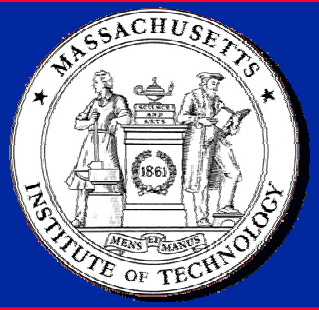
Harvard-MIT Division of Health Sciences and Technology
HST.535: Principles and Practice of Tissue Engineering
Instructor: Myron Spector



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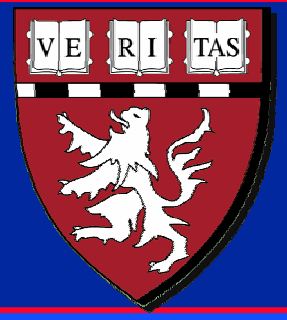

HST 535

PRINCIPLES AND PRACTICE OF TISSUE ENGNEERING:

Review/Discussion

M. Spector, Ph.D.

IMMEDIATE FUNCTION

- The degree to which the implant needs to support immediate function dictates the degree to which the tissue engineered construct needs to be mature before implantation.
- Properties cannot degrade with time.

Vessels

- Can the tissue engineered vessel be isolated from flow for a certain time period after implantation?

Musculoskeletal Tissues (*e.g.*, bone and cartilage)

- Can the tissue/joint be immobilized (unloaded) post-operatively (using metal rods and plates)?

LAYERED-TISSUE ORGANS

- Cardiovascular tissues
  - Endothelium-smooth muscle-connective tissue
- Genito-urinary tissues
  - Endothelium-connective tissue -smooth muscle

EXAMPLE OF A HOLLOW, LAYERED STRUCTURE

Epithelial cells

Muscle cells

Connective tissue cells

Diagrams removed for copyright reasons.
Coronary artery structure: from Netter, F. H. *Heart* (Ciba Collection), 1969.

Male Genito-Urinary System

http://www.bartleby.com/107/255.html#i1135

Diagram removed for copyright reasons.

See Gray's Anatomy, downloadable from Bartleby.com at http://www.bartleby.com/107/.

Urinary Bladder

http://www.bartleby.com/107/255.html#i1135

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Urinary Bladder

Epithelium

Connective Tissue

Smooth Muscle

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http://www.bartleby.com/107/255.html#i1135

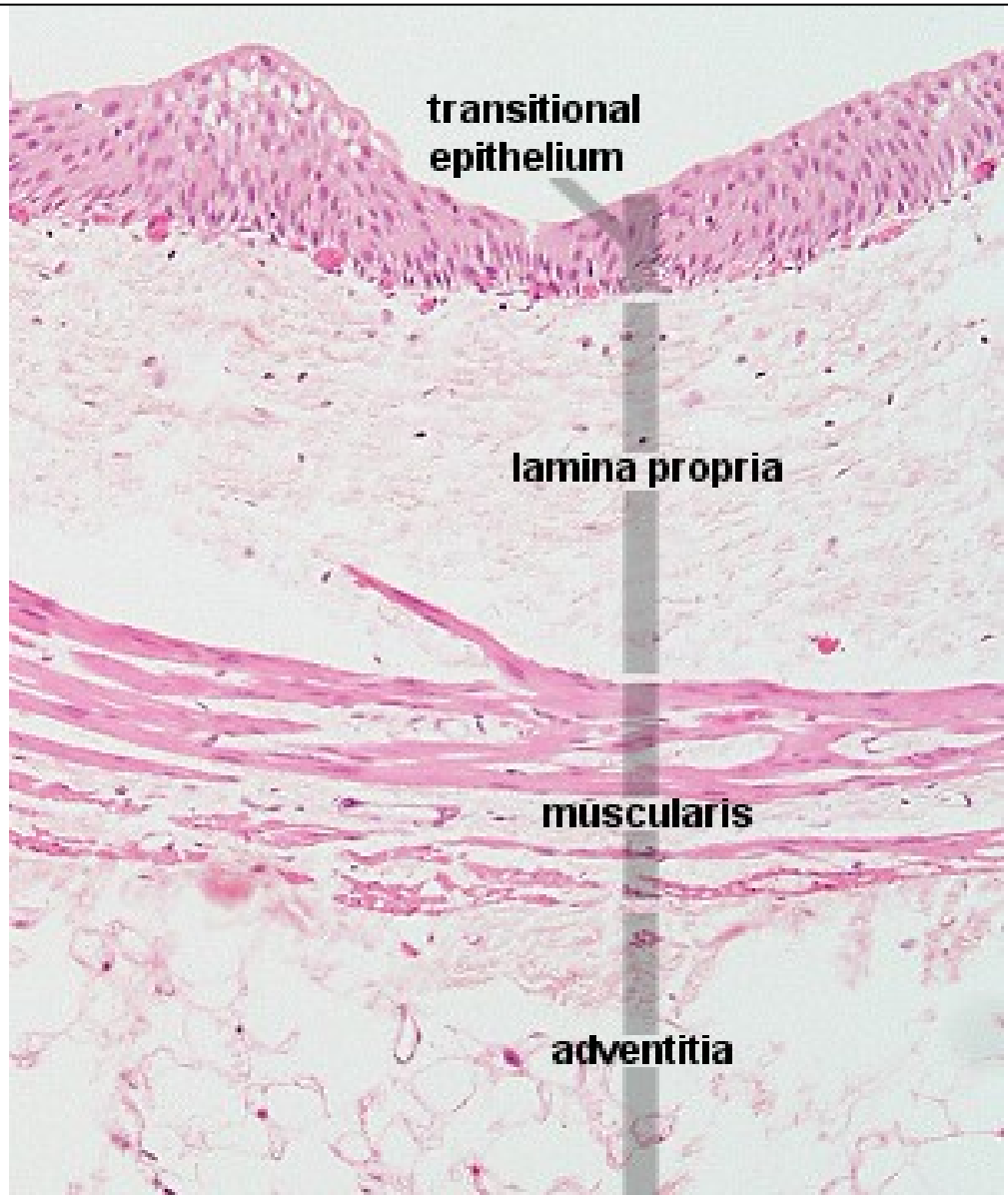
Urinary Bladder (Relaxed)

