University of California, Department of Bioengineering

Course Number: BioE114

Course Title: Cell Engineering

Instructor: Irina Conboy (iconboy@berkeley.edu)

GSI: Ruhollah Moussavi-Baygi (ruhollah@berkeley.edu) Stanley Hall 104

Units: 4 units

Lectures: Moffitt library, 103; TuTh 5:00PM - 6:29PM

Discussion: Moffitt Library, 103; Th 4:00PM - 4:59PM

Final Exam: Moffitt Library, 103; 12/15/16 11:30-2:30pm.

Course Format: three hours lecture per week and two discussion sessions per week .

Prerequisites: Bio1A or BioE 11; or consent of instructor

Grading: Letter

Textbook: Freeman Biological Sciences as a reference textbook.

Course Description:

This course will teach the main concepts and current views on key attributes of animal cells (somatic, embryonic, pluripotent, germ-line; with the focus on mammalian cells), will introduce theory of the regulation of cell function, methods for deliberate control of cell properties and resulting biomedical technologies.

Techniques for primary cell-line derivation, propagation characterization and therapeutic use (transplantation and drug-screening) will be outlined.

Current bioengineering strategies will be discussed, i.e., microfluidics – based sorting and culture, single-cell analysis, high resolution reporter-based MRI imaging, RAMAN microspectorscopy for cell fate determination, fluorescent and mechano-sensors of cellular and sub-cellular events, de-cellularized macro-organs, organs on Chip, and reconstruction and calibration of signal transduction networks.

The course will provide an overview of the gene expression: epigenetic, transcriptional, post-transcriptional, translational and post-translational regulation of cell properties and behavior, introducing the concepts of global genome, epigenome and proteome analyses, genome editing and genetic code reprogramming. Specific examples include Next-Generation Sequencing, RNA Seq and Chip Seq, Reporter systems, Cre-Lox and CRISPR methods, single cell Western Blotting, orthogonal translation and signal transduction pathway reconstruction.

Overview of cell organelles and the use of sub-cellular nanoprobes for monitoring the activity of organells and enzymes will be provided. Specific examples include structure, function, and dynamics of mitochondria in normal and pathological cells; regulation of apoptosis; Nano-sensors for subcellular thermal changes and NADH. Lysosomes and lysosomal diseases; Autophagy; Physiologic and engineered plasma membranes, Cell polarity and asymmetry.

Cell cycle of embryonic, pluripotent, multipotent and cancer cells will be discussed with the introduction of key regulatory determinants (cyclins, CDKs, CDKIs, G1-S and G2-M check-points). Gene expression changes during cell cycle and the relevance of this phenomenon for single cell analysis will be discussed.

Important objectives of currently developing regenerative medicine therapies will be also introduced and discussed, such as methods for derivation of embryonic stem cells, generation and therapeutic use of pluripotent stem cells and discovery of endogenous pluripotent stem cells. Biomaterials and tissue engineering approaches for combatting degenerative disorders; CRISPR and gene therapy approaches for restoring genome in genetic diseases will be outlined. Specific examples include biomaterial scaffolds and tissue-specific differentiation of stem and other regenerative cells, microfulidics and micro-patterning single-cell platforms for characterization of gene expression in regenerative cells, engineering artificial niches for cell transplantation, directed protein evolution and deciphering signal transduction pathways. Specific focus is given to applications for tissue engineering, cell replacement therapies and regenerative medicine.

Course Objectives:

The purpose of this course is to introduce the student to problems associated with the molecular regulation of cell properties, proper selection of in vitro and in vivo conditions and experimental techniques best suited for derivation, propagation and characterization of primary cell lines and provide knowledge of the currently developing cell and tissue engineering technologies. The level of course-work presupposes knowledge of fundamentals of cellular and molecular biology and of biomaterials at the freshman/sophomore undergraduate level. Through class lectures and readings in the theory and experimental methods of cell science, material science and bioengineering the student will gain a fundamental understanding of the principles and techniques guiding the current cell and tissue engineering research. In addition, this course will aid the student in cultivating broad knowledge of the stem cell and regenerative medicine field and in learning about the interface with biomedical and translational sciences.

Course Policies*:*

Students are required to attend lectures and participate in one discussion section a week. Readings from the clinical, life and materials science literature will be assigned. Additionally, students are encouraged to seek out reference material to complement the reading assignments.

