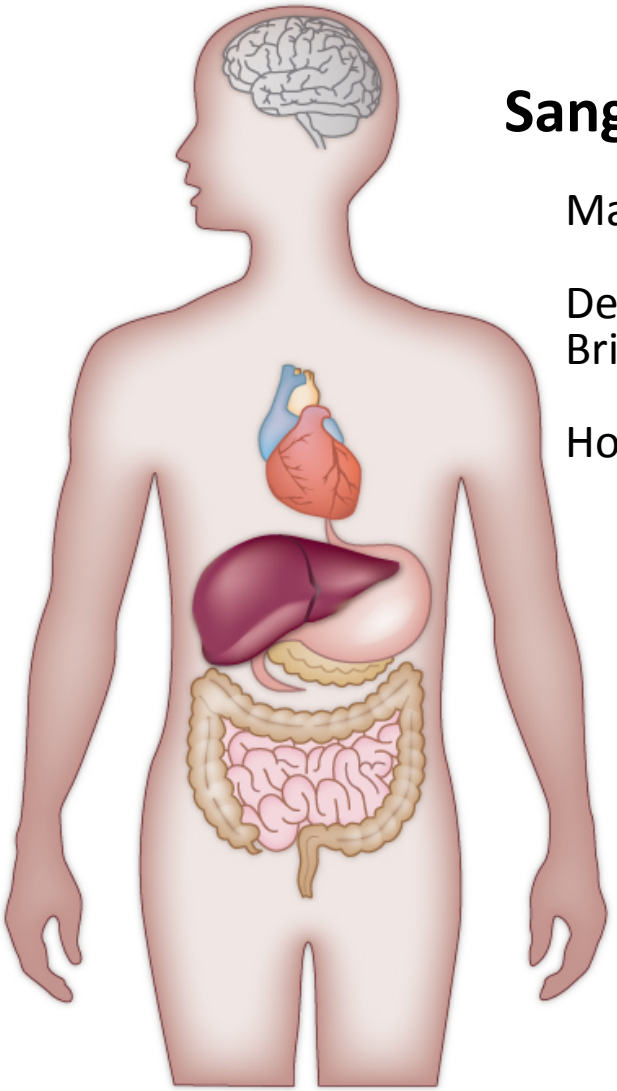
Tissue Engineering

Part 1: Engineering Tissue Replacements



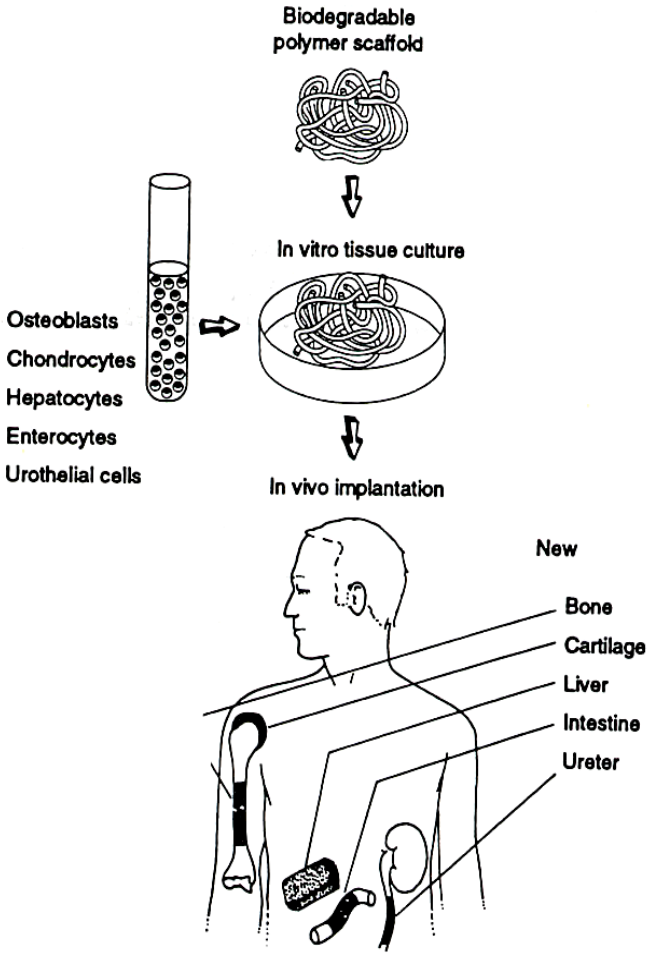
Sangeeta N. Bhatia, MD, PhD

Massachusetts Institute of Technology

Department of Medicine
Brigham & Women's Hospital

Howard Hughes Medical Institute

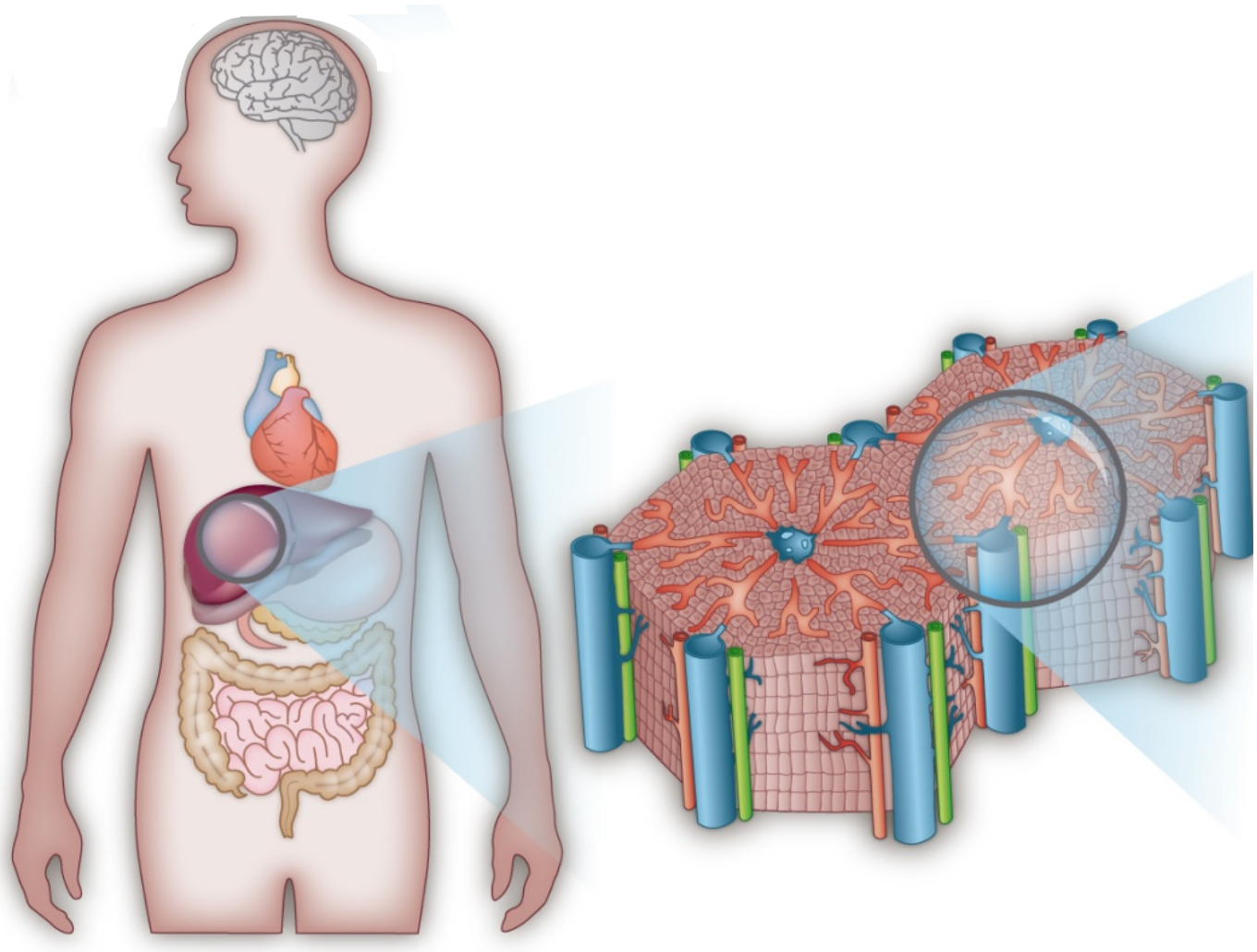
The Need for Tissue Replacements



Organ	Procedures/Yr (MM)
Skin	4.75
Bone	1.34
Cartilage	1.15
Blood vessel	1.36
Tendon/ Ligament	0.123
Pancreas	0.738