http://www.bu.edu/histology/p/16501oca.htm

Images of urinary tract histology removed for copyright reasons.
See http://www.bu.edu/histology/p/16501oca.htm

Ureter (Primate)

http://www.lab.anhb.uwa.edu.au/mb140/CorePages/Urinary/urinary.htm



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TISSUE CHARACTERISTICS AND APPROACHES

Tissue	Lec.	Hollow (Tube) v. Solid	Layered Y or N	Immed. Funct. Y or N	Blood Contact Y or N	Cell Type	Scaff.
Periph Nerve	Yannas Gong	S	N	N	N	Nerve	Collag. Chitin
Blood Vessel	Schoen	H	Y	Y	Y	Ep, CT, Muscle	Collag. PGA
Heart Valve	Schoen	S	Y	Y	Y	Ep, CT, Muscle	PGA
Urin.	Atala	H	Y	Y	N	Ep, CT, Muscle	SIS Others
Bone	Liu/Xu	S	N	N	N	CT,stem	Coll/HA
Cart.	Liu/Spe	S	N	N	N	CT	Collag.

LAYERED STRUCTURES*

How to engineer a layered structure?

- Separately seed layers of a scaffold with different types of cells
- If all the cell types are mixed and added to a scaffold will they segregate eventually to form separate layers?

*Some connective tissues like bone have a lamellar architecture, but these are layers of the same bone materials (*i.e.*, same cell type in each lamella or layer)

TISSUE ENGINEERING VS. REGENERATIVE MEDICINE

TISSUE ENGINEERING

Regeneration *In Vitro*

Advantages

- Evaluation of tissue prior to implantation

Disadvantages

- For incorporation, must be remodeling
- Stress-induced architecture cannot yet be produced *in vitro*

REGENERATIVE MED.

Regeneration *In Vivo*

Advantages

- Incorporation and formation under the influence of endogenous regulators (including mechanical strains)

Disadvantages

- Dislodgment and degrad. by mech. stresses *in vivo*

TISSUE ENGINEERING
CLINICAL APPLICATIONS

Define the clinical problem.

- **What type of tissue/organ to be engineered (connective, epithelial, muscle, or nerve)?**
- **Location and specific features of the tissue that distinguish it from other members of the tissue category.**
- **Function of the tissue at the location at which is has been lost.**
- **The degree to which the tissue has to be regenerated to restore meaningful clinical function (including histology, biochemistry, and functional properties).**

Which Tissues Can Regenerate Spontaneously?

	Yes	No
Connective Tissues		
• Bone	√	
• Articular Cartilage, Ligament, Intervertebral Disc, Others		√
Epithelia (e.g., epidermis)	√	
Muscle		
• Cardiac, Skeletal		√
• Smooth	√	
Nerve		√

CELL-MATRIX INTERACTIONS REQUIRED FOR TISSUE ENGINEERING

Connective Tissues (Musculoskeletal)	Mitosis[1]	Migration[2]	Synthesis[3]	Contract.[4]
Bone	+	+	+	+
Articular Cartilage	-	-	-	+
Ligament/Tendon	+	+	?	+
Intervertebral Disc	?	?	?	+
Meniscus	?	?	?	+

[1] Inadequate mitosis requires exogenous cells.

[2] Inadequate migration may require a scaffold.

[3] Inadequate biosynthesis require growth factors or their genes.

[4] Contraction ?

TISSUE ENGINEERING CLINICAL APPLICATIONS

How the *in vivo* environment differs from that *in vitro*

- Vascular and lymphatic systems
  - blood elements (cells and circulating molecules)
  - fibrin clot
  - endocrine factors
- pH and electrical effects
- Many cell types in the tissue producing paracrine factors
- Complex mechanical loading
- All of the above change with time

FACTORS THAT CAN PREVENT REGENERATION

- **Limited vascular invasion of large defects**
  - ***e.g.*, bone does not regenerate in the central portion of large defects**
- **Collapse of surrounding tissue into the defect**
  - ***e.g.*, periodontal defects**
- **Excessive mechanical strains in the reparative tissue**
  - ***e.g.*, unstable fractures**