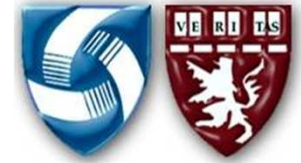




WYSS INSTITUTE  
for Biologically Inspired Engineering



# An introduction to microengineered hydrogels for stem cell bioengineering and tissue regeneration



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## Collaborators

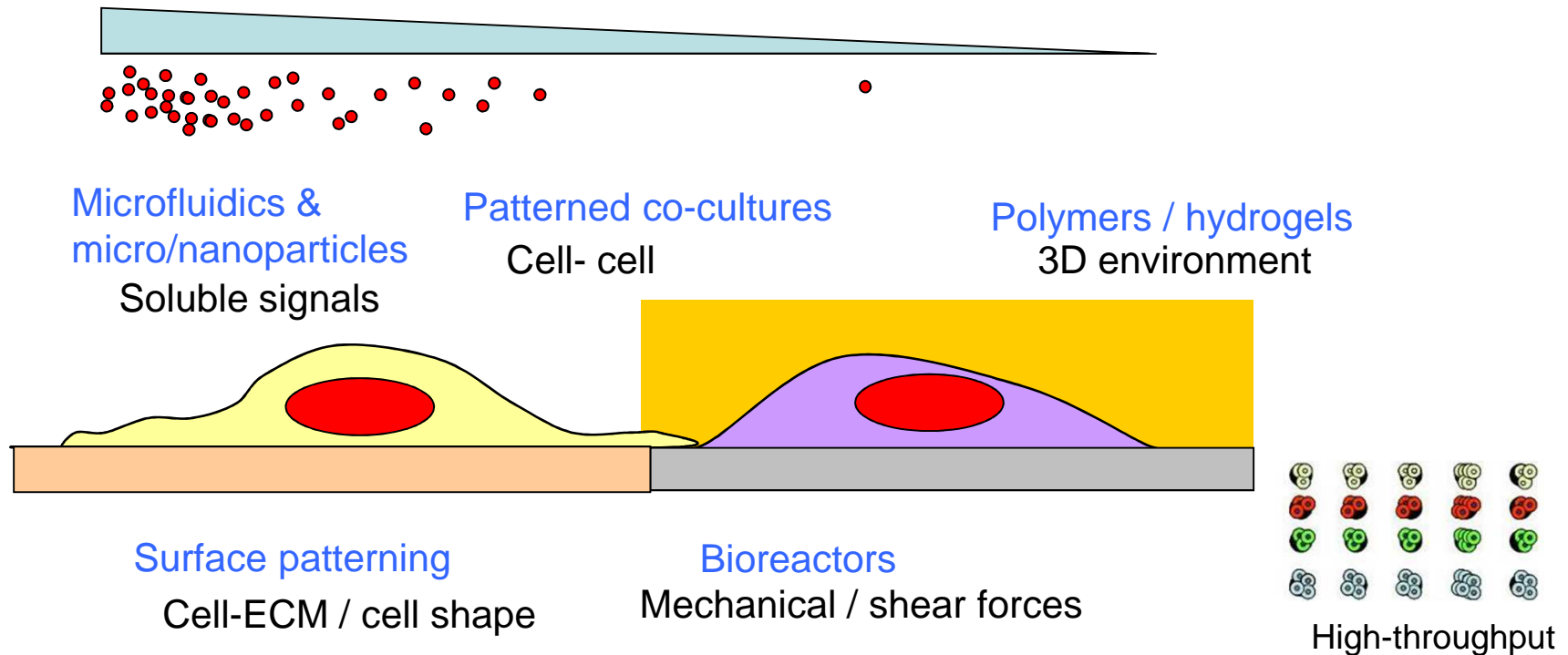
- Prof. Robert Langer
- Prof. Joseph Vacanti
- Prof. Fariba Dehghani
- Prof. Don Ingber
- Prof. Nicholas Peppas
- Prof. Matthias Lutolf
- Dr. Jeff Borenstein
- Prof. Joey Barnett
- Prof. Jianjun Cheng
- Prof. Utkan Demirci
- Prof. Peter Yang
- Prof. Jian Yang
- Prof. Rui Reis
- Prof. Vasif Hasirci
- Prof. Jason Burdick
- Prof. Junji Fukuda
- Prof. Matteo Morreti
- Prof. Kahpyang Suh
- Prof. Richard Maas
- Prof. Ronglih Liao
- Prof. Shaochen Chen
- Prof. SangHoon Lee
- Prof. Eben Alsberg
- Prof. J.W. Hong
- Prof. Junji Fukuda
- Prof. Scott Baldwin

## Friends / Family

- Parents / Salomeh
- Sefton Lab
- Zandstra Lab
- Langer Lab
- Peppamers
- ...



# Microscale approaches to regulate cellular environment

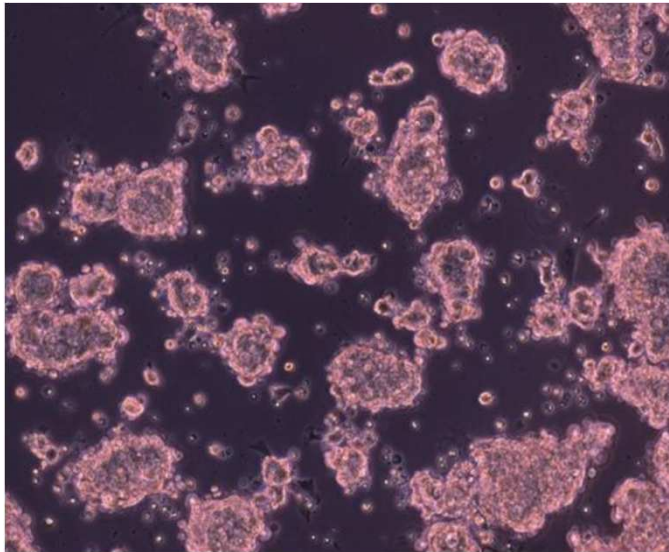


Microfabrication can be used to **generate microscale structures** and miniaturize experiments for **high-throughput analysis**

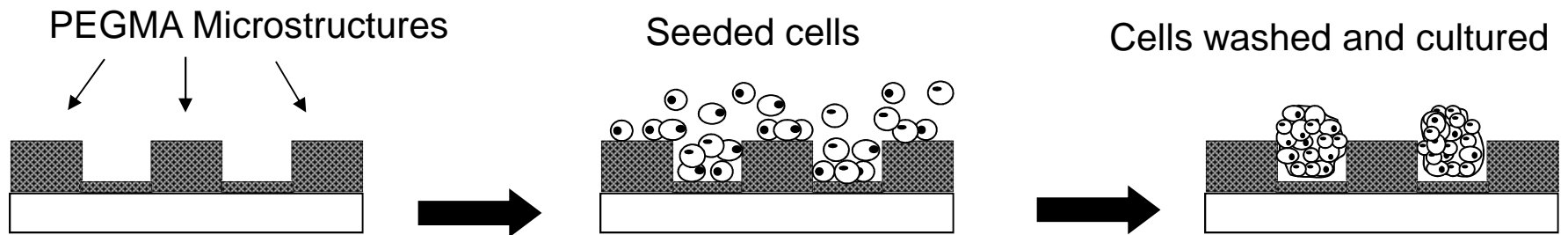
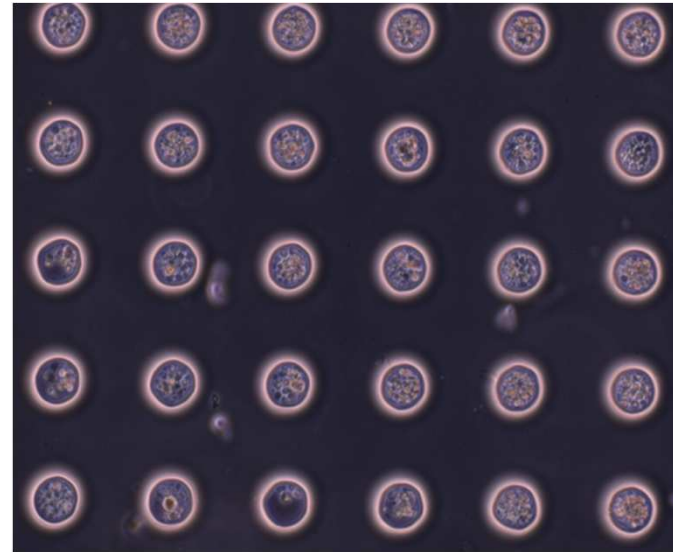