Langer & Vacanti, Science, 1993

Tissues Across Length Scales



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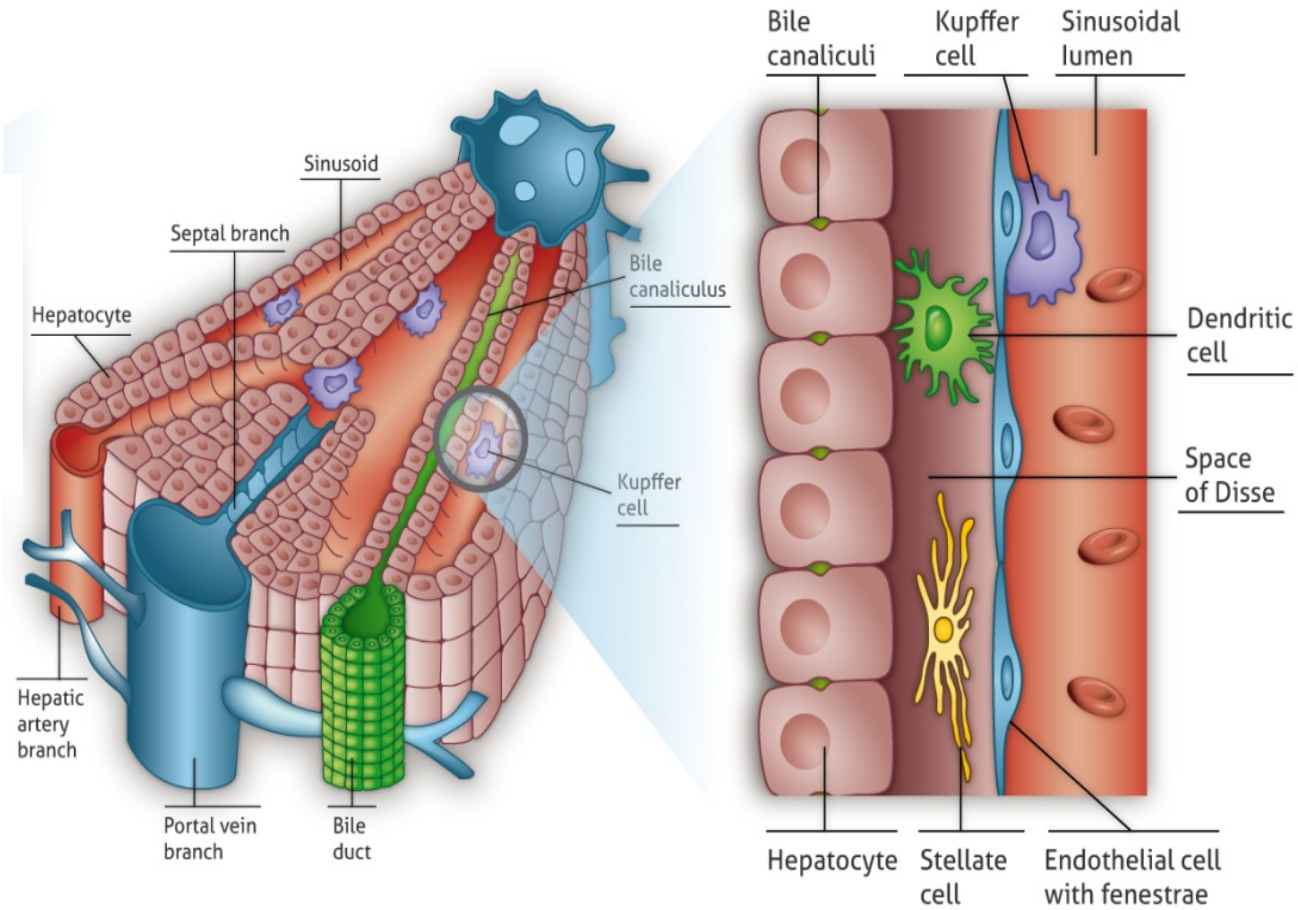


Why a Bioengineered Tissue?

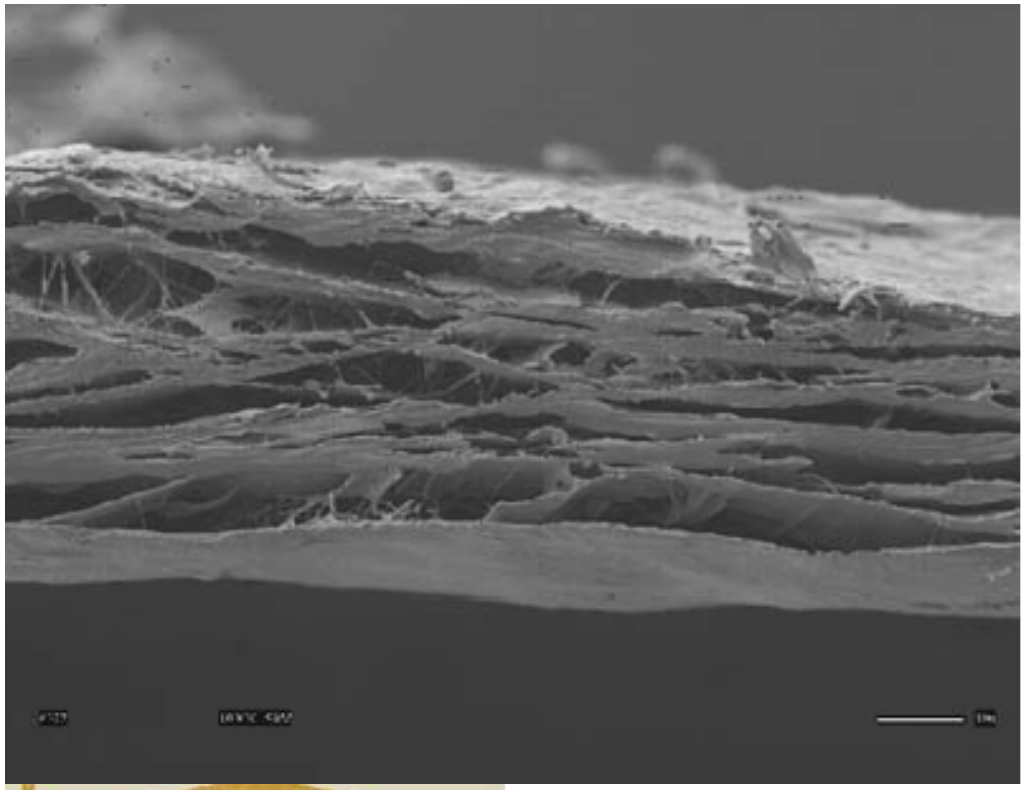
If one can improve upon:

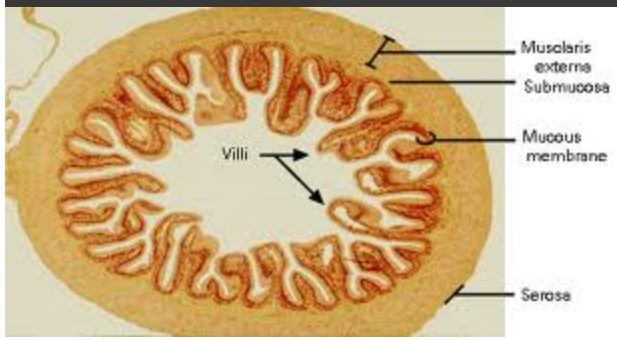
- a device
- a drug
- a minimally-manipulated cell
- surgical reconstruction
- a transplant (unos.org)

- **Engineered tissues = biomaterials + cells**
  - Biomaterials that recruit cells (acellular)
  - Biomaterials that house cells (hybrid)
  - Biomaterial-free structures (hybrid w/ cell-derived ECM)

Vacanti, 1997 [image]

Small Intestine Submucosa (Acellular)

