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Editorial

3D Imaging and Organoid Bioprinting

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Three decades ago, Charles Hull laid the foundation for 3D bioprinting by initiating a mechanical procedure intended for the fabrication of solid scaffolds. Since then, this field has evolved significantly, transforming into a promising technique for precisely depositing biological substances, living cells, and growth factors to generate bioengineered constructs through computer-assisted deposition and assembly methods [1].

Bioinks for organoid fabrication

Bioinks are printable biomaterials for 3D printing, requiring properties such as biodegradability, bioactivity, and non-toxicity. Natural polymers like agarose, alginate, and collagen are preferred due to their similarity to the Extracellular matrix. Hybrid bioinks, such as matrigel–agarose, support intestinal stem cell growth [2]. Alginate-gelatin blends are common for micro-extrusion printing, combining thermo-sensitive properties and cross-linking. Gelatin and its derivative GelMA form thermoreversible hydrogels. Synthetic polymers like polycaprolactone and polyethyl glycolate offer strong mechanical properties, often combined with natural bioinks [3].

Enhanced bioprinting methods for organoid printing

Crucial for the fabrication of computer-aided designs and scaffolds mirroring native tissues, bioprinters use a range of techniques, including inkjet, micro extrusion, laser-assisted, and stereolithography printers. Inkjet bioprinting, utilizing piezoelectric actuators or thermal microheaters, ejects micrometric droplets of bioink, offering high resolution but limited to low viscosity bioinks due to clogging issues. Extrusion bioprinting deposits cellularised filaments with micrometric resolution, allowing for printing with a multitude of bioink materials and scalable construct sizes. Laser bioprinting, a nozzle-free approach, prints high-viscosity biomaterials and high cell densities with precision and high cell viability. At the same time, stereolithography uses layer-by-layer curing of photosensitive polymers using either ultraviolet or visible light to enable rapid and precise fabrication, enabling directed self-organization and regulated differentiation [4].

In the field of stem cell and organoid bioprinting, two prominent methods have emerged: the direct printing of undifferentiated stem cells and the immediate printing of differentiated cells. Various techniques, spanning from extrusion to laser-based methods, have been used for printing pluripotent cells. Extrusion-based printing, employing polysaccharide-based bio-inks, preserves pluripotency in human iPSCs, while laser-assisted bioprinting ensures precise tissue fabrication with enhanced cell viability [5].

Organoid vascularisation

Efforts to vascularise organoids have encountered significant challenges despite advancements in understanding vascular development. In small-scale cultures, static conditions suffice for adequate nutrient supply. However, large-scale 3D cultures require vascularisation to prevent necrosis, especially in thick tissue arrangements where dynamic nutrient flow is essential. The limitations of organoid cultures, such as ceasing proliferation and developing necrotic cores at certain sizes, emphasize the need for vascularization alongside biofabrication. Extrusion bioprinting has been widely used to print endothelial cells alongside other cells directly [6]. As an example, the fusion of hepatic progenitor cells

(HPC) and liver sinusoidal endothelial cells (LSECs) in a 1:1 proportion has resulted in the formation of hepatobiliary organoids featuring liver-specific vasculature, leading to improved survival and liver functions [7].

For the development of brain organoids, several approaches have been explored. The combination of human embryonic stem cell-derived endothelial cells, neural progenitor cells, microglia, and pericytes in artificial hydrogels has created perineural vascular plexus (PNVP) networks [8]. These networks demonstrate functional attributes, including heightened secretion of neurotrophic factors. Self-organizing human blood vessel organoids, derived from pluripotent stem cells, seamlessly integrate into mouse circulation upon transplantation. At the same time, microfluidic techniques enable the spontaneous vascularization of engineered tissues, facilitating the recreation of tissue- and organ-specific vascular architectures [9].