# Control of EB size, homogeneity and shape

suspension cultures



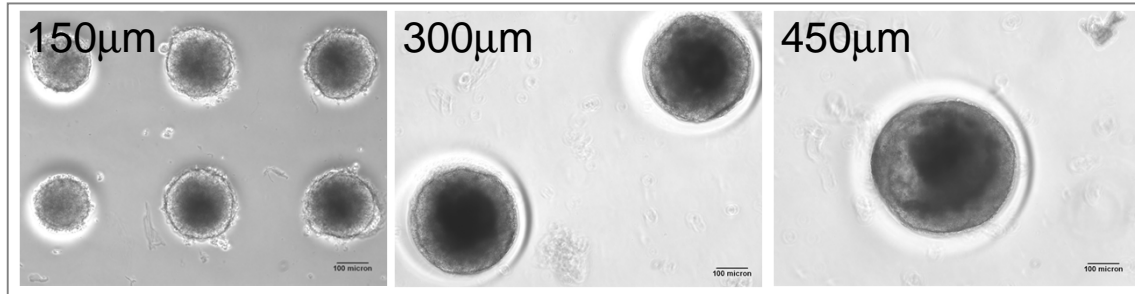
microwells



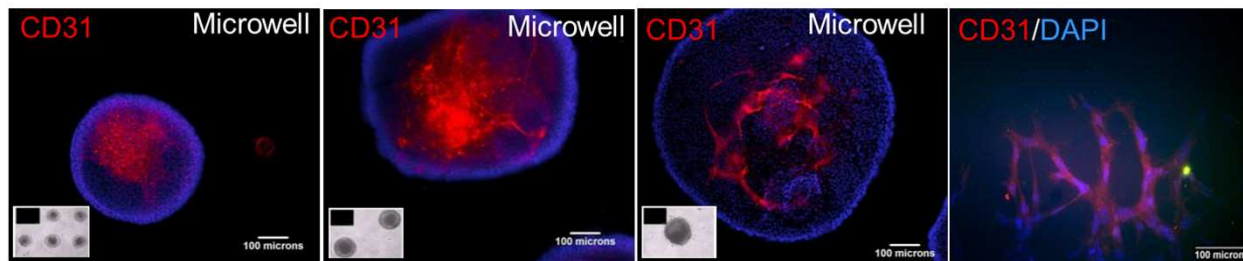
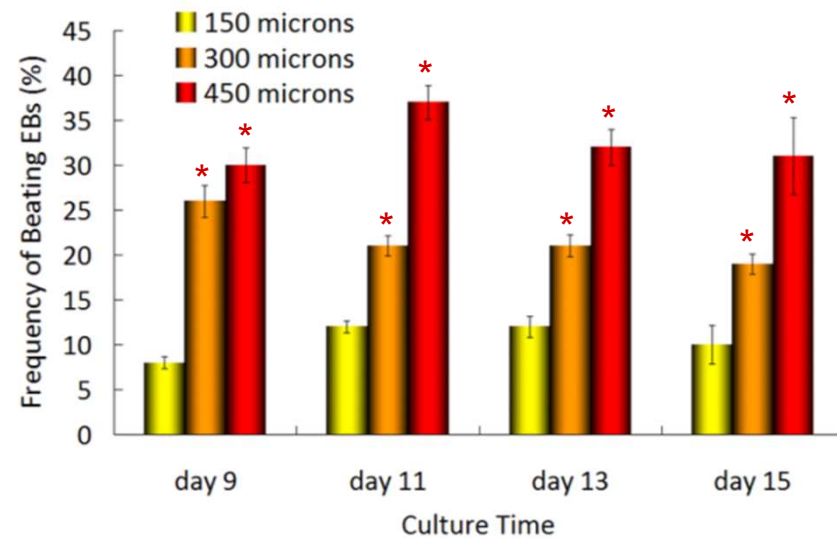
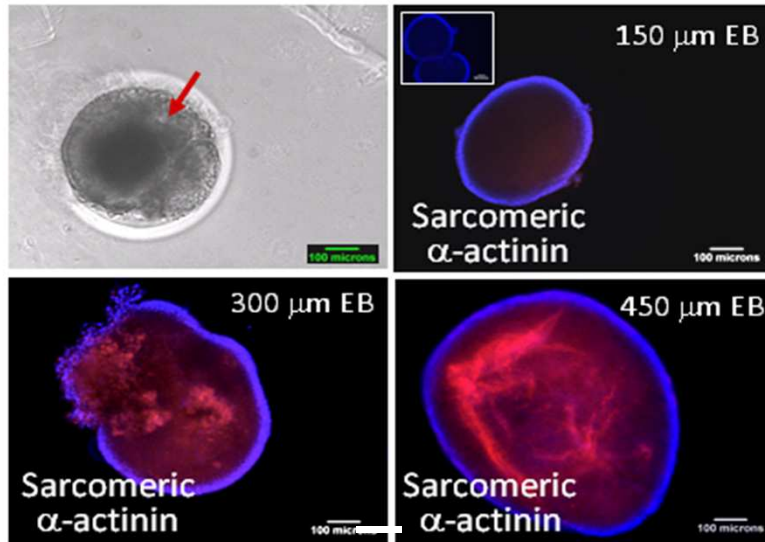
Lab on a Chip (2007); Biomaterials (2007); PNAS (2009); JACS (2011)



