Bioprinting morphogen gradients using granular hydrogels to guide spatial patterning of iPSCs along mesoderm and cardiac lineages

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STATE-OF-THE-ART

Current cardiac bioprinting approaches rely on pre-differentiating iPSCs into cardiomyocytes in 2D before encapsulating them in a bioink[1]. This bypasses core developmental processes that occur in vivo where morphogen gradients spatially pattern progenitor cells along mesodermal and cardiac lineages (e.g., ventricular and atrial cardiomyocytes)[2]. Recapitulating such multicellular patterning in bioprinted heart tissues is challenging, as existing platforms cannot deliver morphogens with the spatial and temporal control required to guide iPSC differentiation.

HYPOTHESIS

Granular hydrogels can be engineered to deliver spatially defined morphogen gradients around bioprinted iPSCs, thereby guiding their differentiation along mesoderm and cardiac lineages.

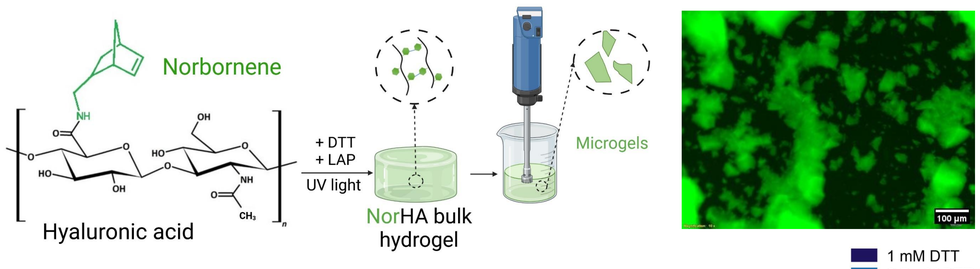
OBJECTIVES

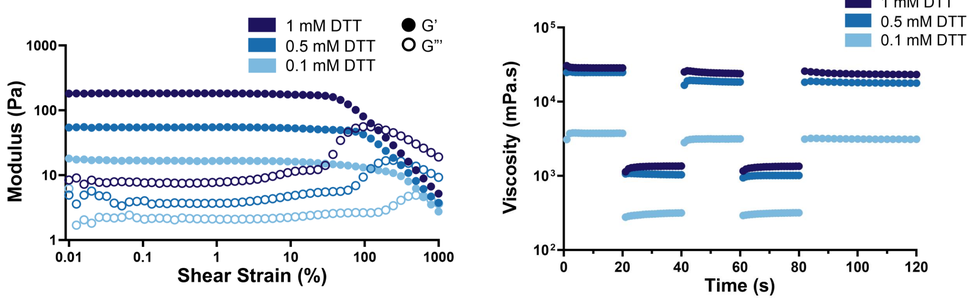
Develop granular hydrogels that enable:

1. Embedded bioprinting of pluripotent iPSC tissue constructs
2. Spatiotemporal release of morphogens from the surrounding support bath
3. Gradient-directed patterning of iPSCs along mesoderm and cardiac fates

