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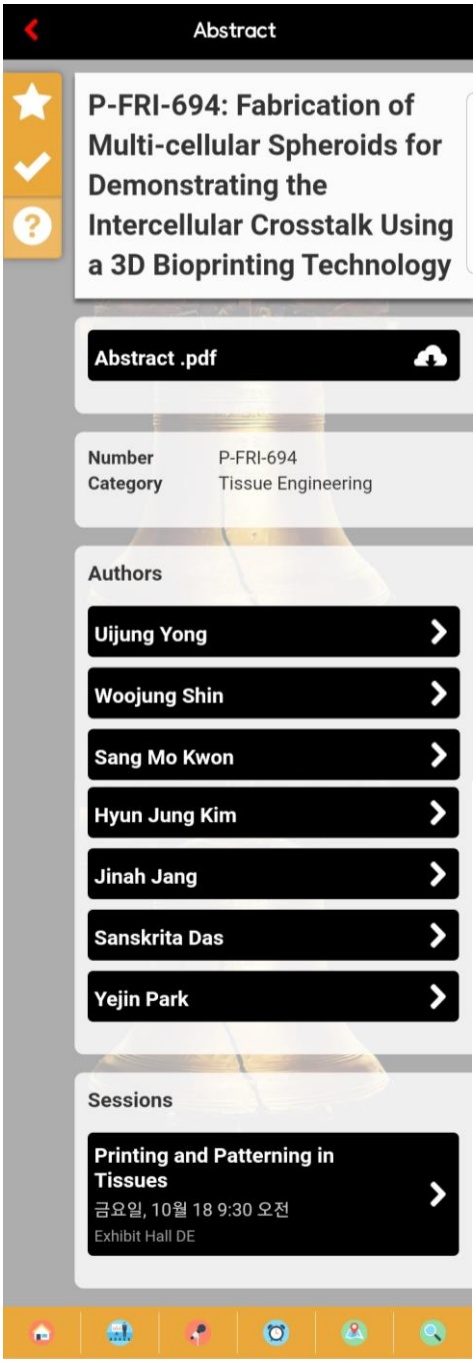
Abstract
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Printing and Patterning in Tissues
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Exhibit Hall DE

Fabrication of Multi-cellular Spheroids for Demonstrating the Intercellular Crosstalk Using a 3D Bioprinting Technology

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Introduction: Intercellular interaction is known as one of the essential characteristics to recapitulate the intrinsic cellular functions in an engineered system. Among the various shapes of the cell-laden construct, the form of spheroids is suitable for mimicking the minimum unit of the cellular ecosystem in the body. The standard methods of fabricating spheroids deal with the difficulties of producing uniform sized spheroids in a standard high throughput manner and cost considerations. To expedite the fabrication process of size-controlled cell-laden spheroids in a cost-effective way and high throughput production, novel approaches should be targeted to accelerate its performance. The present study focused on demonstrating a promising approach to fabricate cell-laden spheroids in a high throughput manner in standard Petri plate format using three-dimensional (3D) bioprinting technology. We use a mixture of alginate solution (1%) and tissue-specific decellularized extracellular matrix (dECM) to confine the cells by printing the bioink drops into a coagulation bath of calcium chloride (0.1M) and Pluronic F-127. Upon the crosslinking of the bioink, we can control the size of spheroids and the density of encapsulated cells. Exploiting the 3D bioprinting technology to confine the cells in the form of size-controlled spheroids accelerates the process of spheroid production for a wide range of applications such as cell delivery, co-culture of multi-species microbial cells, and drug screening.

Materials and Methods: 3D bioprinted uniform sized cell-laden spheroids were fabricated via a 3D bioprinter where cardiac progenitor cells (CPCs) were encapsulated in 1% (w/v) hdECM with alginate bioink. By varying parameters such as mixing ratio, nozzle size, and applied pressure, an optimal condition to produce size-controlled spheroids were determined. To validate the versatility of the current strategy in fabricating different types of cellular spheroids, MIN6, a pancreatic beta cell line, and various light-emitting bacterial cell lines were encapsulated in pancreatic tissue-derived decellularized extracellular matrix (pdECM) and colon tissue-derived decellularized extracellular matrix (CL-dECM) respectively to produce cell-laden spheroids in a high throughput manner.