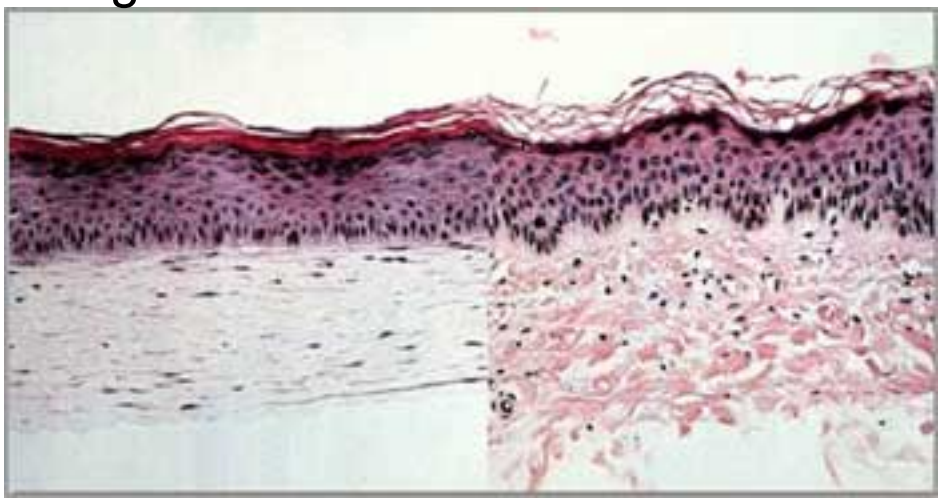


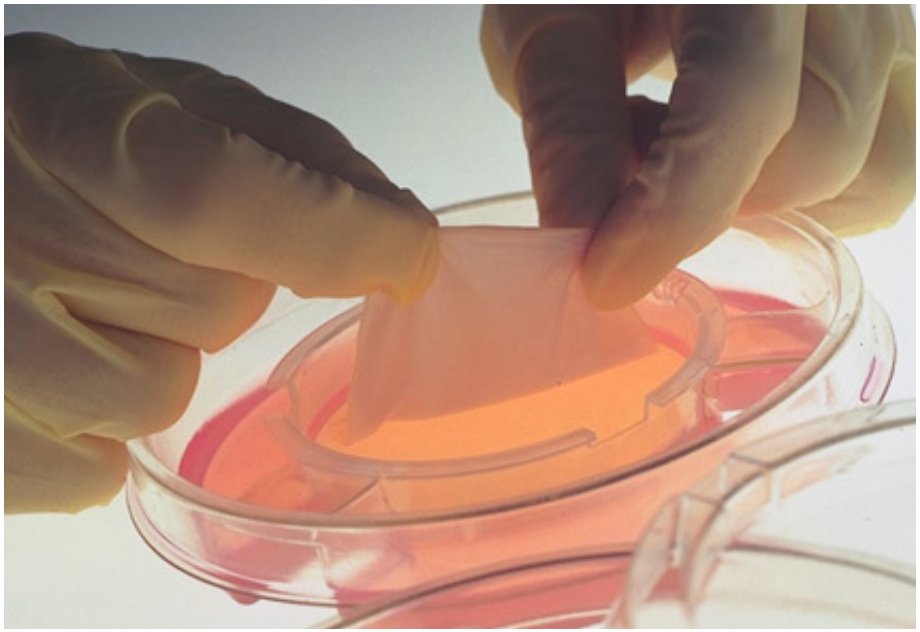


Hales M et al: Int J Urogynecology (2006) 17: S39-S43
www.student.loretto.org
Badylak and coworkers

Skin (Hybrid)

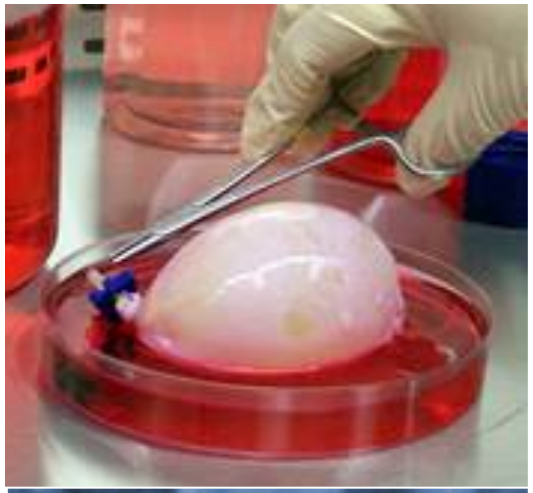
Engineered Skin Human Skin

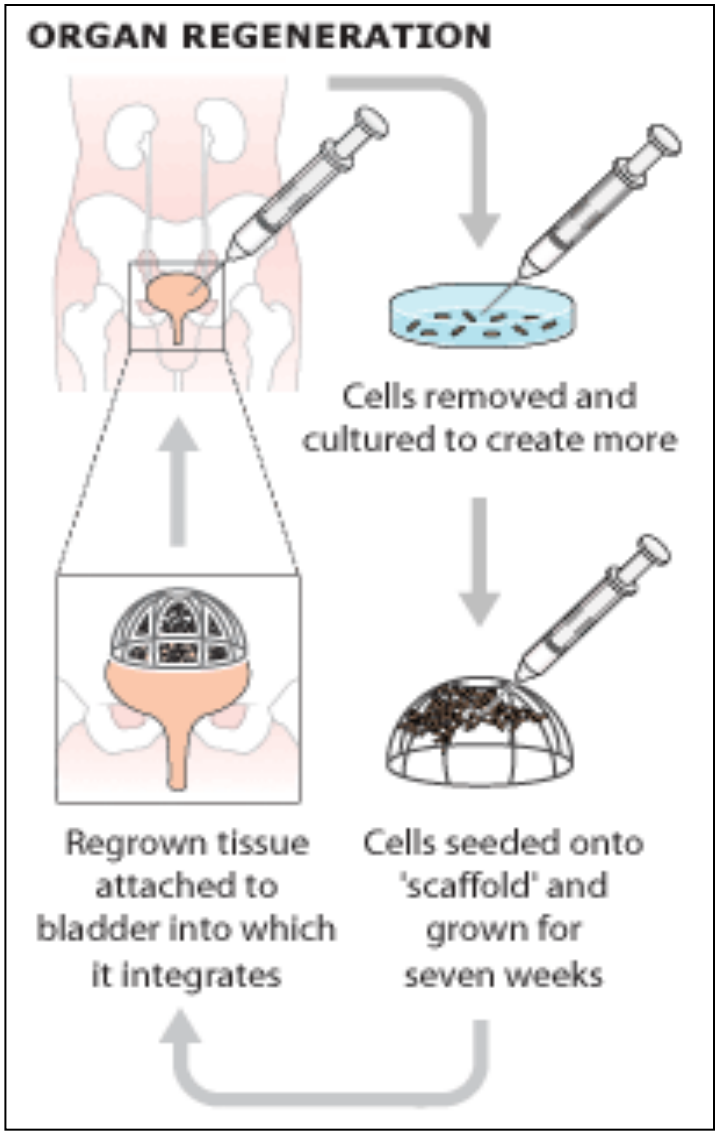




Organogenesis, Inc.

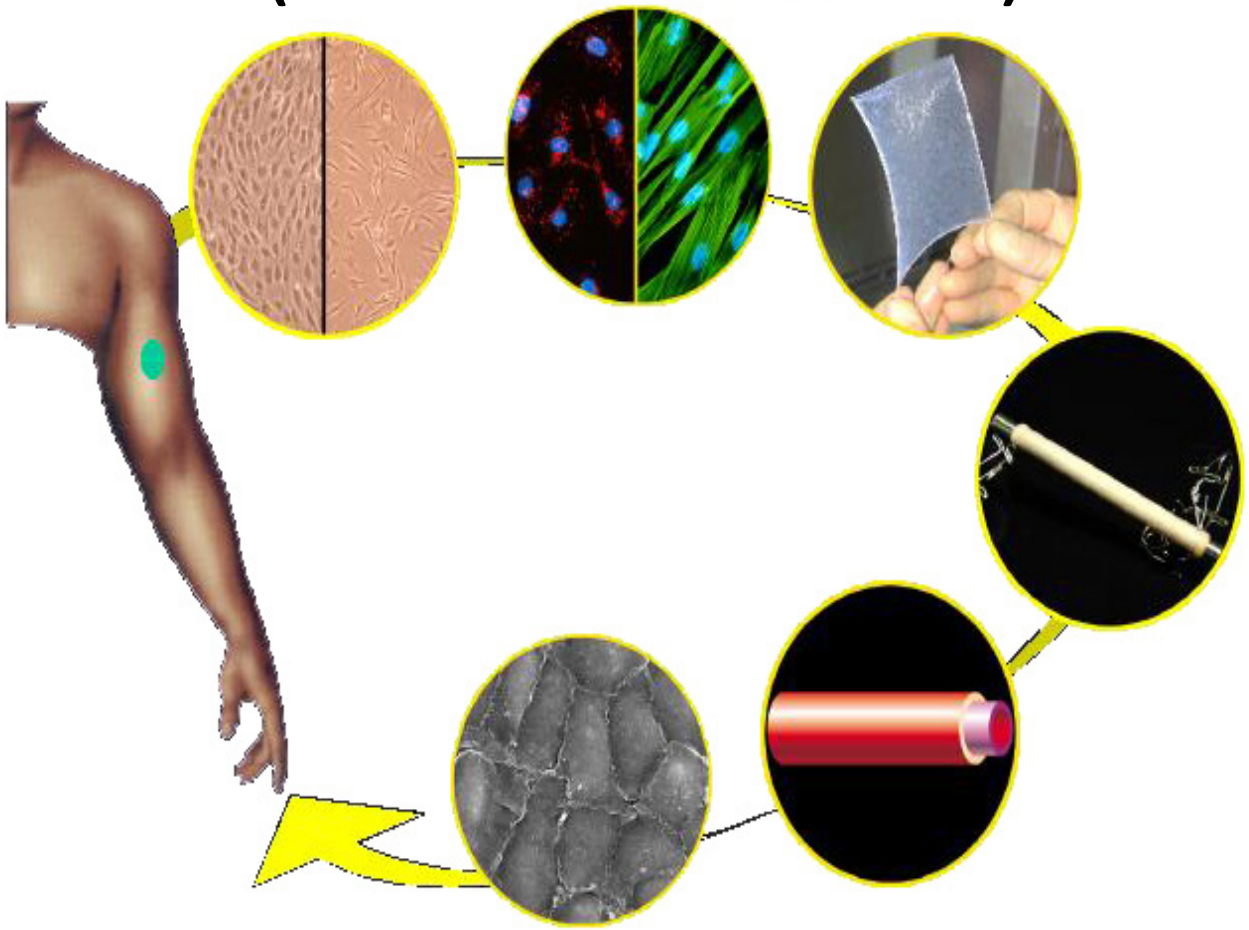
Bladder (Hybrid)