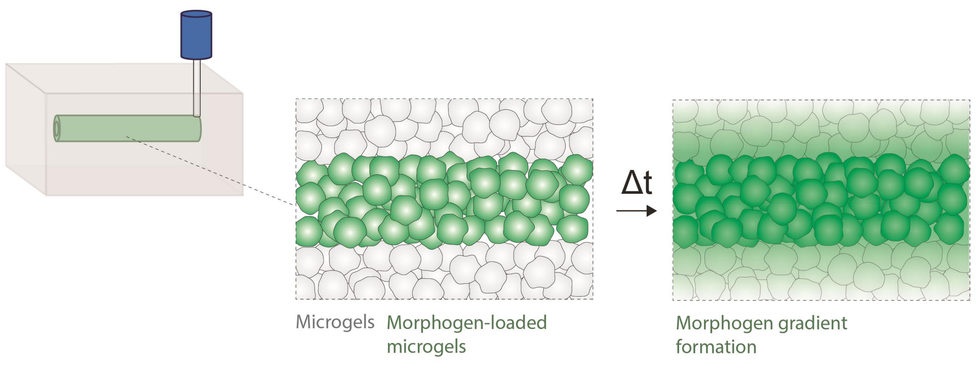
METHODOLOGY

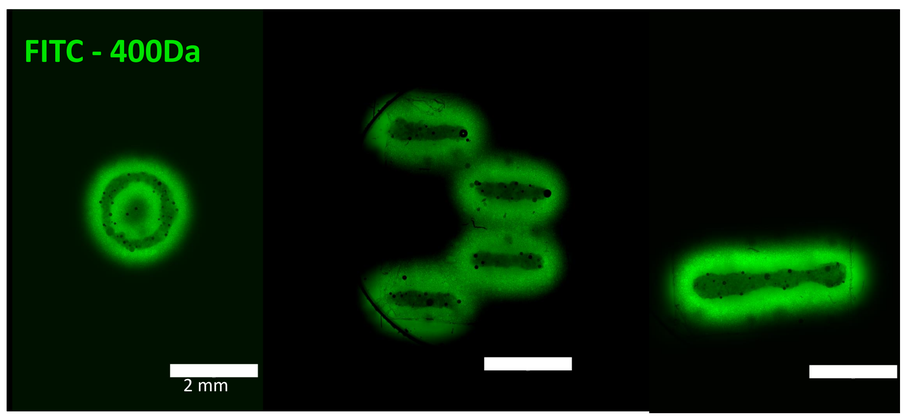
a) Granular hydrogel fabrication using hyaluronic acid





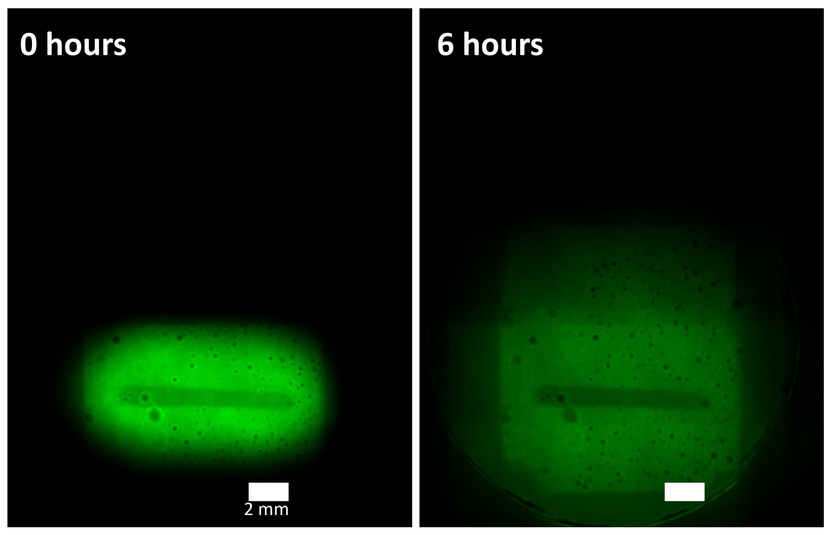
b) Bioprinting morphogen gradients using granular hydrogels