# EB size mediates stem cell differentiation into cardiac and endothelial cells

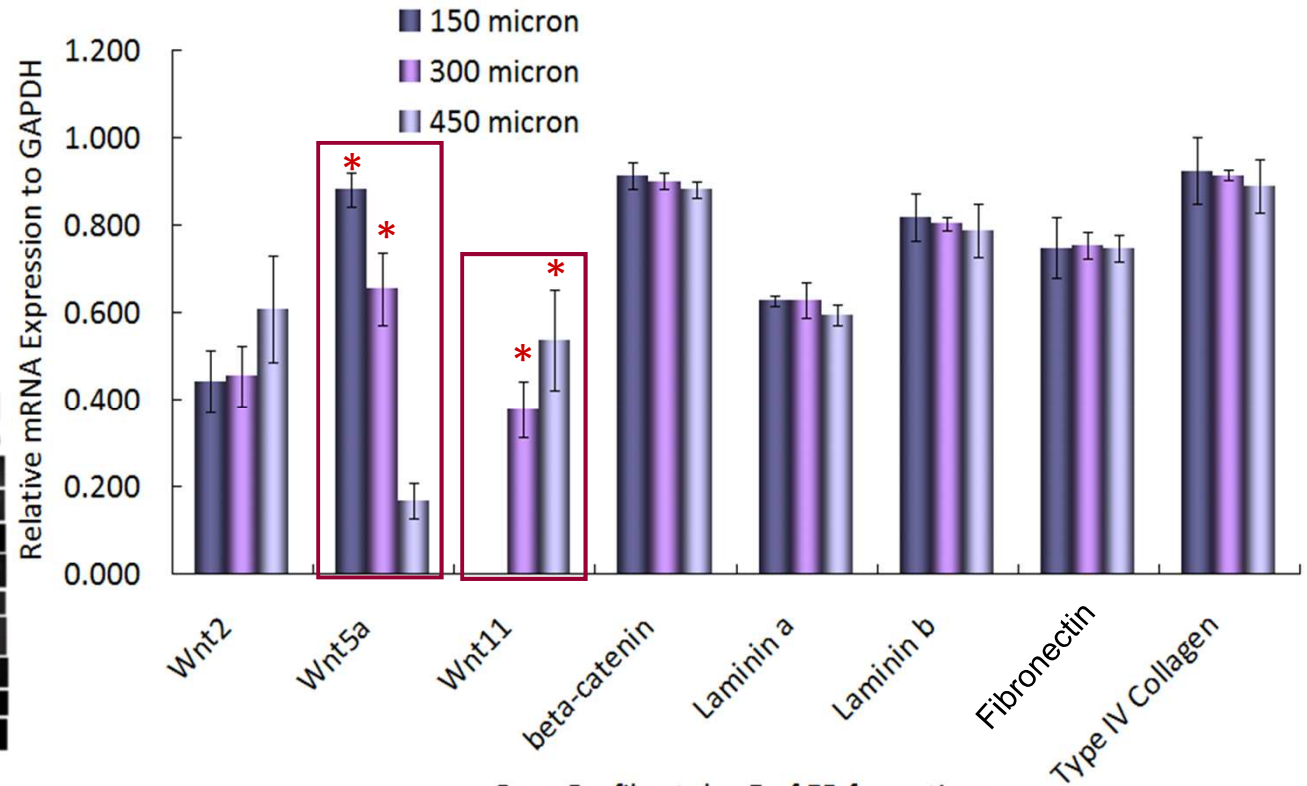
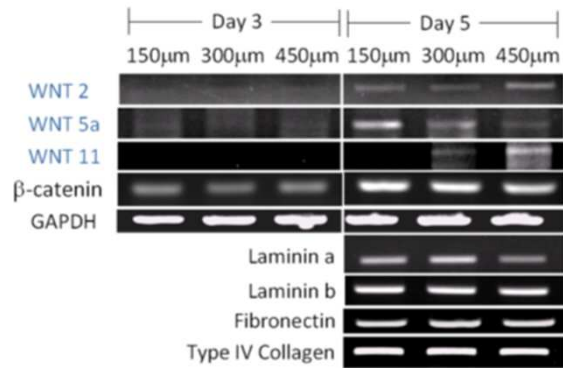


Hwang et al.  
PNAS (2009)



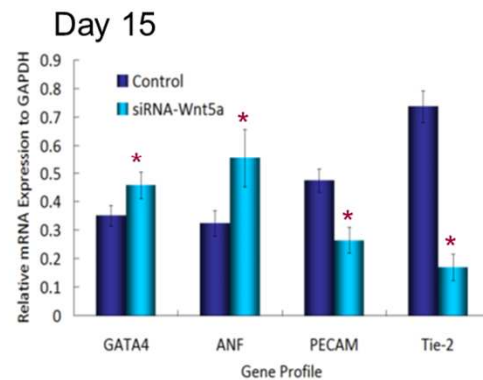
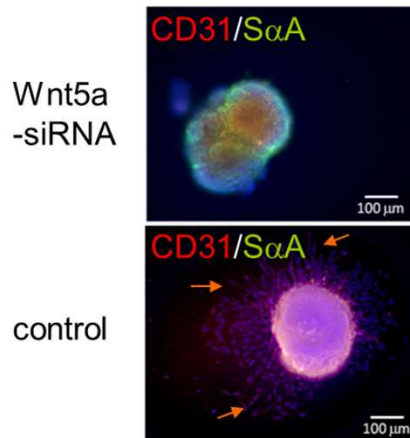


## Non-canonical Wnt Signaling (Wnt 5a & Wnt 11) regulate EB differentiation



Gene Profile at day 5 of EB formation

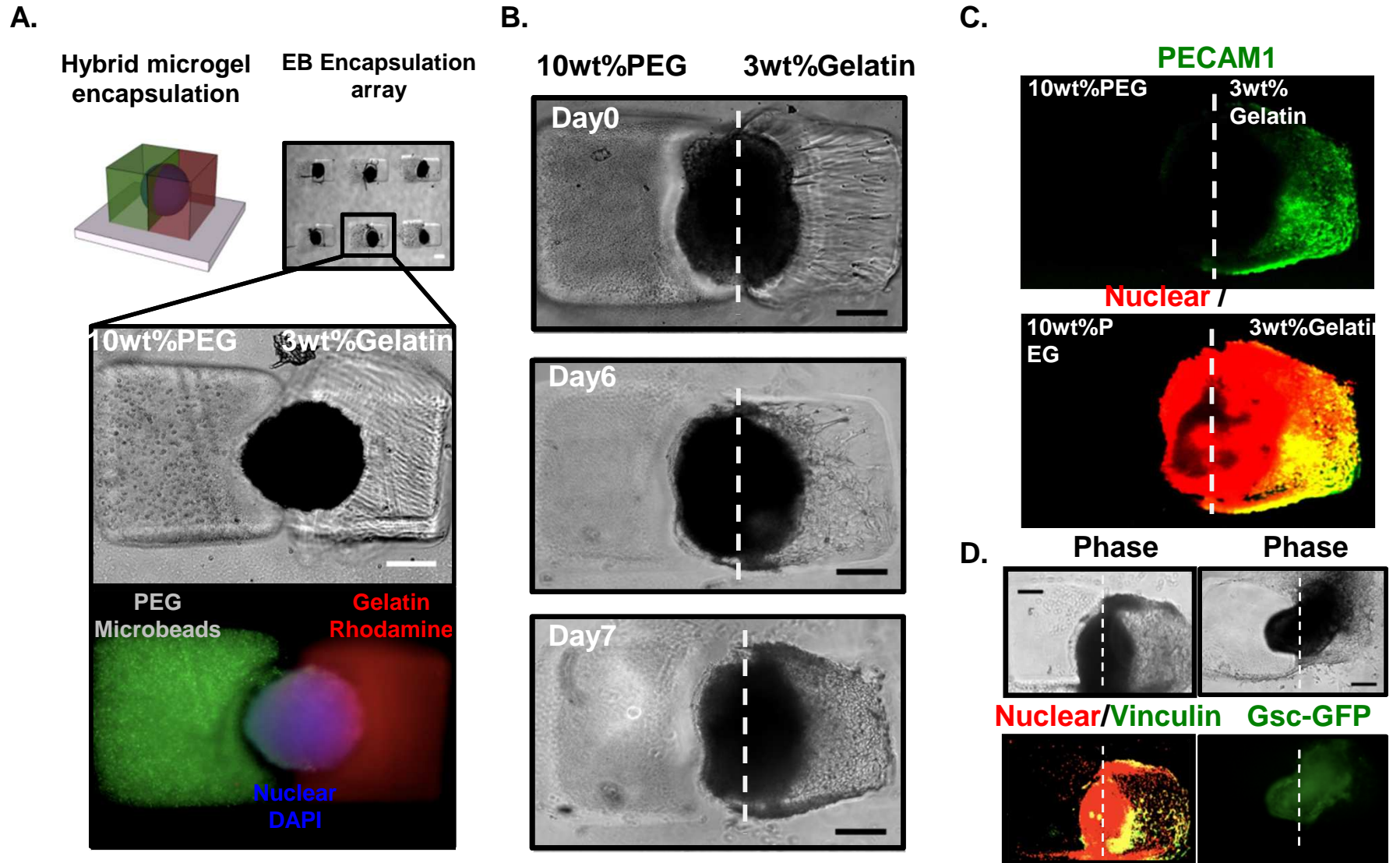
## Wnt5a-siRNA transfection inhibits angiogenesis