Tengion; Atala A et al; Lancet 2006: 367 124-6

Blood Vessel (Biomaterial-free)



www.cytograft.com; L'Heureux, FASEB J, 1998

Blood Vessel

www.cytograft.com

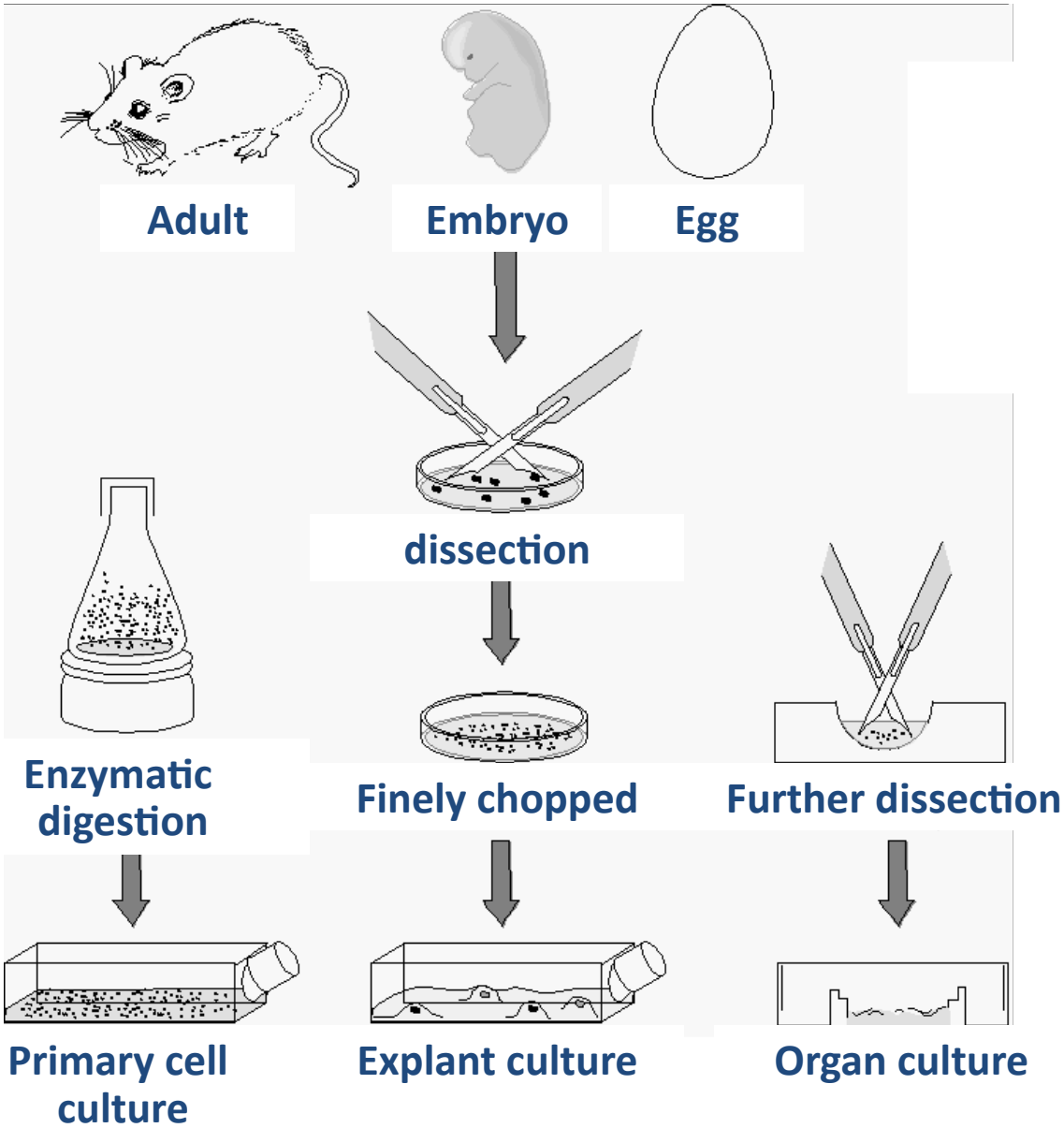
Designing bioengineered tissues I: Pick a function

Organ	Function
Skin	Barrier
Kidney	Secretory
Pancreas	Insulin production
Cartilage	Space filling
Bladder	Compliance

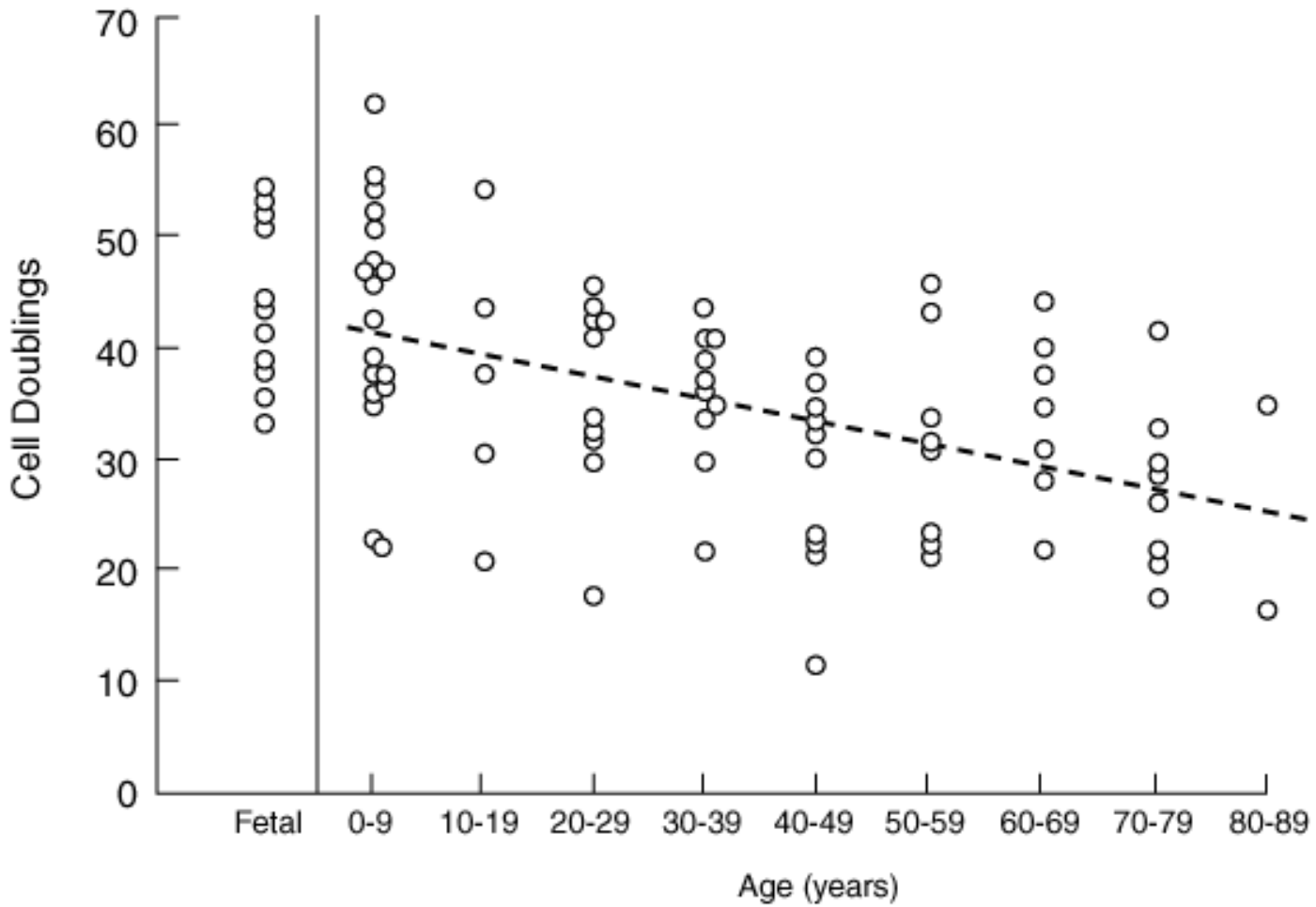
II: Pick ingredients & fabrication method