Homeworks consist of self-graded Check Your Understanding quizzes for each lecture and graded directed reading and in-class presentations of relevant published articles (from the assigned list) describing the use of cell technologies in biomedicine or bioengineering. Each presentation will be developed in discussion with Prof. Conboy or GSIs and delivered by the group of 4-5 students. Each directed reading lecture will have the introduction into the covered material and conclusion given by Prof. Conboy. The student presentations are a valuable asset to the course as they allow the students to participate in discussions of a relevant papers showing how the material learned in class is used for a plethora of applications ranging from basic research to clinical therapy. This aspect of the class also provides training in public speaking and enhances communication skills of the students. The final exam, which is based on the fundamental principles of cell science and technology as these apply to key areas of bioengineering and regenerative medicine will be given in class. All in-class examinations are open-book and open-notes; the use of internet is not allowed.

GRADING:

Class participation	10%
Midterm Exam	30%
Homeworks (Paper presentations)	20%
Final Exam	40%
Total	100%

Wk 1	8/25	Introductory Lecture
Wk 2	8/30	Basic principles of cell science and cell engineering; overview

	9/1	Genetic control of cell fate and behavior. Editing genomes and deliberately controlling the levels of gene expression.
Wk 3	9/6	Reporters, Transgenes, Knock-outs,-ins, Cre-Lox and barcoding methods for monitoring and regulating cell behavior.
	9/8	Master-switch of Epigenetics.
Wk 4	9/13	Organelle homeostasis and pathologies; sub-cellular nano-probes.
	9/15	Cell-cell and cell-matrix interactions. Matrix rigidity and tethering.
Wk 5	9/20	Reverse engineering of organogenesis. Macro-organs and organs on Chip.
	9/22	Cell cycle 1: comparison between somatic, stem and cancer cells
Wk 6	9/27	Cell cycle 2: check-points, deliberate control and considerations in single cell analysis.
	9/29	Immune system1: cell transplantation technologies.
Wk 7	10/4	Immune system2: rejection of non-self and considerations for tissue engineering.
	10/6	Protein engineering: Tim-barrel, and directed protein evolution. GSI guest lecture.
	10/11	**Midterm (open book)**
Wk 8	10/13	Engineering pluripotency and cell-fate switches. Safeguards and implications for regenerative medicine and understating human diseases.

		1. Directed reading and group presentation: Cell. 2006 Aug 25;126(4):663-76.
Wk 9	10/18	Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors.
	10/20	2. Directed reading and group presentation: Nat Chem Biol. (Links to an external site.) 2016 Jan;12(1):29-34. Designing Tim-barrel protein with atomic level accuracy.
	10/25	Use of micro-patterning and micro-fluidics for single cell analysis: implications for drug screening.
Wk 10	10/27	3. Directed reading and group presentation: Lab Chip. 2008 Jan;8(1):68-74. A microfluidic processor for gene expression profiling of single human embryonic stem cells.
Wk 11	11/1	4. Directed reading and group presentation: Human iPSC-based cardiac microphysiological system for drug screening applications. (Links to an external site.) Sci Rep. 2015 Mar 9;5:8883.
	11/3	In vivo cell imaging.
		5. Directed reading and group presentation: MRI-based detection of alkaline phosphatase gene reporter activity using a porphyrin solubility switch. (Links to an external site.) Chem Biol. 2014 Mar 20;21(3):422-9.
Wk 12	11/8	6. Directed reading and group presentation: Stem Cells. 2008 Apr;26(4):864-73. Comparison of reporter gene and iron particle labeling for tracking fate of human embryonic stem cells and differentiated endothelial cells in living subjects.
	11/10	Cell aging and rejuvenation.
	11/15	7. Directed reading and group presentation: Nature. (Links to an external site.)2005 Feb 17;433(7027):760-4.

		Rejuvenation of aged progenitor cells by exposure to a young systemic environment.
Wk 13		8. Directed reading and group presentation: Nat Med. (Links to an external site.)2014 Jun;20(6):659-63. 2014 May 4. Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice.
	11/17	Ethical considerations and responsible conduct of research in Science and Technology.
Wk 14	11/22	9. Directed reading and group presentation. Science. 2005 Jun308(5729):1777-83. (+concerns and retractions). Patient-specific embryonic stem cells derived from human SCNT blastocysts. 10. Directed reading and group presentation.Nature. (Links to an external site.)2014 Jan 30;505(7485):641-7. doi: 10.1038/nature12968. Stimulus-triggered fate conversion of somatic cells into pluripotency. Scientific and ethical evaluation of the retracted paper.
	11/25	Thanksgiving, no class
	12/5-9	Review Week
	12/15-16	**FINALS:** Moffitt library, 103; 11:30-2:30pm. **Open book.**