### Angiogenesis

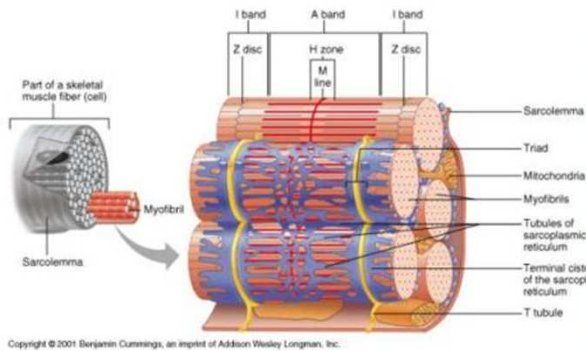
Day 11	Control (150μm EB)	Wnt5a -siRNA (150 μm EB)
Sprouting Frequency	77 ± 12 %	24 ± 3%

# EBs with spatially patterned microenvironments



# Tissue microarchitecture

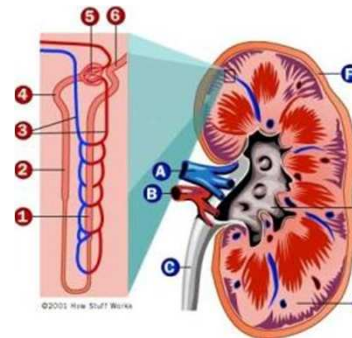
myofibers



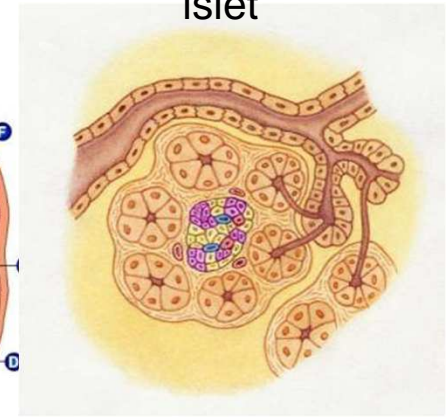
lobules



nephron



islet



Nat Rev Mol Cell Bio (2006) 7:211

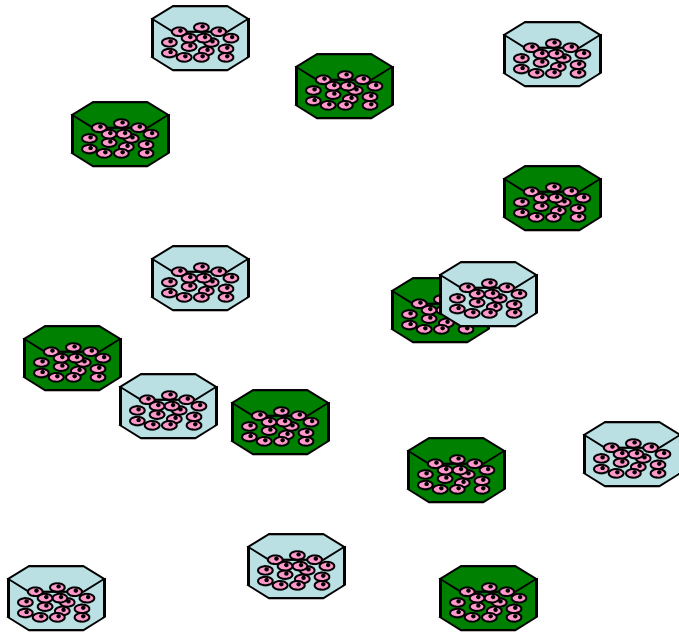
Living tissues are usually constituted by smaller repeating units (hundreds of microns), containing different cell types, in a well-defined 3D architectures.

## Challenge

Mimic the complexity of native tissue architecture such as repeating tissue units with well-defined 3D architecture, and synergistic interactions of multiple cell type.

