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Abstract submission deadline: June 23th, 2023
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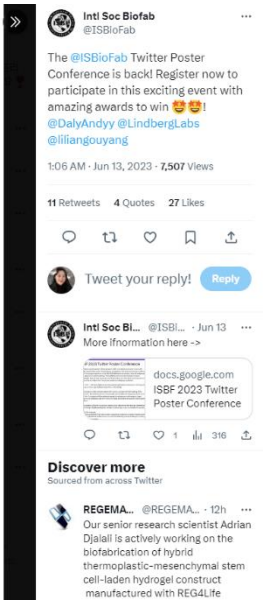

https://twitter.com/MyungjiKIM_/status/1678769247101812744

Bioprinting of Bespoke Pancreatic Niche for Human Islet-like Cellular Aggregates and Vasculatures to Model Diabetic Diseases

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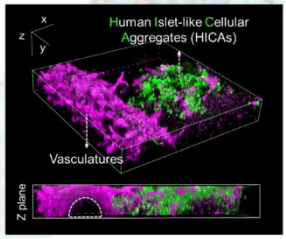
Abstract

The interplay between pancreatic islets and the surrounding microenvironment (e.g., neighboring vascular cells and basement membrane-enriched extracellular matrix) is pivotal for the maturation of insulin-producing beta cells and metabolic homeostasis. In this study, we suggest two engineering strategies to improve the glucoregulatory functions of stem cell-derived islets, (1) **creation of the bespoke niche to generate an islet-specific environment with pancreatic tissue-specific matrix supplemented with basement membrane proteins** and (2) **bioprinting based-structural guidance of islets and vasculatures to recapitulate spatial arrangement of islet periphery**. Geometrically controlled human islet-like cellular aggregates and vasculatures within the realistic pancreatic niche significantly improved glucose responsiveness of stem cell-derived islets and reproduced **physio-mimetic phenomena in native islets, encompassing both healthy and diabetic states**. Our engineering insights into the manipulation of niche properties to recreate tissue-specific organization pave the way for demonstrating the microenvironmental effects on differentiation of islets, functional maturation, and diabetic disease modeling.

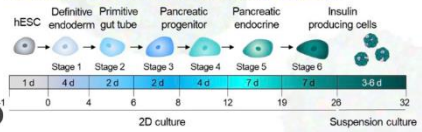


Background

Can geometrically controlled stem cell-derived human islet-like cellular aggregates (HICAs)-vasculatures within the tailored pancreatic-specific niche reproduce the physio-mimetic responses of native islets via facilitating metabolic functions of islets?

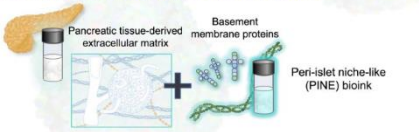
Methods

1. Differentiation of insulin-producing beta cells



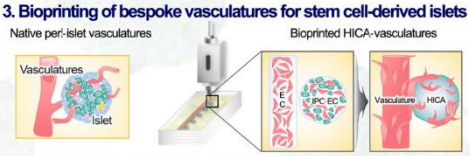
To mainly elucidate insulin secretory functions of the islets, differentiation of insulin-producing beta cells was performed via a standardized 6 stages protocol. After differentiation, cells were dissociated into single cells and encapsulated for 3D culture and bioprinting applications.

2. Development of peri-islet niche-like bioink



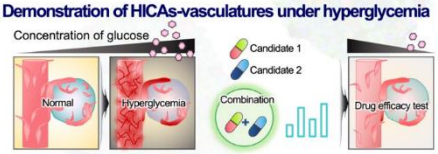
To recreate the pancreatic-mimetic niche for enhancing functional maturation capacity of islets, laminin and type IV collagen, which are principal ECM components of native peri-islets, were supplemented to the pdECM bioink.

