserving cell integrity (**Figure 2**).

Mechanistic Insights

Unlike many other hydrogels, PGmatrix provides controlled degradability that supports cell-driven remodeling and natural signaling exchange. Degradability was identified as the key determinant for hiPSC pluripotency maintenance via YAP/TAZ-regulated Hippo signaling. This balance promotes sustained self-renewal and scalable 3D growth.

Applications

- Scalable hiPSC expansion, and somatic cell and organoid manufacturing.
- High-throughput drug screening and toxicity testing.
- Bioprinting of large sheet-like tissue constructs for regenerative medicine.

Figure 1. hiPSC physiologically developed into 3D natural luminal cyst spheroids in PGmatrix. a. Morphology of hiPSCs cultured in PGmatrix 3D Cells (Cat. EM1004-010-BF) at 0.5% gel content and a seeding density of 2×10^5 cells/mL after five days of culture. Scale bar: 200 µm; **b.** Morphology of hiPSCs cultured in 2D on a Matrigel coated surface. Scale bar: 50 µm; **c.** 3D hiPSC cultured in PGmatrix exhibited significantly upregulated expression of UTF1 and hTERT markers, indicating enhanced differentiation potential and reduced spontaneous differentiation compared to 2D cultures.

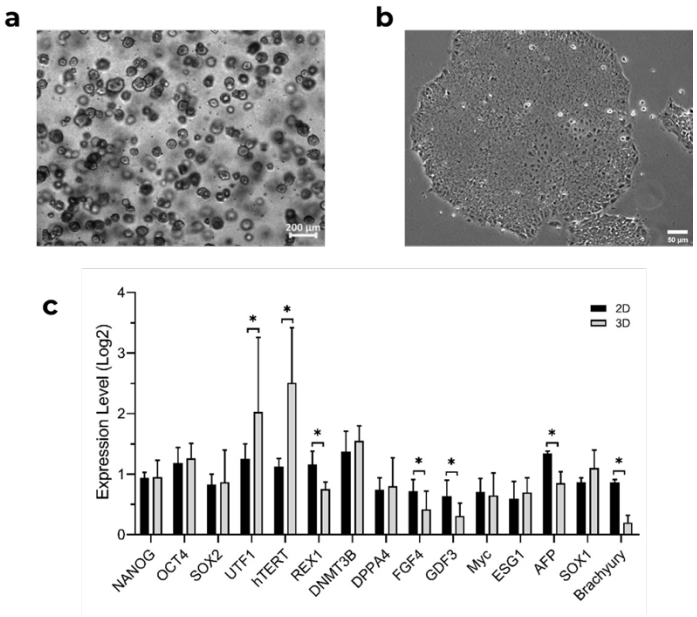
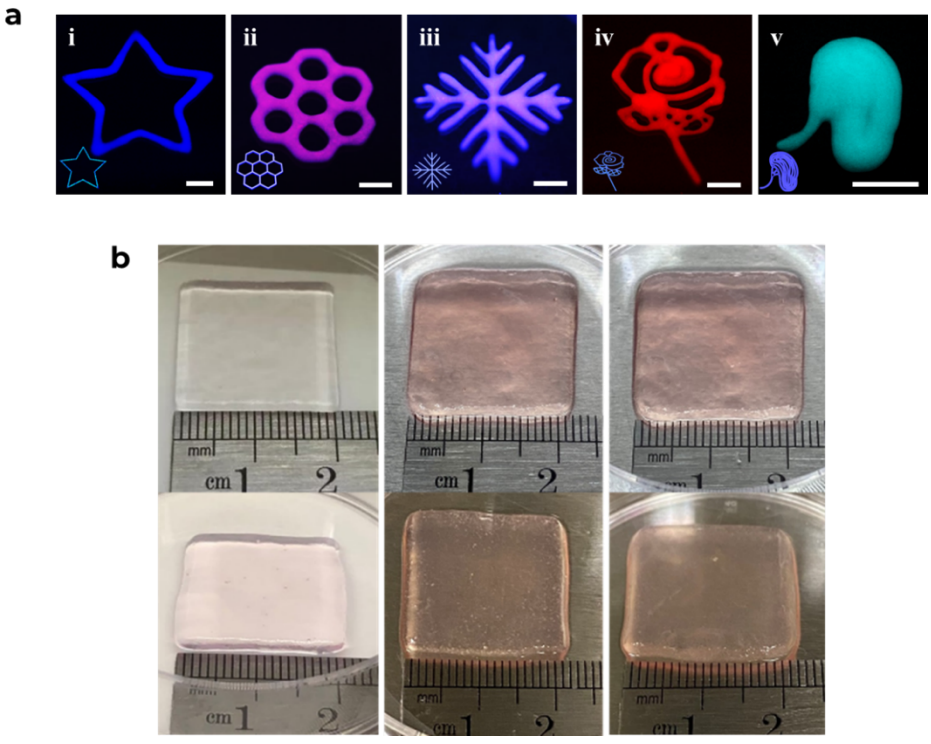


Figure 2: PGmatrix enables large-sheet bioprinting of 3D hiPSCs with superior cell integrity. a. Bioprinted PGmatrix sheet constructs in various patterns. Scale bar 5 mm; **b.** The PGmatrix sheet construct (2 mm thick) remained stable for over six days both with or without hiPSCs. Constructs were intentionally disrupted on day six for cell isolation and subsequent analysis.



Summary

PGmatrix™ establishes a physiologically authentic, xeno-free 3D culture platform that enables consistent, long-term maintenance and scalable expansion of hiPSCs. Its tunable mechanical strength, controlled degradability, and biomimetic extracellular matrix (ECM)-like architecture collectively sustain pluripotency and promote organized 3D colony formation without spontaneous differentiation.

Unlike conventional hydrogels that rely on undefined animal-derived components or rigid matrices, PGmatrix supports dynamic cell–matrix remodeling through natural YAP/TAZ-regulated Hippo signaling, ensuring balanced self-renewal and differentiation capacity. The system's intrinsic bioprintability further allows fabrication of stable, large-scale, tissue-like constructs without chemical or photo-crosslinking, preserving cell integrity and functionality.

By integrating physiological relevance, reproducibility, and scalability, PGmatrix bridges laboratory research and translational biomanufacturing, advancing applications in stem cell expansion, tissue engineering, organoid production, and regenerative medicine.

Adapted from:

Li, Q. et al. (2021). Universal Peptide Hydrogel for Scalable Physiological Formation and Bioprinting of 3D Spheroids from Human Induced Pluripotent Stem Cells. Advanced Functional Materials, 31(2104046).