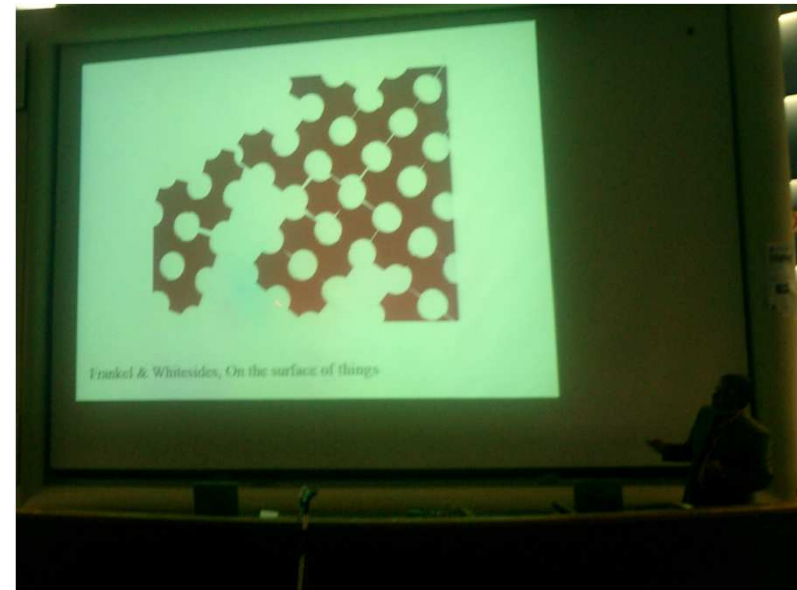


# Bottom-Up (Modular) Tissue Engineering

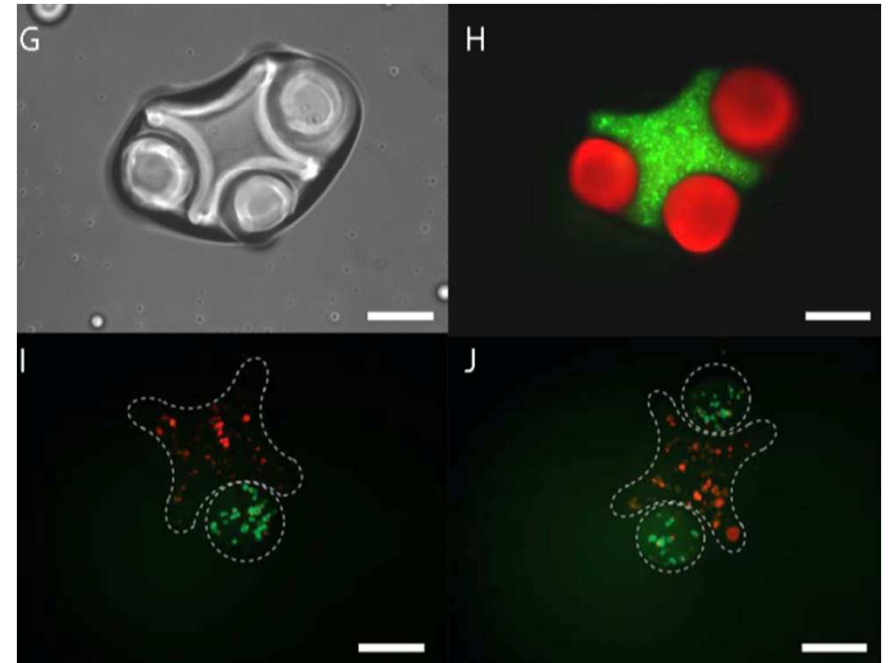
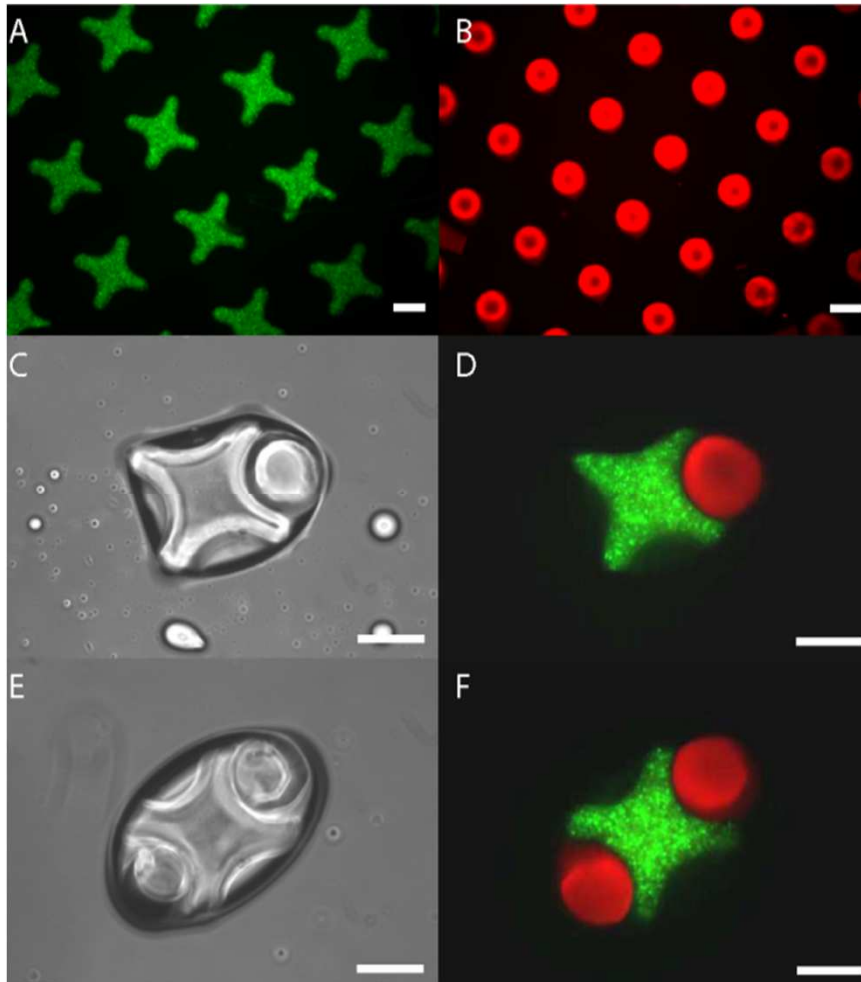


Advantage:

- Controlled 3D homotypic and heterotypic tissue architectures
- Homogeneous initial cell distribution



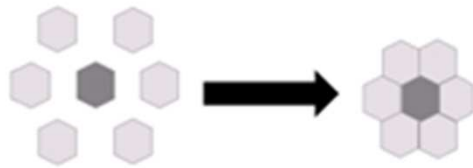
# Controlled assembly of microgels



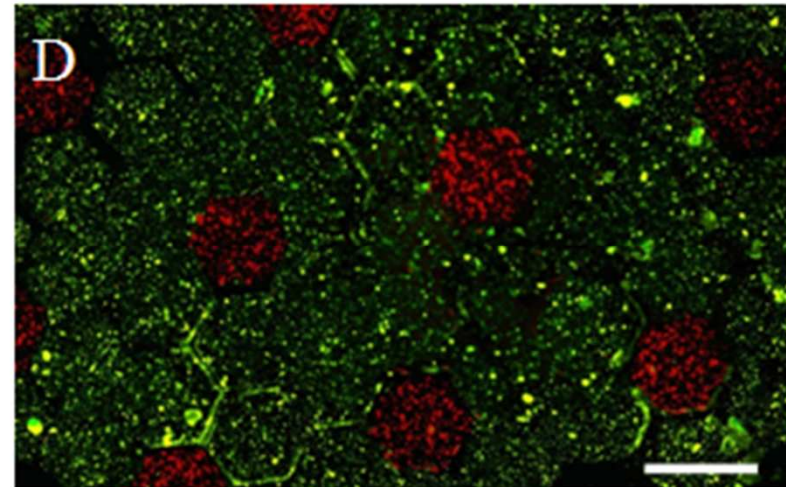
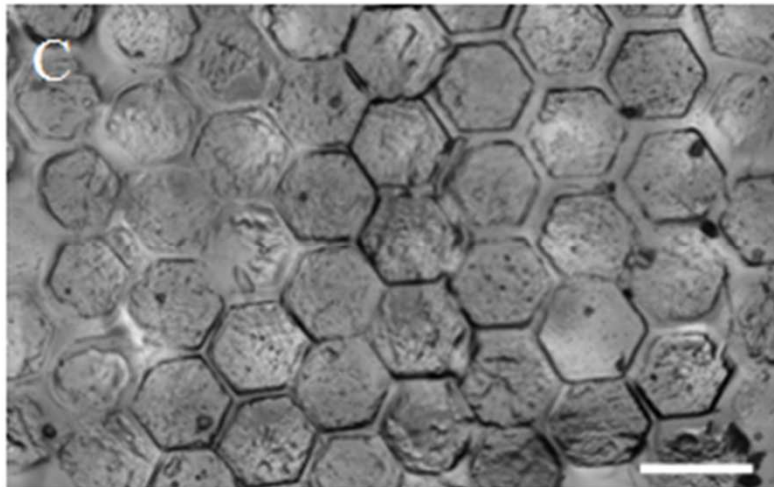
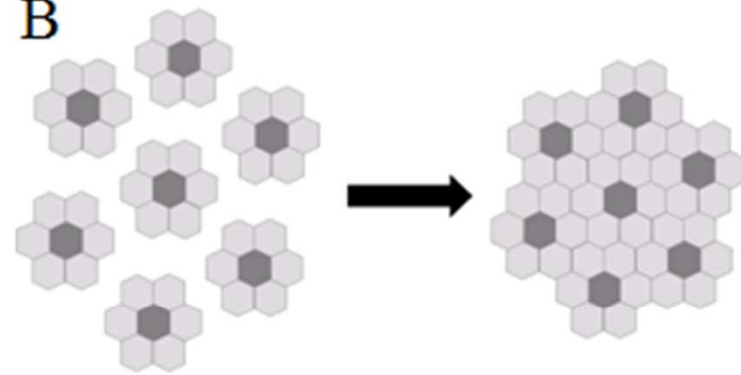
- Using lock and key shapes
- Provides additional control of hydrogel aggregation and cell co-culture