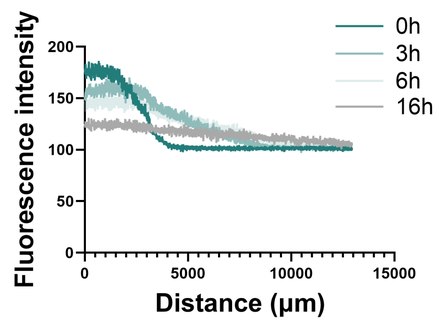


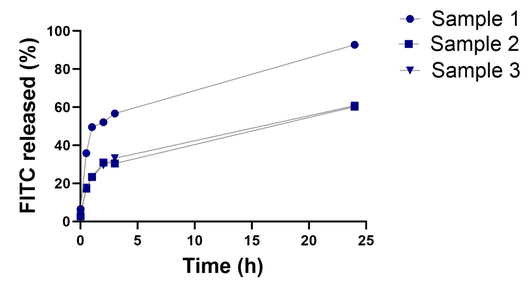


RESULTS

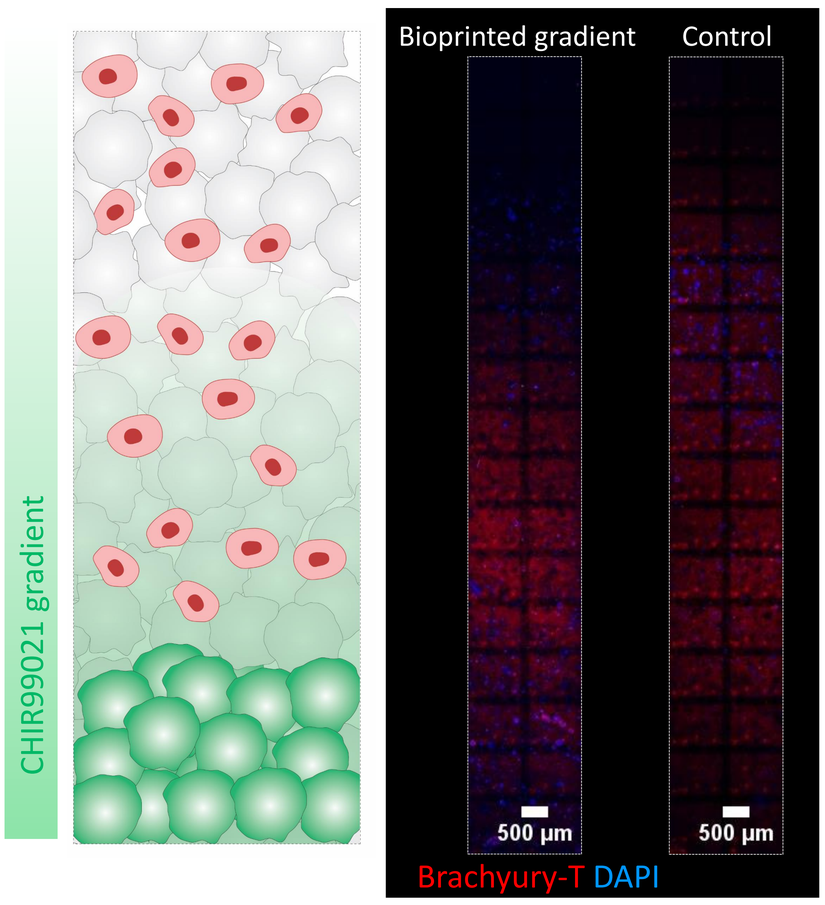
a) Spatiotemporal control of diffusion gradients via embedded printing in granular hydrogels