3. Bioprinting of bespoke vasculatures for stem cell-derived islets



We used in-bath printing technique to mimic native islets, which are embedded within the ECM and have robust vascular networks in the periphery. EC-laden bioink were linearly patterned and IPC-EC-laden bioink, which contain high cellular density 1×10⁶ cells per mL, were printed for 0.8 s within the bath.

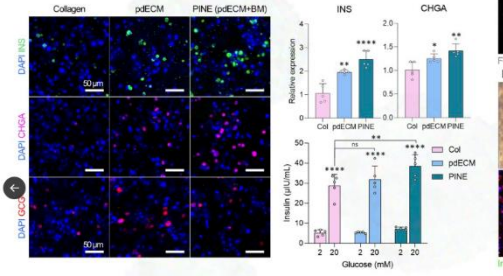
4. Demonstration of HICAs-vasculatures under hyperglycemia



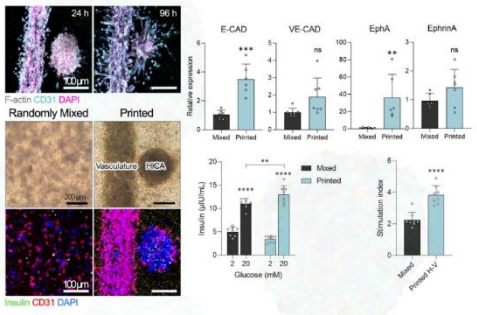
Diabetic condition was induced by high concentration of glucose in culture media. Physio-mimetic pathophysiology in the printed HICAs-vasculatures was observed. Moreover, we tested a representative anti-diabetic drug, Metformin, to further evaluate the physiological responses of the HICAs-vasculatures.

Results

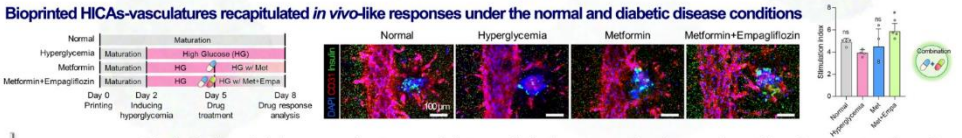
PINE bioink enhances functional maturity of stem cell-derived islets



Bioprinting of islet-specific vasculatures facilitates insulin release



Bioprinted HICAs-vasculatures recapitulated *in vivo*-like responses under the normal and diabetic disease conditions



Conclusion

Manipulation of niche properties to recapitulate realistic tissue organization can boost functional maturation of pancreatic islets and vasculatures and induce physio-mimetic responses for the studies of diabetic diseases.

Myungji Kim @MyungjiKIM_

Excited to have my work on bioprinting of bespoke pancreatic niche for stem cell-derived islets and vasculature to model diabetic diseases in #Biofab2023 @ISBioFab !!

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Gabriella Li... @Lind... · Jul 12
Exciting work with the fabrication of islet-specific vasculatures for drug testing @MyungjiKIM_! Does the placement (um distance) between vasculature and islet impact the functional maturation, is there a critical limit of proximity needed for the crosstalk to be effective?

Myungji ... @Myungji... · 22h
I'm grateful for the kind comments @LindbergLabs ! We hypothesized that the proximal condition(~30 um) could induce active crosstalk in the printed cellular networks, generating diverse signaling molecules that are critical in the glucoregulatory functions of islets.

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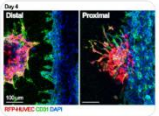

rlevato @RicLevato · Jul 12
Congrats for the nice work @MyungjiKIM_! It is nice to see a system with both pancreatic endocrine cells and vasculature. Did you have to develop a co-culture media to grow both cell types together? Which components/formulation worked better for you?

Myungji ... @Myungji... · 22h
In this process, we verified that the viability of endothelial cells was significantly reduced in the EGM-2+ESFM condition. Based on this result, we utilized a combination of EGM-2 with 1 % p/s and CMRL with 10 % FBS, 1 % p/s, and 1x glutaMAX, maintaining a 1:1 ratio.