# Controlled assembly of microgels at a liquid-air interface

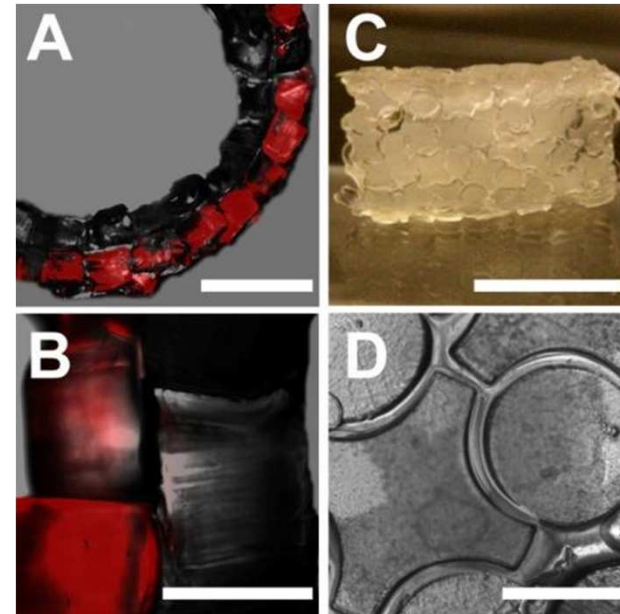
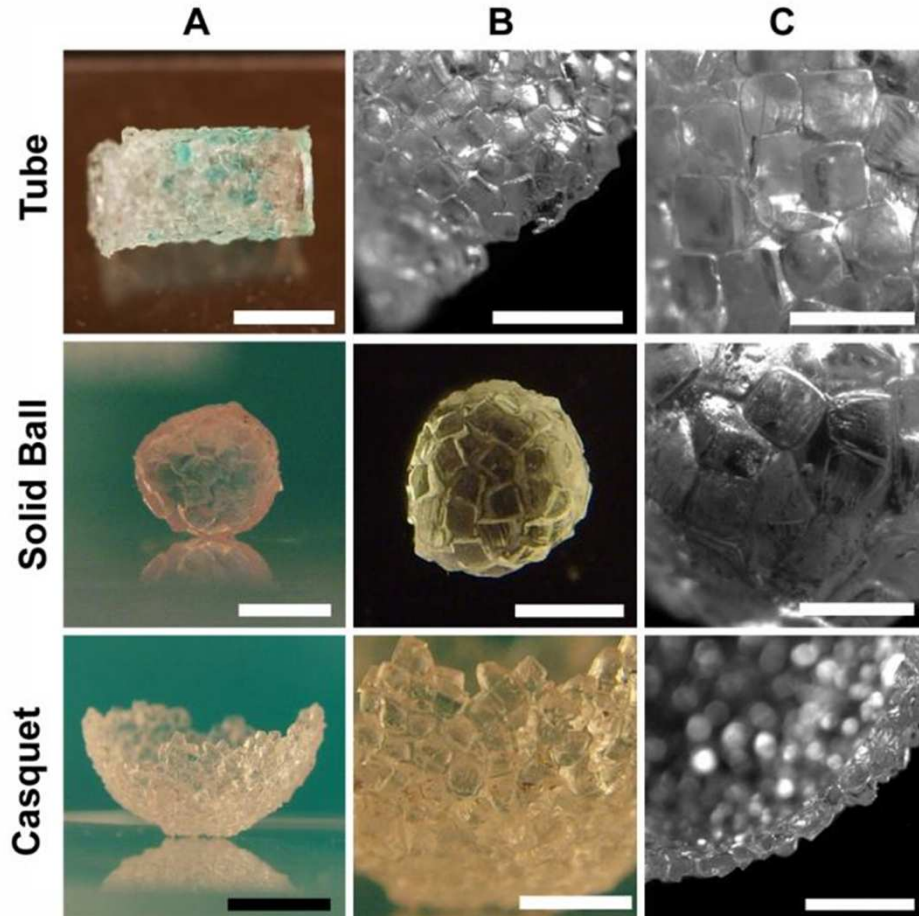
A