- **Raw Ingredients:**
  - Cells
    - Somatic (auto-, allo-, xeno-)
    - Stem cells
  - Biomaterials
  - Nutrients
- **Fabrication:**
  - Assembly
  - Bioprocessing
  - Preservation

Culturing Primary Cells

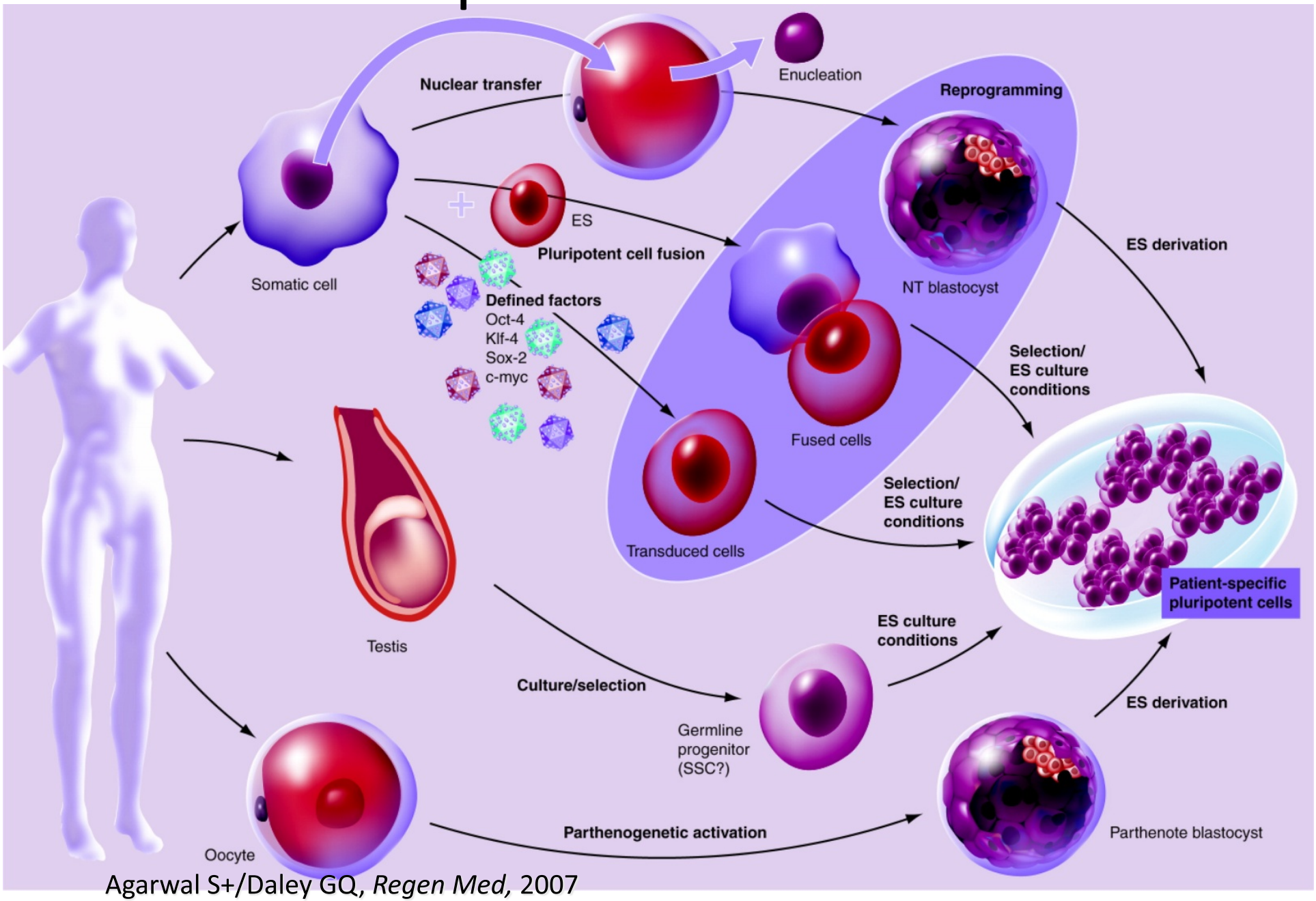


Hayflick Limit



Hayflick, 1965

Pluripotent Stem Cells



Agarwal S+/Daley GQ, *Regen Med,* 2007

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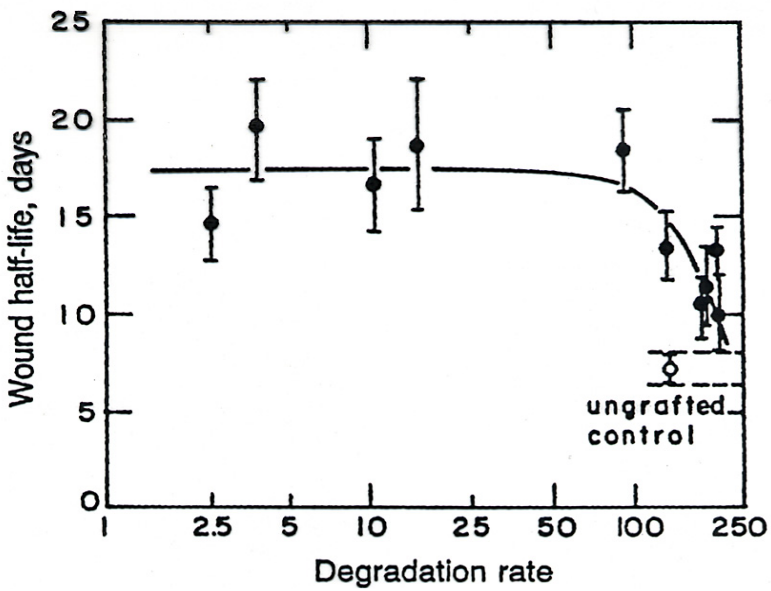
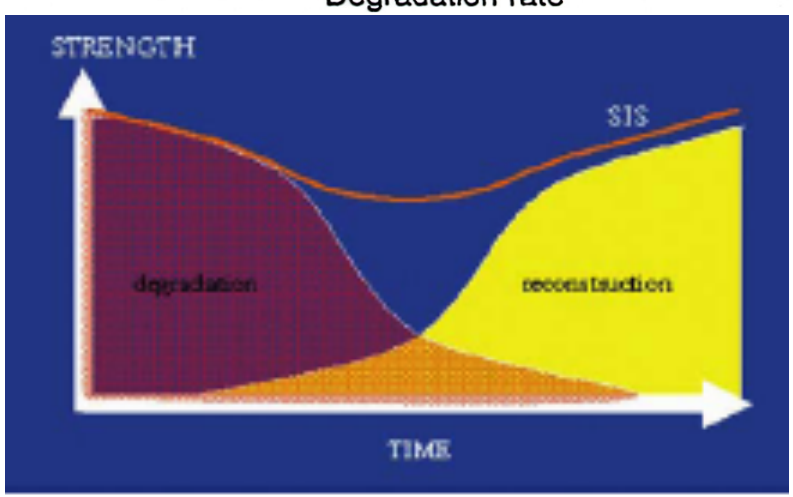
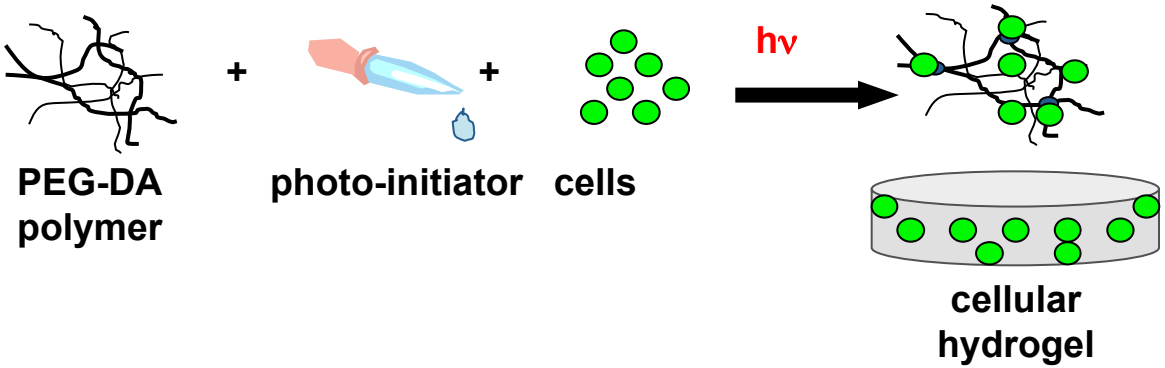
Matching Degradation with Synthesis