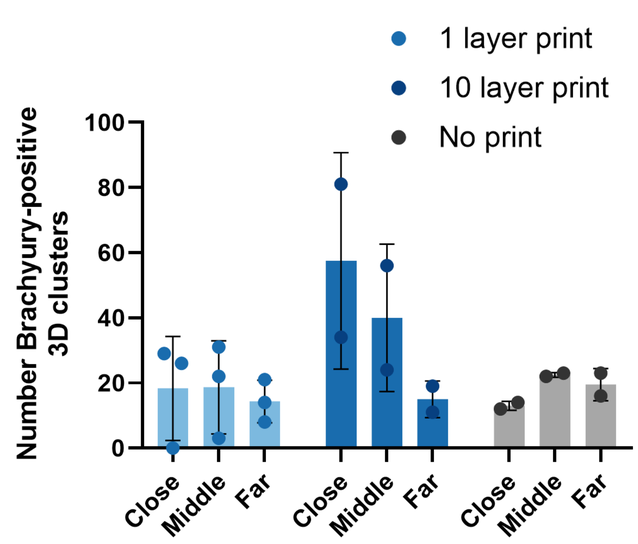




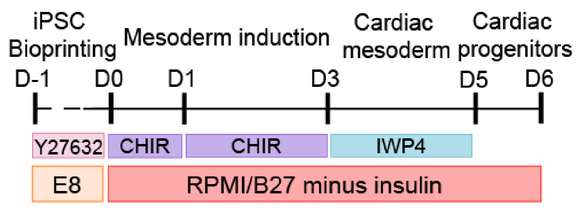


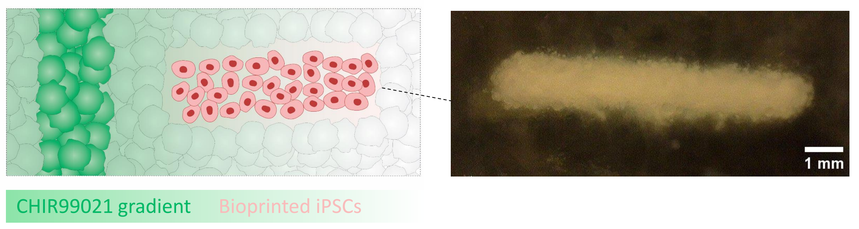
b) Spatial mesodermal differentiation of iPSCs using bioprinted CHIR gradients

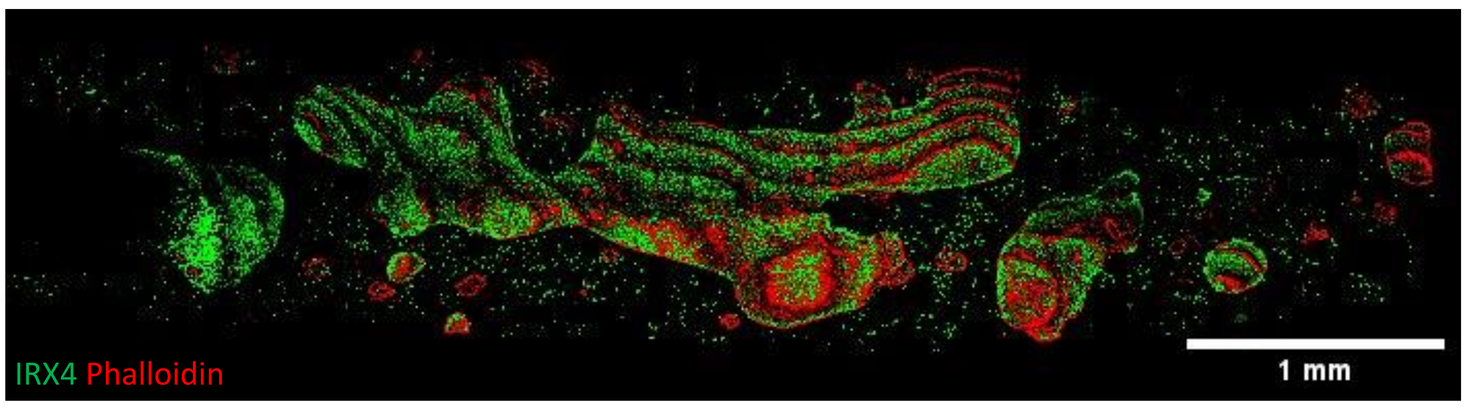




c) Controlling cardiac differentiation of iPSCs using bioprinted CHIR gradients







CONCLUSIONS

- NorHA granular hydrogels can serve as both inks and support baths for embedded bioprinting of spatiotemporally controlled morphogen gradients.
- iPSCs undergo mesoderm and cardiac differentiation in response to bioprinted gradients of CHIR99021.
- Future work will apply this platform to spatially control 3D in situ differentiation of iPSCs into multicellular cardiac tissues.

REFERENCES

1. Noor N., et al., Advanced Science. 2019
2. Farah E.N., et al., Nature. 2024

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