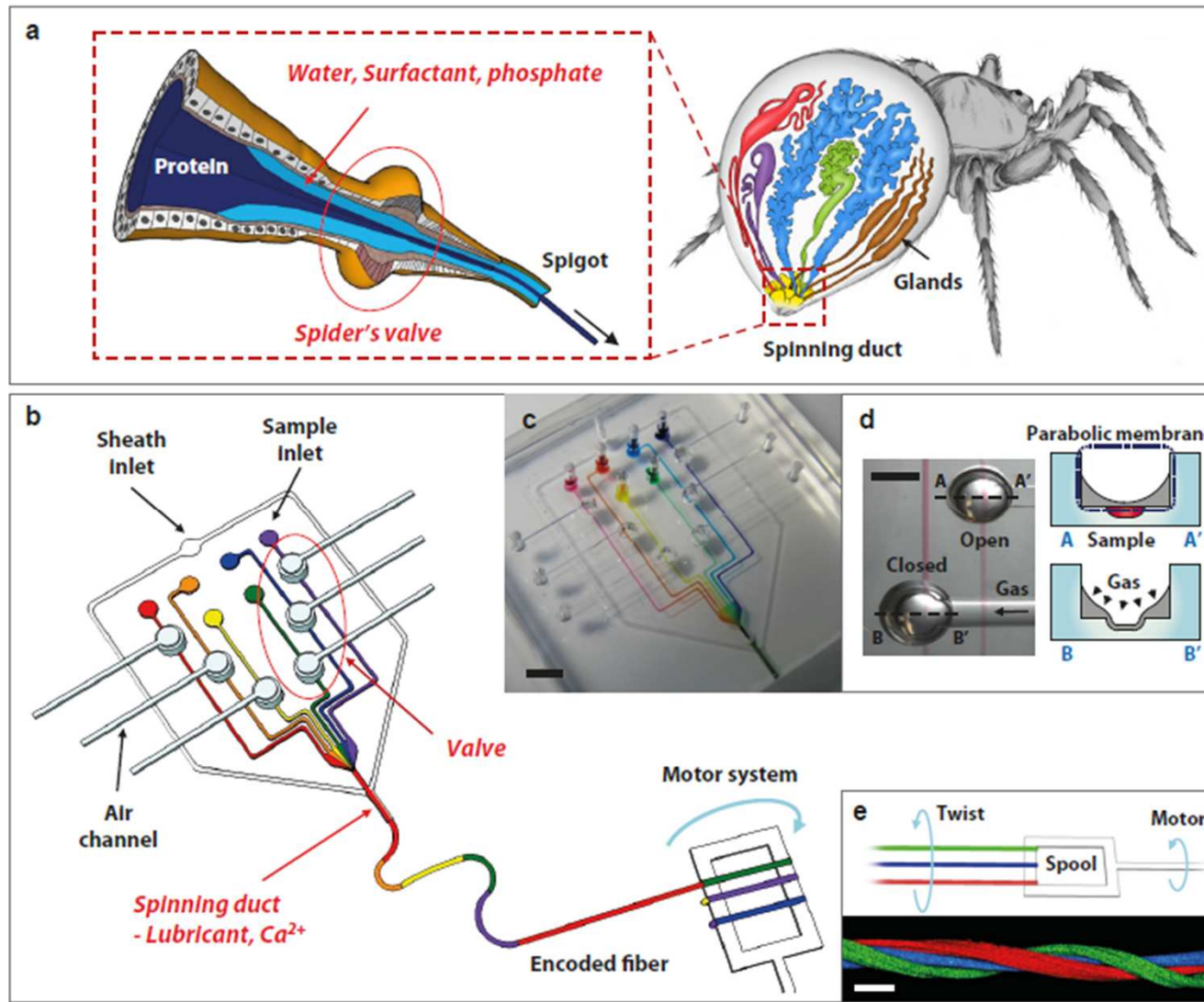
B



# Microscale template-based directed assembly of microgels



# Biomimetic approach for generating microfibers

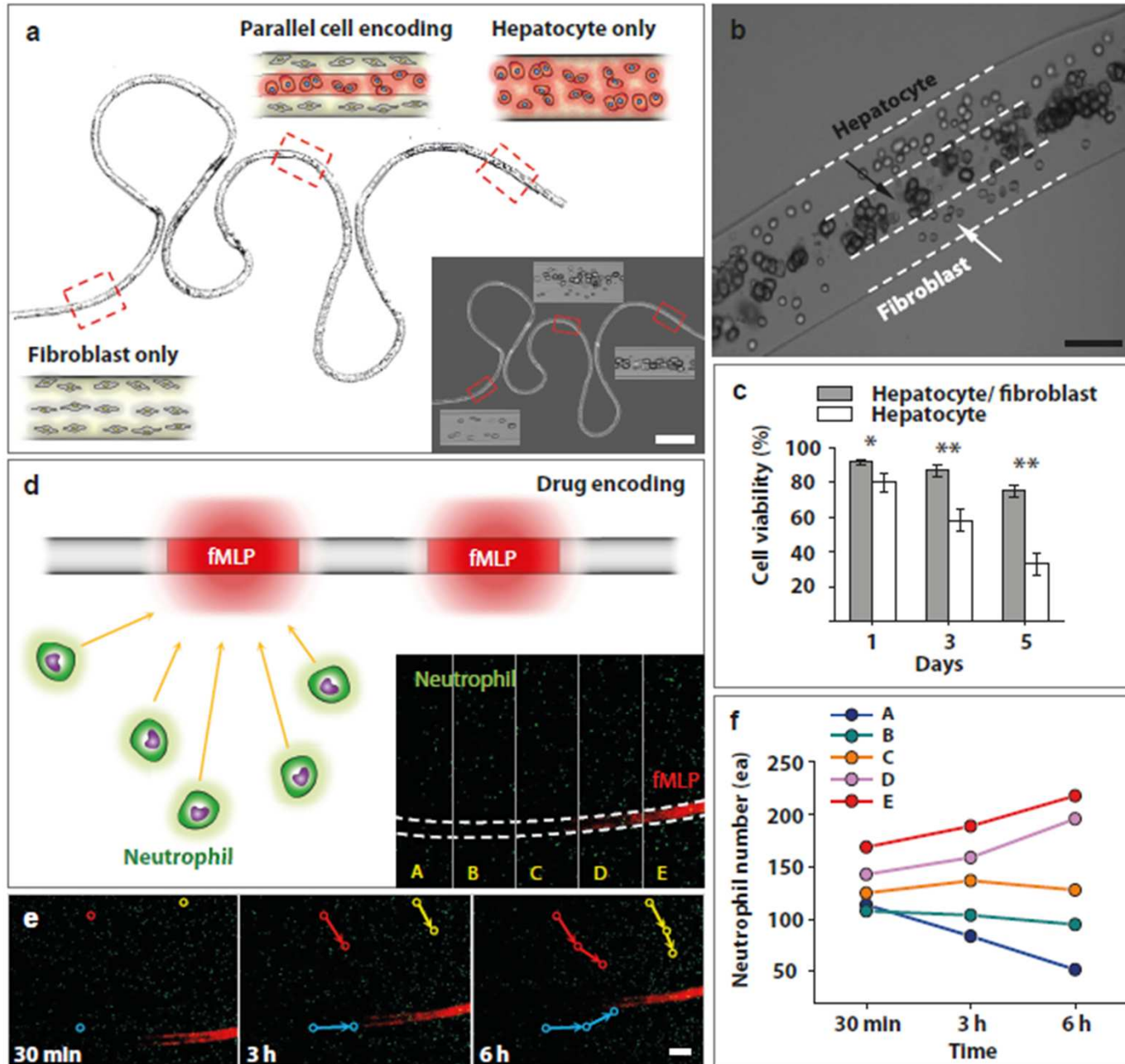


w/ S.H. Lee (Korea U.)

Nature Materials (2011)

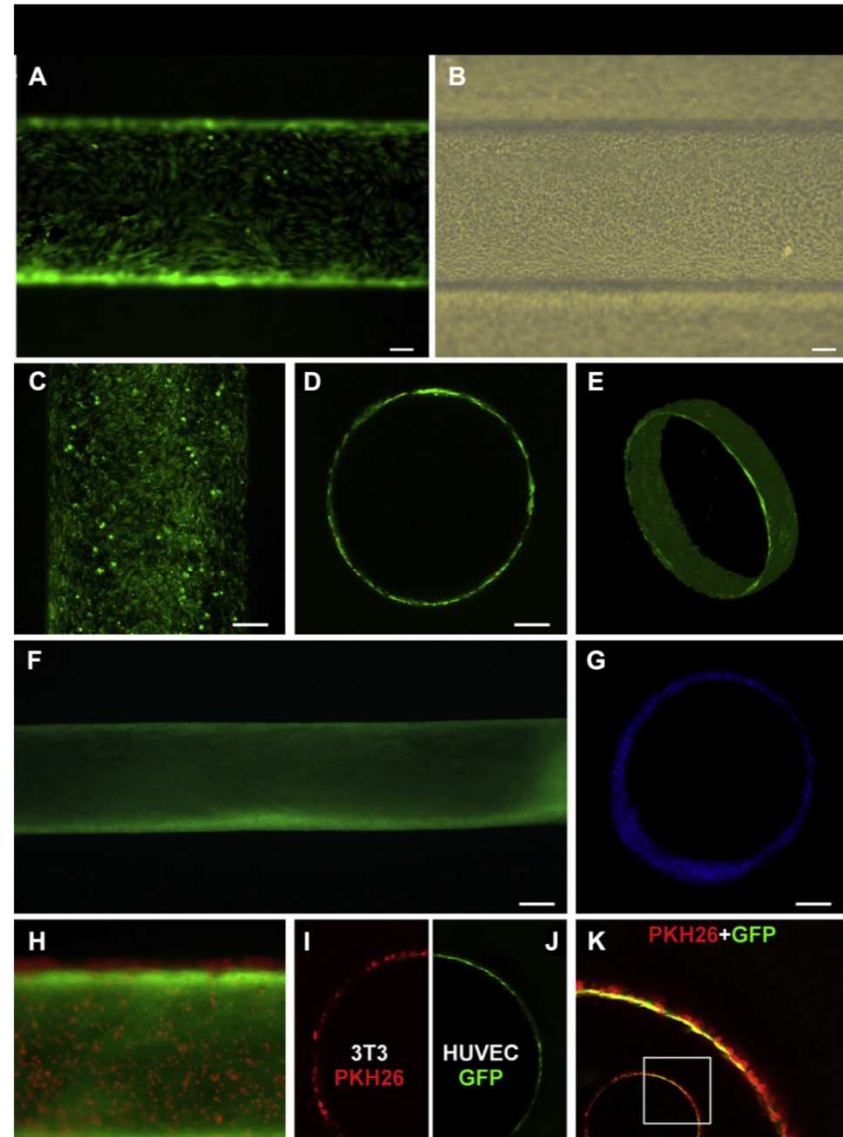
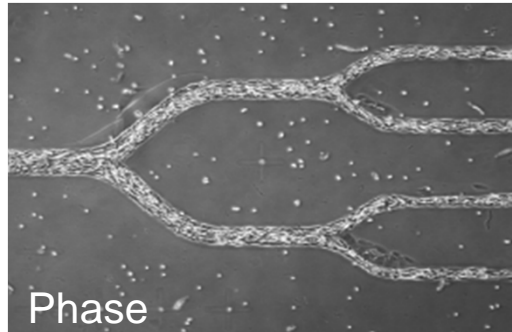