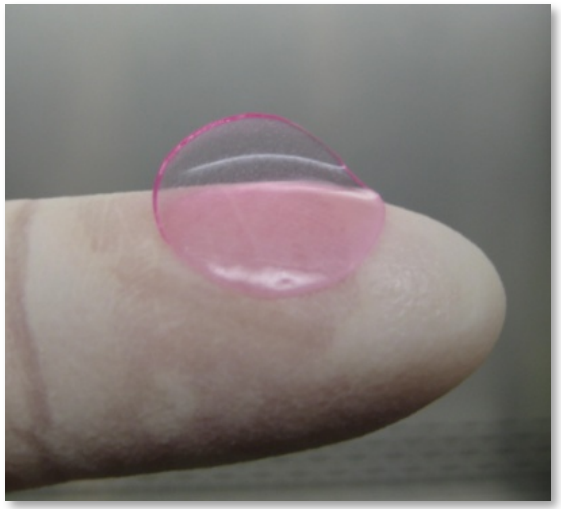




Yannas & coworkers, PNAS, 1989; J&J and Cook Biotech

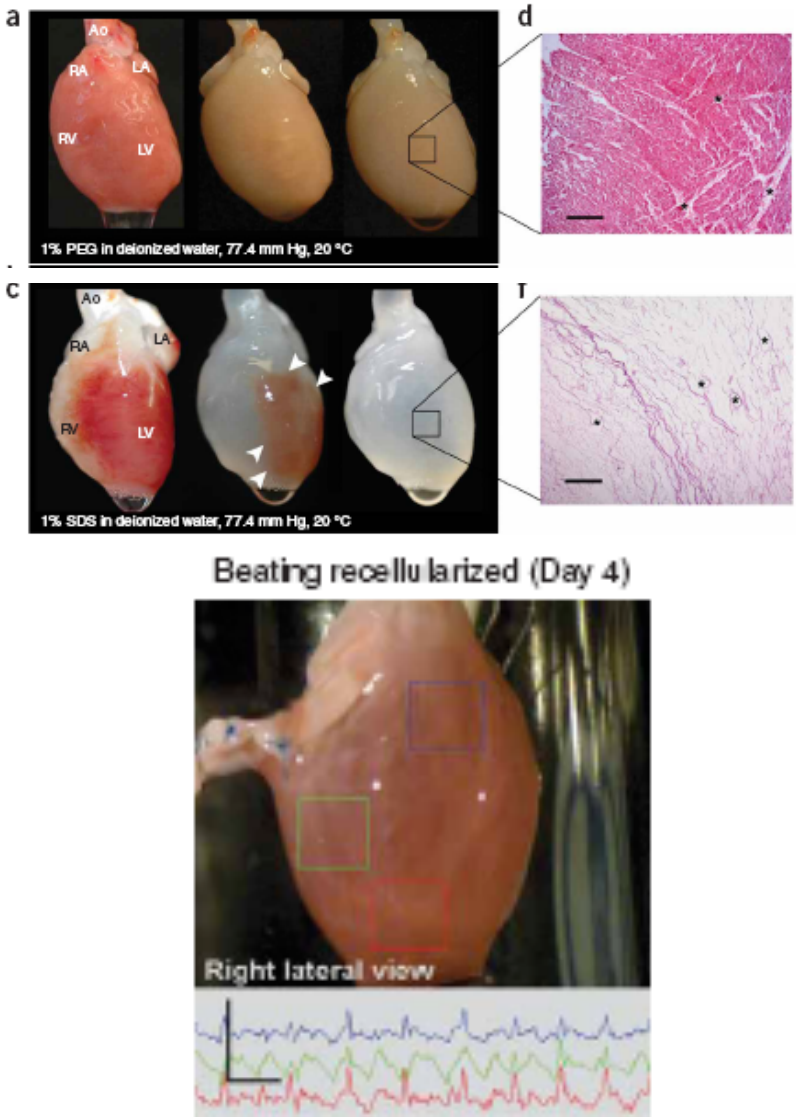
Synthetic Scaffolds





- PLGA, PCL
- PEG
- ePTFE
- Glycans
- Titanium

Natural Scaffolds



Ott HC, Mattiesen TS, Goh S, Black LD, Kren SM, Netoff TI, Taylor D, *Nat Medicine*, 13 January 2008

