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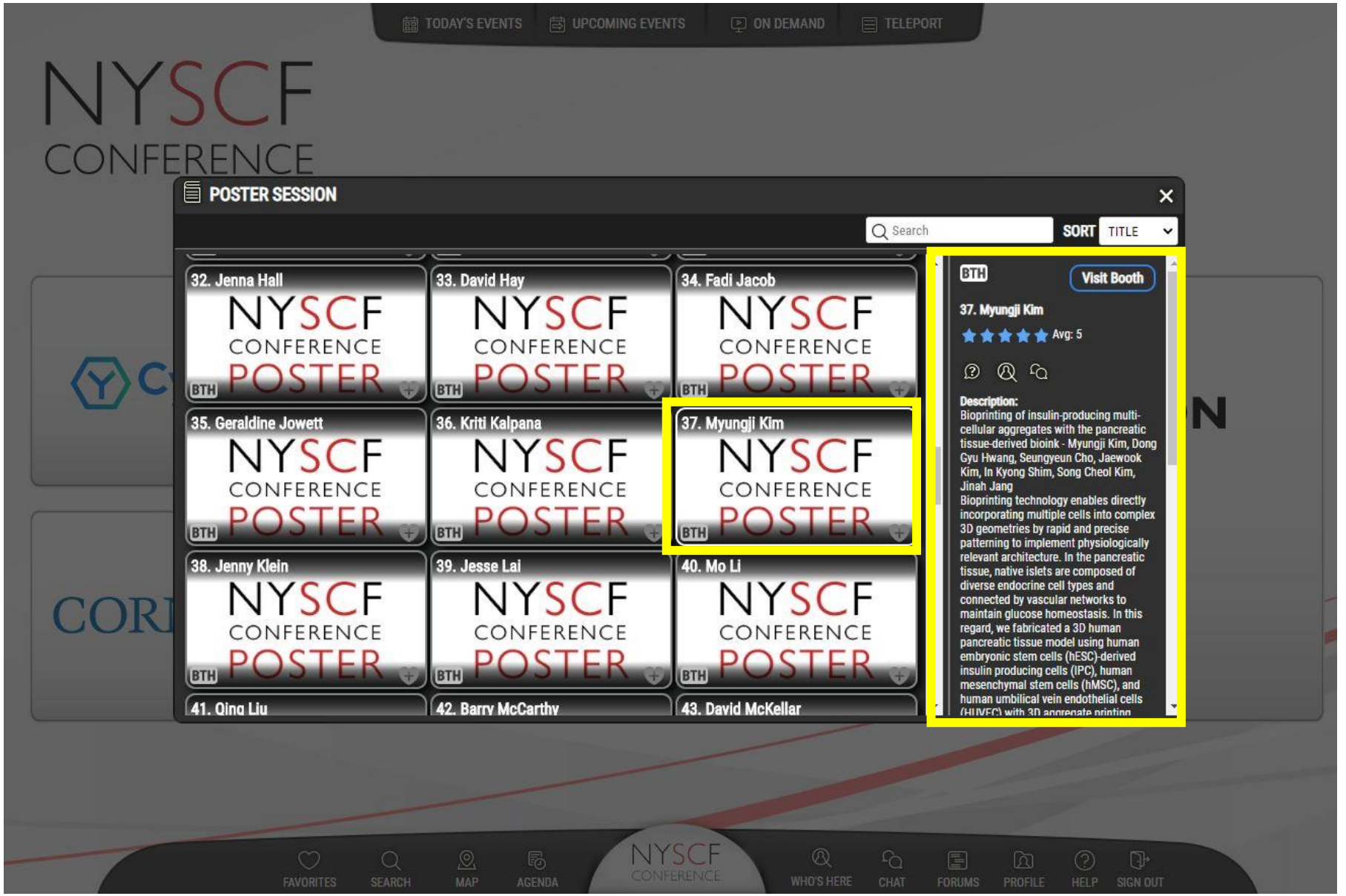
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Description:
Bioprinting of insulin-producing multi-cellular aggregates with the pancreatic tissue-derived bioink - Myungji Kim, Dong Gyu Hwang, Seungyeun Cho, Jaewook Kim, In Kyong Shim, Song Cheol Kim, Jinah Jang
Bioprinting technology enables directly incorporating multiple cells into complex 3D geometries by rapid and precise patterning to implement physiologically relevant architecture. In the pancreatic tissue, native islets are composed of diverse endocrine cell types and connected by vascular networks to maintain glucose homeostasis. In this regard, we fabricated a 3D human pancreatic tissue model using human embryonic stem cells (hESC)-derived insulin producing cells (IPC), human mesenchymal stem cells (hMSC), and human umbilical vein endothelial cells
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NYSCF 2020

- Bioprinting of insulin-producing multicellular aggregates with the pancreatic tissue-derived bioink - (October 20, 2020 – October 21)

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Abstract

Bioprinting technology enables directly incorporating multiple cells into complex 3D geometries by rapid and precise patterning to implement physiologically relevant architecture. In the pancreatic tissue, native islets are composed of diverse endocrine cell types and connected by vascular networks to maintain glucose homeostasis. In this regard, we fabricated a 3D human pancreatic tissue model using human embryonic stem cells (hESC)-derived insulin producing cells (IPC), human mesenchymal stem cells (hMSC), and human umbilical vein endothelial cells (HUVEC) with 3D aggregate printing approach to emulate native pancreatic islet-like structure and function.

Development of bioink as a functional building block, which can support robust cell differentiation and proliferation, is a critical step towards creation of engineered tissue constructs. In previous study, we proposed that pancreatic tissue derived-decellularized extracellular matrix (pdECM) bioink is compatible with advanced pancreatic tissue engineering as encapsulated islets in pdECM bioink revealed functional stability in glucose responsiveness over typical bioink. Here, we organized the list of major components in the pdECM bioink through gene ontology and proteomic analysis to assess whether tissue-derived bioink can provide sufficient pancreatic cell niche. The representative protein of pdECM bioink was collagen type VI, and other important ECM proteins were also abundant compared to that of the collagen bioink.

Moreover, differentiation of hESC into IPC using four-stage protocol was performed to generate functional human pancreatic cells and differentiated cells were characterized by gene expression profile and flow cytometry analysis. As a result, beta cell-specific markers including NKX6.1, PDX1, and insulin exhibited high expression level. After generation of IPC, spatial organization of IPC aggregates via 3D bioprinting were validated for recapitulating native pancreatic tissue geometry. Rapid induction of cellular networks between IPC aggregates comprising IPC, HUVEC, and hMSC was observed after 2 days of printing. Future efforts on functional tests will be able to improve the established 3D human pancreatic tissue model, expanding the application of in vitro and in vivo studies for diabetes research.

Conclusion

- Proteomic analysis results revealed that the representative protein of pdECM bioink was collagen type VI, and other important ECM proteins were also abundant compared to that of the collagen bioink.
- Representative flow cytometry plots of S4 cells showed that beta cell-specific markers including NKX6.1, PDX1, and insulin exhibited high expression level. Moreover, rapid induction of cellular networks between bioprinted aggregates comprising IPC, HUVEC, and hMSC was observed after 2 days of printing.
- Future efforts on functional tests will be able to improve the established 3D human pancreatic tissue model, expanding the application of in vitro and in vivo studies for diabetes research.

Reference

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Acknowledgement

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