# Coded microfibers can be read by cells





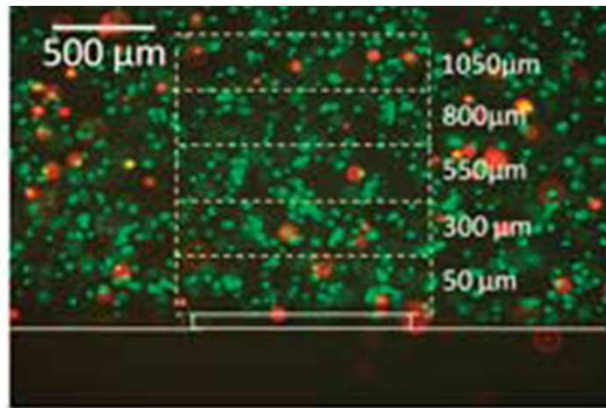
# Seeding endothelial cells within microchannels



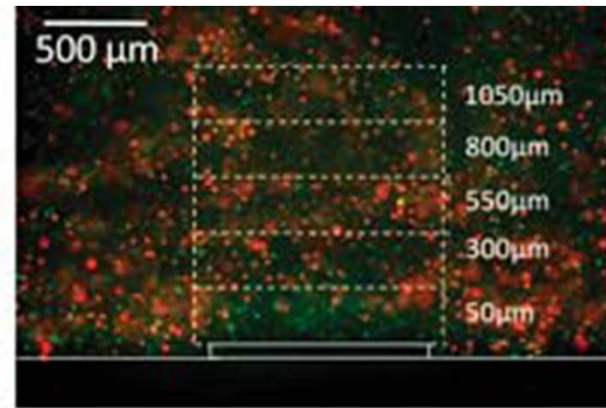
w/ J Fukuda



# Cells in close proximity of microchannels remain viable

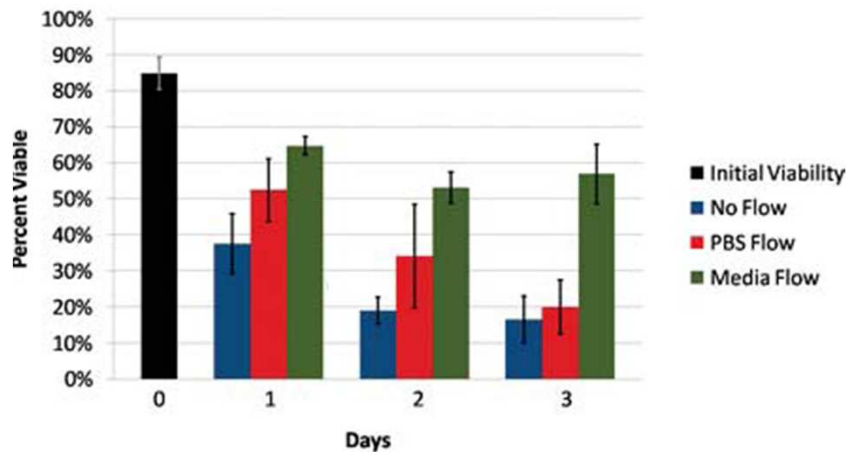


0 Hours

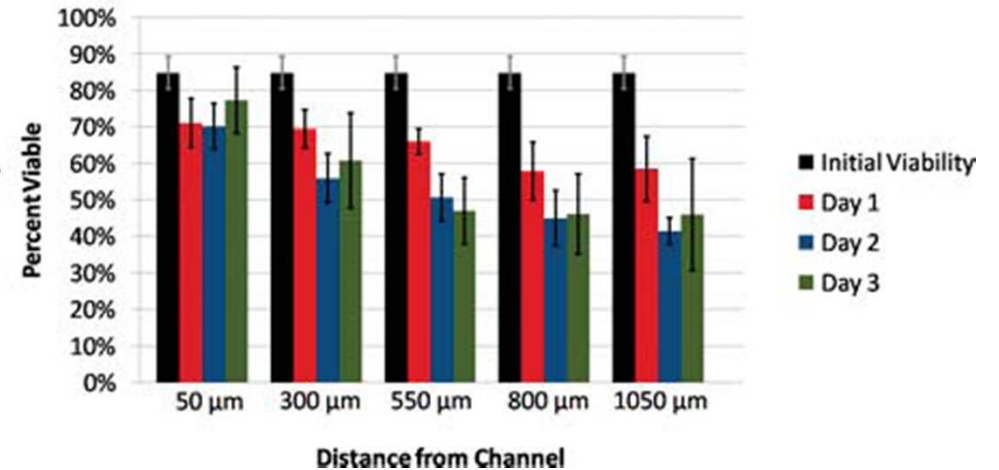


72 Hours

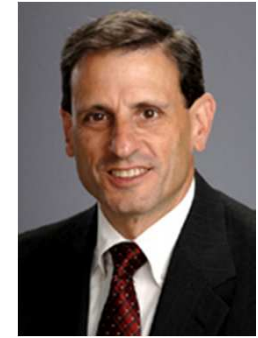
Time Course Viability



Viability vs. Distance from Channel



Ling et al. Lab on a chip (2007)



Age related  
diseases

Cardiovascular /  
Neural diseases

Personalized  
medicine

**Biomedical Engineering Grand Challenges**

Cancer

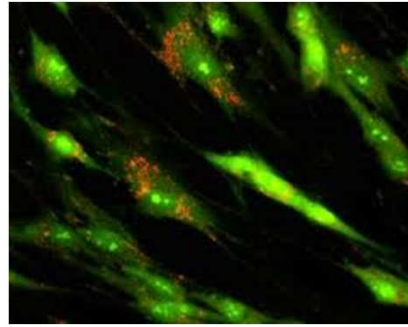
Food supply

Biomedical  
Robotics

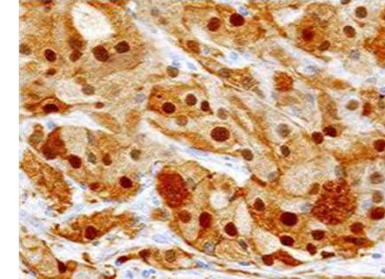




Regenerative  
Medicine

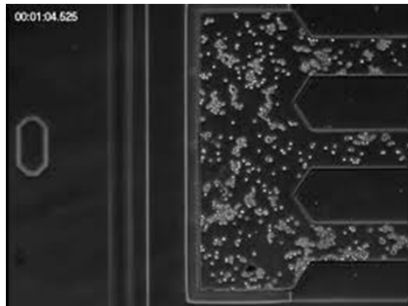


Biological studies



Disease models  
/ drug discovery

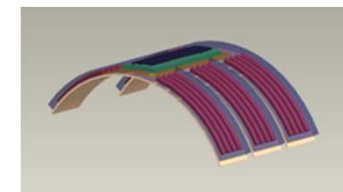
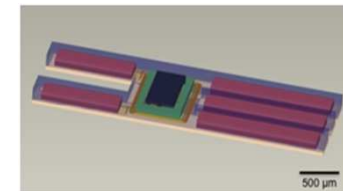
**Applications of Engineered Biological Tissues**



Biosensing



Artificial food



Biorobotics /  
Bioenergy



# Acknowledgements

## *Funding*

NIH (NIDCR, NIGMS, NIAMS, NHLBI, NIBIB), NSF CAREER, ONR YIP, DOD, ISN, US Army Corps of Engineers, Draper, KOSEF, MIT-Portugal, NSERC, FQNRT, Samsung, Australia-Harvard Club



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