

## Principles and Practice of Tissue Engineering and Organ Regeneration (TEOR)

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### SYLLABUS

#### DESCRIPTION

The subject presents the principles and practice of tissue engineering (TE) and Organ Regeneration (OR). Emphasis is on the clinical translation and the development of workable medical devices. Topics include factors that prevent the spontaneous regeneration of tissues/organs in the adult (following traumatic injury, surgical excision, disease, and aging), and molecular and cell-biological mechanisms that can be harnessed for induced regeneration. The subject presents the principles underlying strategies for employing select biomaterial scaffolds, exogenous cells, soluble regulators, and mechanical stimuli, for the formation of tissue *in vitro* (TE) and regeneration of tissues/organs *in vivo* (regenerative medicine/OR). Describes the methodologies for producing biomaterial scaffolds to accommodate the infiltration of endogenous cells (*e.g.*, for the treatment of stroke; Fig. 1) and for incorporating cells and regulatory molecules (*e.g.*, for the treatment of blindness). Examples of clinical successes and failures of regenerative devices are analyzed as case studies. All lecture materials are posted on the class website.

The topics include:

#### PART I PRINCIPLES UNDERLYING TEOR

- Principles underlying TEOR; distinguishing the approaches of TE and OR
- Defining the clinical problem; impediments to spontaneous regeneration in defects resulting from injury, disease, and aging
- The tools available for facilitating improved healing and regeneration: biomaterial matrices, exogenous cells, and regulators (growth factors and cytokines)

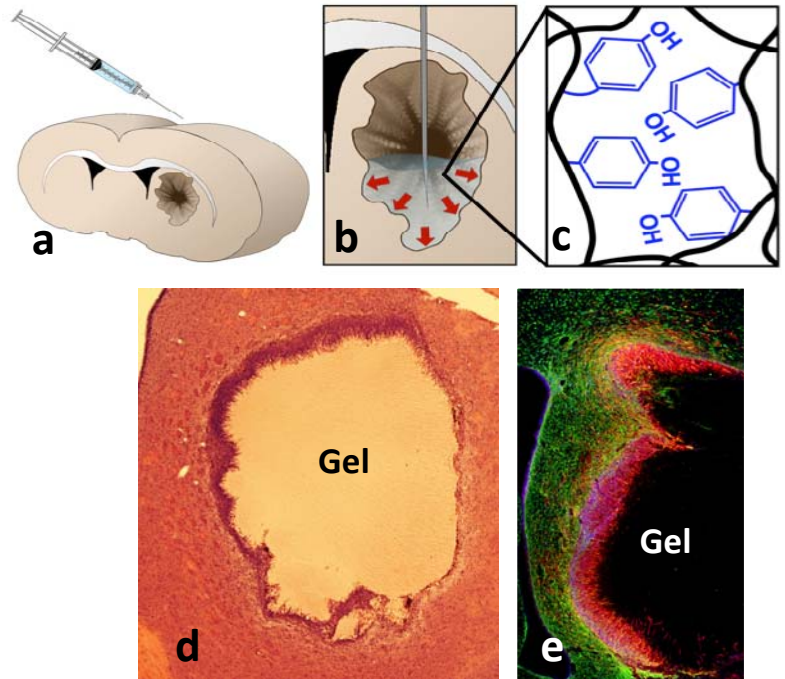


Fig. 1 An injectable gelatin-based hydrogel (gel) to facilitate regenerative processes in the fluid-filled cavitory lesions resulting from hemorrhagic stroke, in a rat model. (TC Lim, MIT HST PhD 2014; and CJ Love MIT Meche PhD 2019).

- (a) Lesion induced in the rat brain by injection of collagenase.
- (b) Injection of gelatin-hydroxyphenyl propionic acid (Gtn-HPA) into the fluid filled lesion. The gelatin solution displaces the fluid in the lesion.
- (c) Within minutes the Gtn-HPA undergoes enzymatic covalent cross-linking, under the action of horseradish peroxidase and peroxide, to form a gel.
- (d) The gel remains for over 10 weeks post-injection, enabling endogenous cells to migrate into the gel-filled lesion; the cells degrade the gel as they infiltrate it.
- (e) Immunofluorescence histology demonstrating nestin-positive endogenous neural precursor cells (red chromogen) migrating into the gel incorporating epidermal growth factor, 2 weeks post-injection, at which time rats display functional improvement.