Applications of bioprinted organoids

The scope of organoids needs to improve regarding structural and physiological relevance, limiting their applicability in functional investigations, pathological emulation, and reparative treatment. Advancements in 3D bioprinting and vascularization tactics offer avenues to enhance their significance. By augmenting complexity and size and providing tissue-specific geometries and architectures, bioprinted organoid structures become valuable tools in developmental modeling, disease simulation, pharmaceutical testing, and tissue repair and rejuvenation. Organoids derived from human stem cells offer unique insights into early human development and disease biology. Unlike conventional 2D cultures, they faithfully recapitulate disease characteristics, making them indispensable for disease modeling and mechanistic investigations. Patient-derived organoids, particularly those derived from induced pluripotent stem cells (iPSCs), are pivotal for studying hereditary diseases and elucidating tumor progression mechanisms [10]. These organoids serve as reliable preclinical models for evaluating pharmacological interventions, potentially mitigating drug development setbacks observed in clinical trials. Organoids hold promise in regenerative therapy. Organoids with integrated vasculature, for instance, can be transplanted *in vivo*, circumventing the need for donor organs [11]. Studies have demonstrated the healing capacity of organoid transplantation in various pathological conditions, such as acute liver failure.

Conclusion and future perspectives

Automated three-dimensional bioprinting technology holds promise for scaling up organoid and tissue construct production. Challenges include enhancing bioprinting resolution, minimizing shear stress-induced cell damage, and developing advanced bioinks for intricate organoid patterning and effective vascularization. Despite these challenges, ongoing refinements in techniques and biomaterials ensure the sustained relevance of bioprinted tissue organoids. In the near future, fully fabricated organs with vascular connections will revolutionize disease modeling and drug testing, offering comprehensive insights and reducing reliance on human trials.

References

1. Kupfer ME, Lin WH, Ravikumar V, Qiu K, Wang L, Gao L, et al. In-situ expansion, diferentiation, and electromechanical coupling of human cardiac muscle in a 3D bioprinted. Chambered Organoid Circ Res. 2020;127(2):207-24.
2. Kaushik G, Gupta K, Harms V, Torr E, Evans J, Johnson HJ, et al. Engineered perineural vascular plexus for modeling developmental toxicity. Adv Healthc Mater. 2020;9(16):e2000825.
3. Creff J, Courson R, Mangeat T, Foncy J, Souleille S, Thibault C, et al. Fabrication of 3D scafolds reproducing intestinal epithelium topography by high resolution 3D stereolithography. Biomaterials. 2019;221:119404.
4. King SM, Higgins JW, Nino CR, Smith TR, Paffenroth EH, Fairbairn CE, *et al.* 3D proximal tubule tissues recapitulate key aspects of renal physiology to enable nephrotoxicity testing. Front Physiol. 2017;8:123.
5. Zaky SH, Lee KW, Gao J, Jensen A, Close J, Wang Y, et al. Poly (glycerol sebacate) elastomer: a novel material for mechanically loaded bone regeneration. Tissue Eng Part A. 2014;20(1-2):45-53.

6. Catros S, Guillotin B, Bačáaková M, Fricain JC, Guillemot F. Effect of laser energy, substrate flm thickness and bioink viscosity on viability of endothelial cells printed by laserassisted bioprinting. Appl Surf Sci. 2011; 257:5142-7.
7. Hirsch T, Rothoeft T, Teig N, Bauer JW, Pellegrini G, De Rosa L, et al. Regeneration of the entire human epidermis using transgenic stem cells. Nature. 2011;551(7680):327-32.
8. Logan S, Arzua T, Yan Y, Jiang C, Liu X, Yu LK, et al. Dynamic characterization of structural, molecular, and electrophysiological phenotypes of human-induced pluripotent stem cell-derived cerebral organoids, and comparison with fetal and adult gene profiles. Cells. 2020;9(5):1301.
9. Silvestri VL, Henriet E, Linville RM, Wong AD, Searson PC, Ewald AJ. A tissue-engineered 3D microvessel model reveals the dynamics of mosaic vessel formation in breast cancer. Cancer Res. 2020;80(19):4288-301.
10. Hiller T, Berg J, Elomaa L, Röhrs V, Ullah I, Schaar K, et al. Generation of a 3D liver model comprising human extracellular matrix in an alginate/ gelatin-based bioink by extrusion bioprinting for infection and transduction studies. Int J Mol Sci. 2018;19(10):3129.
11. Sun W, Starly B, Daly AC, Burdick JA, Groll J, Skeldon G, et al. The bioprinting roadmap. Biofabrication 2020; 12(2):022002.

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