Results and Discussion: We demonstrated that the cell-based 3D bioprinted spheroids maintained its structural integrity when the mixing ratio of alginate to dECM was 1:2. Also, spheroids possessing a constant diameter of 300-350 μm could be obtained using 0.1 M $CaCl_2$ and 15% Pluronic F-127 as a coagulating bath. In *in vitro*, cell-based spheroids demonstrated predominant green fluorescence highlighting the dominated population of live cells and clearly indicates that cells were viable in the biocompatible dECM niche condition. We also used this printed spheroid platform for co-culturing a multi-species microbial community that shows a cross-feeding metabolism in the human gut.

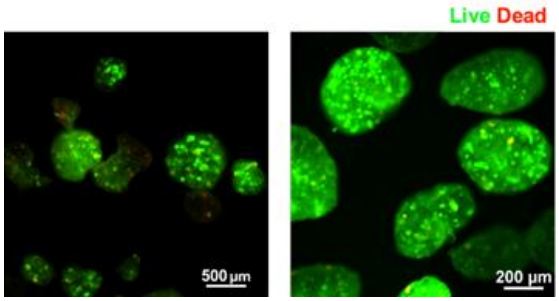

Figure 1. Fluorescence Images of 3D bioprinted spheroids encapsulating cardiac progenitor cells at day 7, scale bar 500μm (left); at day 14, scale bar 200μm (right)

Conclusions: The current strategy presents a novel step toward high throughput production of uniform sized spheroids without the use of any external forces. In addition, creating a microenvironmental niche using tissue derived dECM provides a tissue-mimetic microenvironment for the encapsulated cells thereby, promoting enhanced intrinsic functions. Hence, immobilizing and direct delivery of cells in the form of 3D bioprinted spheroids provide a new platform for the treatment of damaged tissue sites, co-culture of gut microbiome, and opens an avenue for carrying out further studies about drug screening with improved throughput and efficiency. In conclusion, our fabrication strategy can present the versatility in incorporating different types of cells and its co-cultures for understanding the multi-cellular interactions.

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(Oct. 16, 2019 – Oct. 19)

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Abstract

Intercellular interaction is known as one of the essential characteristics to recapitulate the intrinsic cellular functions in an engineered system. Among the various shapes of the cell-laden construct, the form of spheroids is suitable for mimicking the minimum unit of the cellular ecosystem in the body. The standard methods of fabricating spheroids deal with the difficulties of producing uniform sized spheroids in a standard high throughput manner and cost considerations. To expedite the fabrication process of size-controlled cell-laden spheroids in a cost-effective way and high throughput production, the present study focused on demonstrating a promising approach to fabricate cell-laden spheroids using three-dimensional (3D) bioprinting technology. By varying parameters such as mixing ratio, nozzle size, and applied pressure, an optimal condition to produce size-controlled spheroids were determined. In *in vitro*, cell-based spheroids demonstrated predominant green fluorescence highlighting the dominated population of live cells and clearly indicates that cells were viable in the biocompatible dECM niche condition. We also will use this printed spheroid platform for co-culturing a multi-species microbial community that shows a cross-feeding metabolism in the human gut in the future.

Conclusion

- The current strategy presents a novel step toward high throughput production of uniform sized spheroids without the use of any external forces.
- Using tissue-derived dECM provides a tissue-mimetic microenvironment for the encapsulated cells thereby, promoting enhanced intrinsic functions.
- Immobilization and direct delivery of cells in the form of 3D bioprinted spheroids provide a new platform for the treatment of damaged tissue sites, co-culture of gut microbiome, and opens an avenue for carrying out further studies about drug screening with improved throughput and efficiency.

Reference

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