- How to model the clinical problem to guide the selection of the tools; "unit cell processes"
- Understanding the interactions among matrices, cells, and molecular regulators (Fig. 2), and how tissues naturally assemble during development to form organs, to provide models for OR

## **PART II THE TOOLS FOR TEOR; WHAT THEY ARE AND HOW TO USE THEM**

- Design criteria for pre-formed and injectable matrices, and methods of fabrication
- Criteria for the selection of stem and progenitor cells and differentiated cell types, and methods for their use in conjunction with biomaterial matrices
- Determinants of the use of regulatory molecules, and delivery vehicles

## **PART III PRACTICE/TRANSLATION OF TEOR: CLINICAL APPLICATIONS**

- Examples of TEOR solutions to specific clinical problems
- Federal regulatory (FDA) issues which apply to TEOR products



Fig. 2 In a collagen-GAG scaffold that induces organ regeneration, specific motifs (cyan) on the collagen (green) scaffold surface bind specifically with integrin segments (blue) on the membrane of contractile fibroblasts (myofibroblasts).

## **CLASS SESSIONS**

Students will attend two 90-min. classes each week. Prior to the class session, students will have the opportunity to review materials related to the topic to be discussed, accessible on the MIT Stellar website.

## **GRADING**

The final grade will be determined by 3 Quizzes.

Each quiz will be 90 minutes in length and will cover the information presented and discussed in class and in the homework sets. Any notes can be used during the quiz.

## **PREREQUISITES**

Prerequisites are the three Institute requirements in chemistry, biology and physics.

## **READING MATERIALS**

Readings for the subject will comprise lecture notes, PowerPoint slides, journal articles, and selections from textbooks. All of the reading materials will be posted on the Stellar class website as "pdf" files which can be downloaded.

The following book will also serve as reading material: Tissue and Organ Regeneration in Adults, 2015, I.V. Yannas (reserved in the library).

Massachusetts Institute of Technology MIT 2.787J, HST.535J Fall 2021  
 Tuesdays and Thursdays, 11:00-12:30 PM  
 Stellar Website: <http://stellar.mit.edu/S/course/2/fa21/2.787/>

PRINCIPLES AND PRACTICE OF  
 TISSUE ENGINEERING AND ORGAN REGENERATION (TEOR)

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Lec #	Date	Read*		Lecturer
<b>I. BASIC SCIENCE PRINCIPLES UNDERLYING TEOR</b>				
1	Sept 9	1	Course Overview/Clinical Problems for TEOR Solution; What's in the Toolbox.	Yannas/ Spector
2	14	2	"Unit Tissue Structure" Make-up of Tissues/Organs	Spector
3	16	3	"Unit Cell Processes" Underlying TEOR; Modelling the Problem	Spector
4	21	<u>4,1,2</u>	Organ Regeneration I. Physiological Repair vs Regeneration	Yannas
5	23	<u>4,3,4,8</u>	Organ Regeneration II. Scar Formation and Contraction Blockade	Yannas
6	28	<u>4,9</u>	Organ Regeneration III. Molecular Mechanism of Regeneration	Yannas
7	39	<u>4,7</u>	Organ Regeneration IV. Regenerating Tissues vs Organs	Yannas
8	Oct 5	<u>4,9,10</u>	Organ Regeneration V. Criteria for Active Scaffolds. Review	Yannas
9	7		<b>QUIZ #1</b>	
<b>II. THE TOOLS FOR TEOR; WHAT THEY ARE AND HOW TO USE THEM</b>				
10	12	5	UCPs and The Tools: Cells; Scaffolds; and Regulators	Spector
11	14	5	Chemical and Structural Make-up of Scaffolds	Spector
12	19	6, 7	Types of Cells and Regulators	Spector
13	21	<u>8,6</u>	Skin Regeneration in the Clinical Setting	Yannas
14	26		Cell-ECM Interactions <i>In Vitro</i> and <i>In Vivo</i>	Yannas
15	28	<u>9,7</u>	Peripheral Nerve Regeneration. Construct Databases.	Yannas
16	Nov 2	8	Device Development for Skin Regeneration	D. Orgill (HMS)
17	4		<b>QUIZ #2</b>	
<b>III. PRACTICE/TRANSLATION OF TEOR: CLINICAL APPLICATIONS</b>				
18	9	15	Conjunctiva (Eye) Regeneration. Future Directions.	Yannas
	11		<i>No Class; Veterans Day</i>	
19	16	10	Musculoskeletal/Dental Hard Tissue: Bone	Spector
20	18	10	Musculoskeletal Soft Tissues: Cartilages, and Fibrous Tissues	Spector
21	23	11	Dental Soft Tissues: Gingiva, Ligament, and Pulp	Spector
	25	13	<i>No Class; Thanksgiving Day Holiday</i>	
22	30	15	Central Nervous System: Brain and Spinal Cord	Love/Spector
23	Dec 2	14	Central Nervous System: Retina	Dromel
24	7		Federal Regulatory Issues for TEOR Products; Review	Spector Spector/Yannas
25	9		<b>QUIZ #3</b>	

\* Readings Numbers in plain text refer to chapters on the Web site; numbers in bold, italics, and underlined refer to chapters in Tissue and Organ Regeneration in Adults, I.V. Yannas, 2<sup>nd</sup> edition, 2015. MIT Library reserve.