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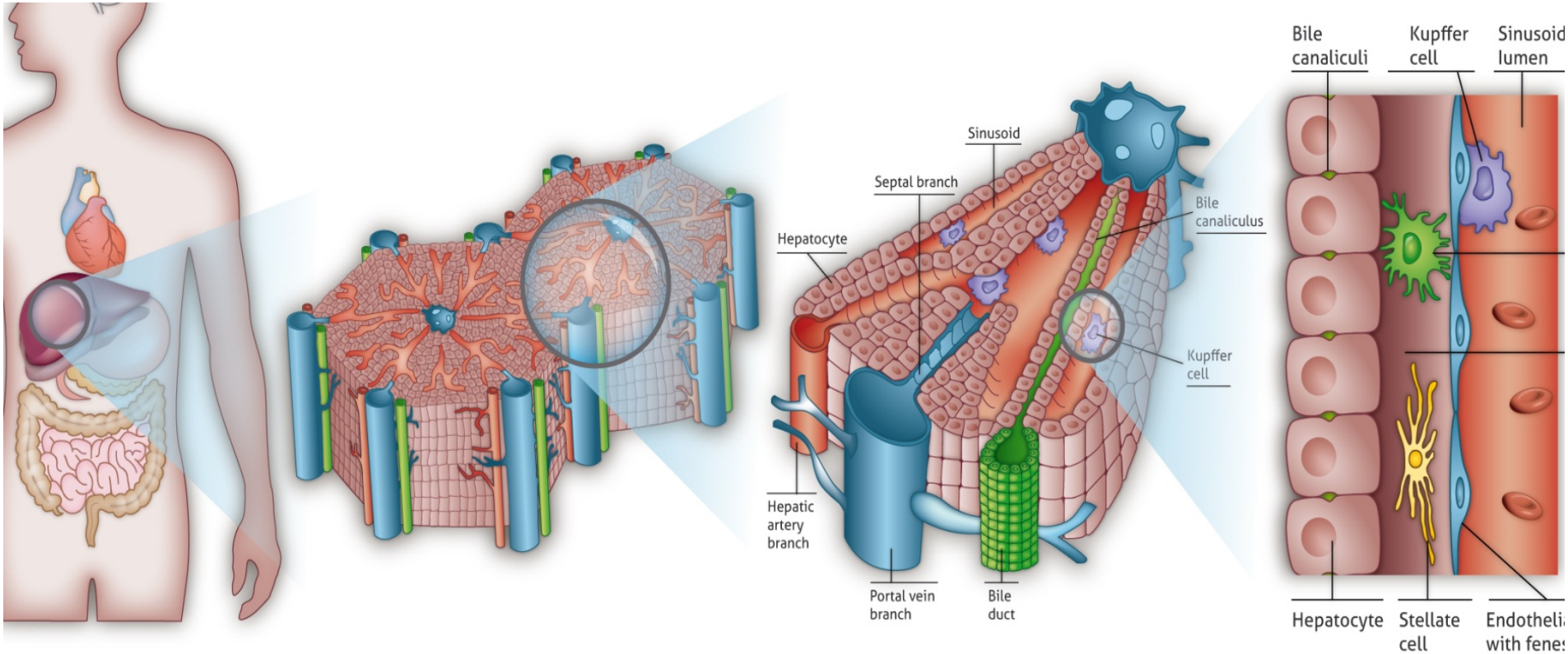
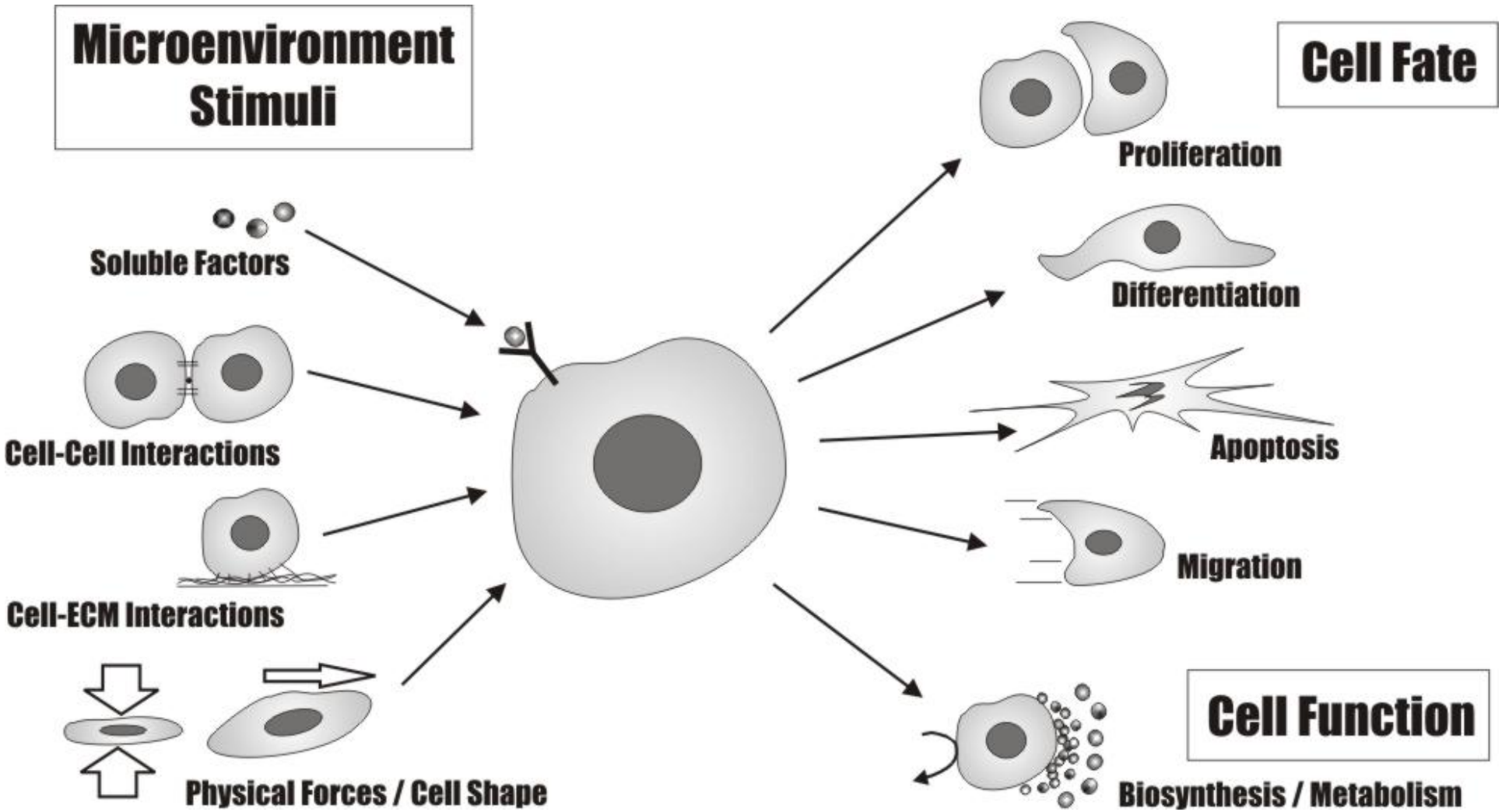
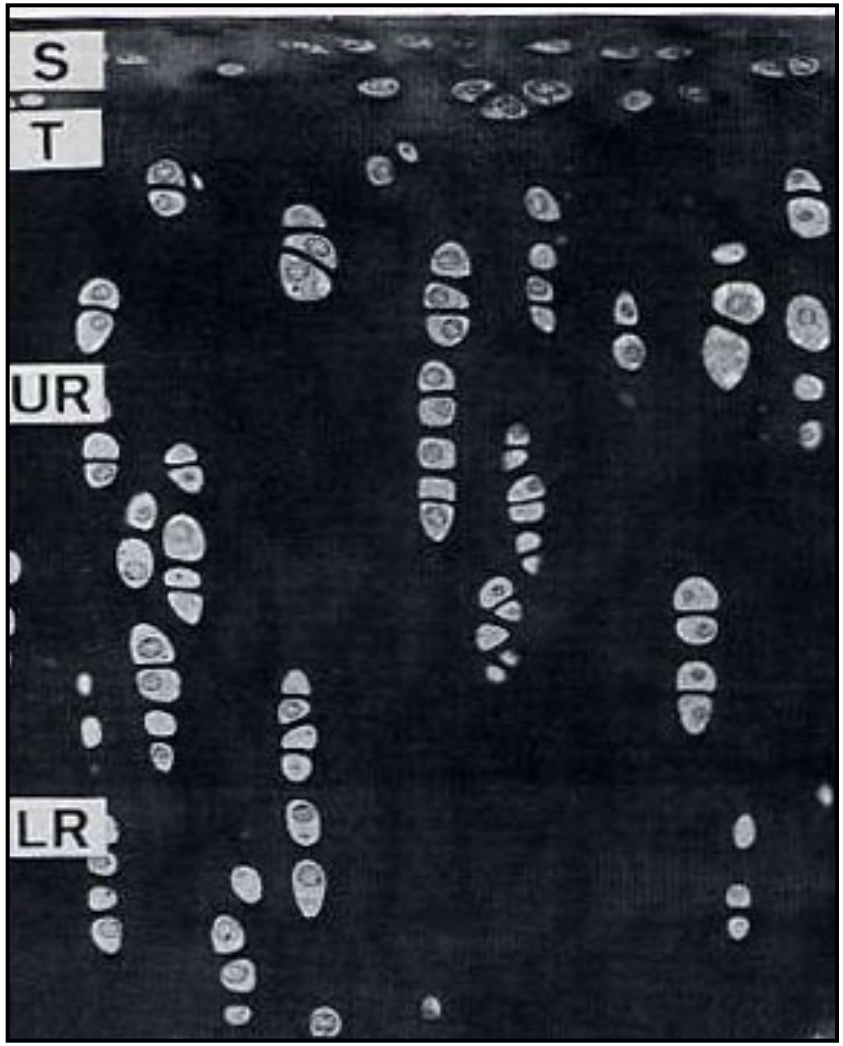
Hierarchical Organization



Cellular Microenvironment

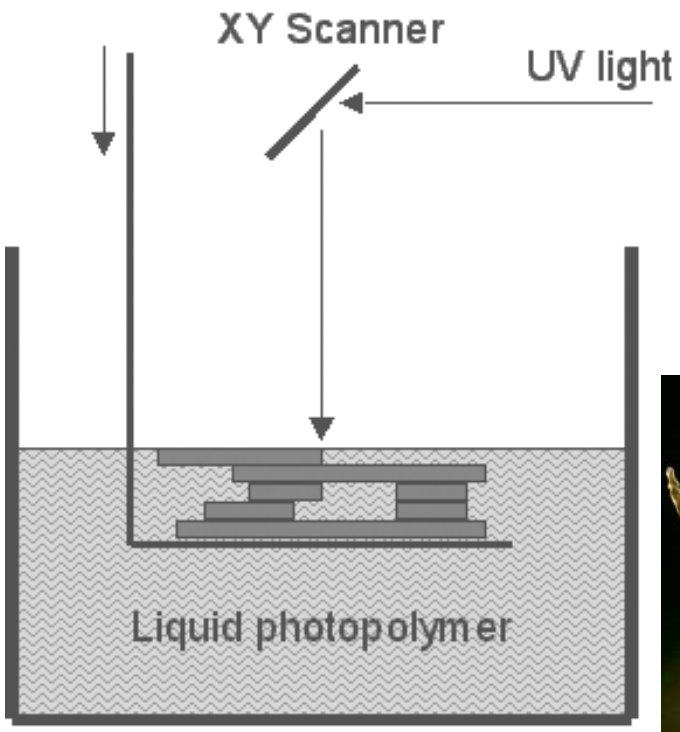


3D Tissue Environments

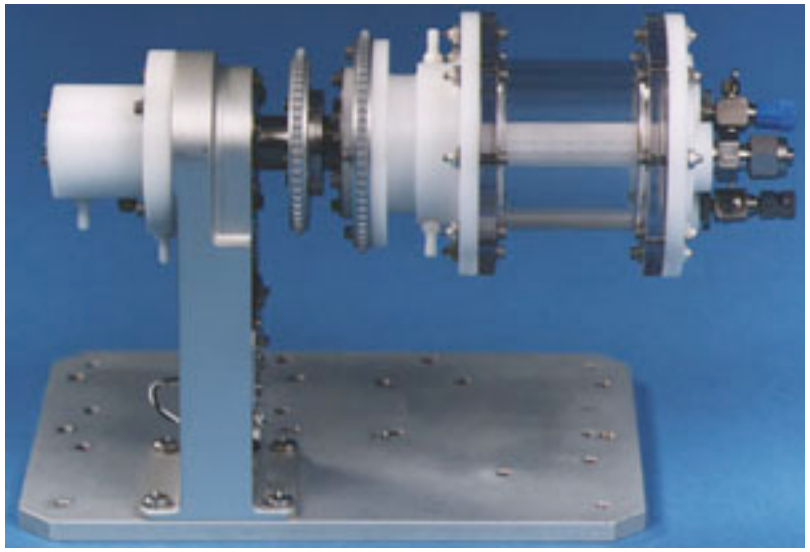


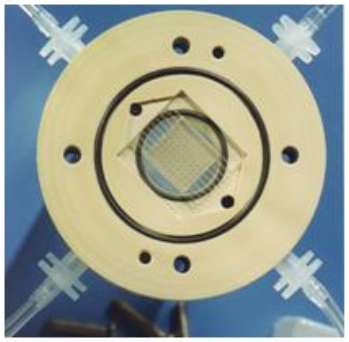
R. Sah: J Orthop Research, 2002

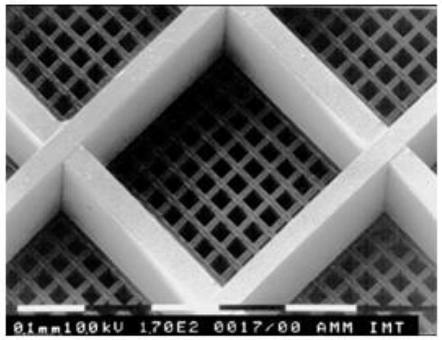
3-D Fabrication & Assembly

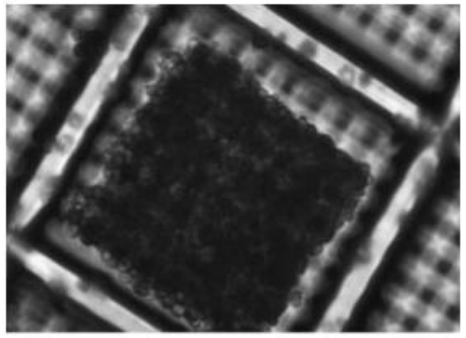


Bioreactor



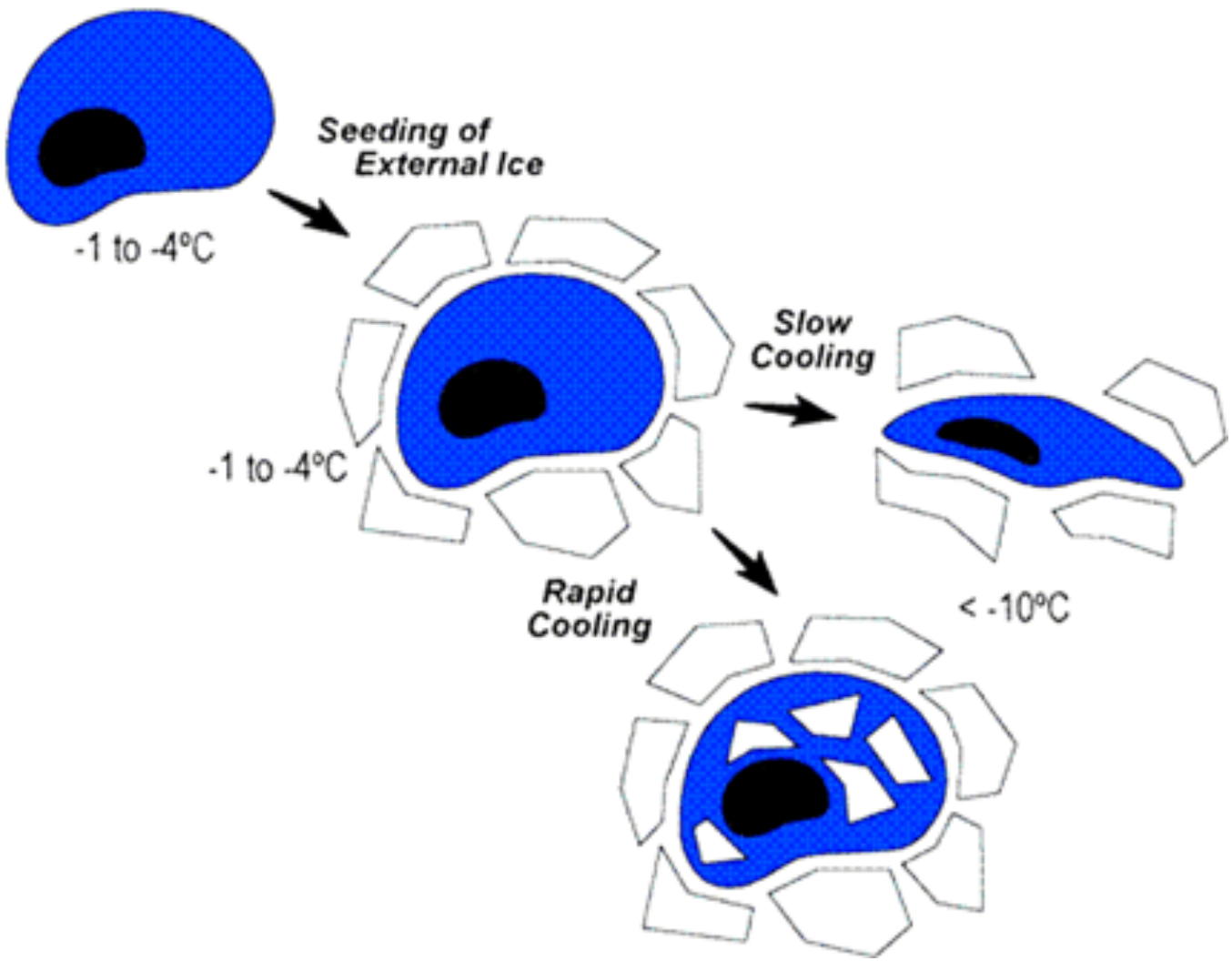






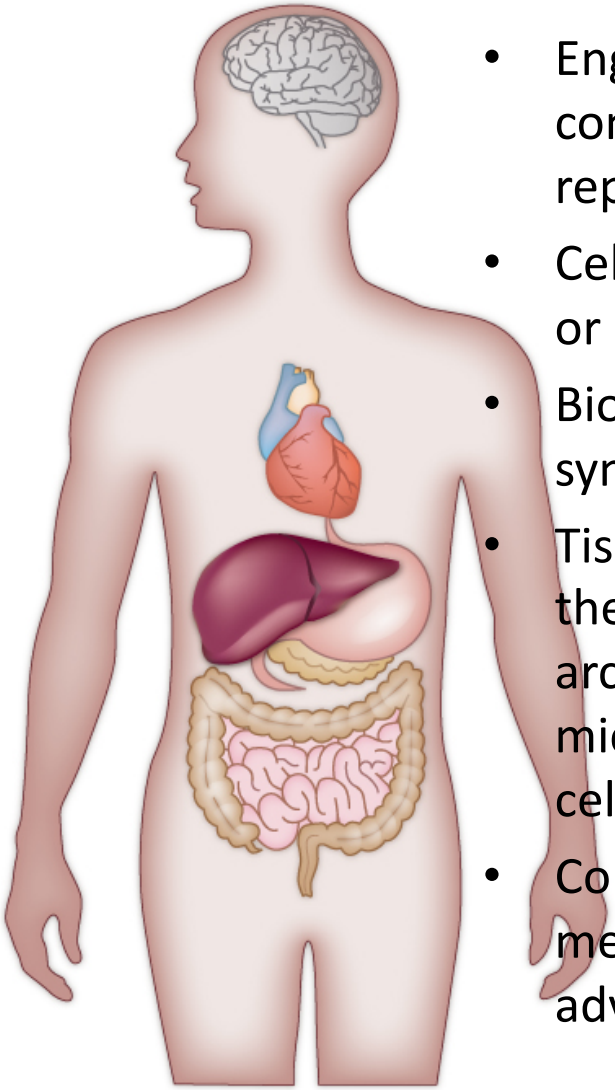
Science.nasa.gov; Gottwald & coworkers

Cryopreservation



Fowler & Toner, PNAS 2005

Conclusions



- Engineered tissue replacements combine cells & biomaterials to replace a subset of tissue functions
- Cells are derived from somatic cells or stem cells
- Biomaterials are natural or synthetic
- Tissue structure is hierarchical and therefore engineered tissue architecture must control microscale environment to control cell function
- Convergence of cell biology, medicine, and engineering is advancing the field