Course Syllabus

University of California, Department of Bioengineering

Course Number: BioE114/BioE202

Course Title: Cell Engineering

Instructor: Irina Conboy (iconboy@berkeley.edu); office hours 4-5pm by Zoom and by appointment.

GSIs: Lindsey Osimiri (**lindseyo@berkeley.edu (mailto:lindseyo@berkeley.edu)**), Kiet Phong (**phongk@berkeley.edu (mailto:phongk@berkeley.edu)**)

Units: 4 units

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

Prerequisites: Bio1A or BioE11; or consent of instructor

Grading: Letter

Time & Location: Lecture: Tuesday & Thursday 2:00 - 3:30 PM, **Zoom (https://berkeley.zoom.us/j/98479148937?pwd=eEhrTzQ4WWdBVXN3ZU5wa0hhRHZrUT09)**

Discussion 101 (Lindsey): Wednesday 4:00 - 5:00 PM, **Zoom (https://berkeley.zoom.us/j/98001846466?pwd=bzY1azYxeEZJOGhUcU5pemp4c1YvUT09)**

Discussion 102 (Kiet): Friday 8:00 - 9:00 AM, **Zoom (https://berkeley.zoom.us/j/98359740939?pwd=WEZYT0hWTGd5RnRBUi9aU2tkc0VDUT09)**

Midterm: Rolling Midterm (as described in Lecture 1).

Final: Tuesday, 12/15/2020 8:00 - 11:00 AM, Online

Room share and graduate content: BioE114 and BioE202 will share the same lectures and exams. However, graduate students will be required to define a biomedical problem and suggest solution(s), whereas undergraduate students will be provided with specific topics from published papers.

Textbook: *Freeman Biological Sciences* as a reference textbook.

Class Syllabus and Full 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 and bioengineering technologies.

The key concepts of cell engineering will be discussed in the light of deriving specific cell types, control of cell behavior and therapeutic use of cells, i.e., microfluidics – based sorting and culture, single-cell analysis, high resolution reporter-based MRI imaging, 2-photon microscopy imaging of cells in their in vivo niches, RAMAN micro-spectroscopy for cell fate determination, fluorescent and mechano-sensors of cellular and sub-cellular events, de-cellularized macro-organs, organs chips, reconstruction and calibration of signal transduction networks, and introduction to protein and peptide engineering and directed evolution.

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 Sequencing and Chip Sequencing, 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 nano-probes for monitoring the activity of organelles 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, microfluidics 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.

Weekly Schedule:

Week 1	08/27/20	Introductory Lecture
Week 2	09/01/20	Basic principles of cell science and cell engineering; overview.
	09/03/20	Genetic control of cell fate and behavior. Editing genomes and deliberately controlling the levels of gene expression.
Week 3	09/08/20	Reporters, Transgenes, Knock-outs, -ins, Cre-Lox and barcoding methods for monitoring and regulating cell behavior.
	09/10/20	Master-switch of Epigenetics.
Week 4	09/15/20	Organelle homeostasis and pathologies; sub-cellular nano-probes. **Example of paper presentation.**
	09/17/20	Cell-cell and cell-matrix interactions. Matrix rigidity and tethering.
Week 5	09/22/20	Reverse engineering of organogenesis. Macro-organs and organs chips.
	09/24/20	Cell cycle 1: comparison between somatic, stem and cancer cells.
Week 6	09/29/20	Cell cycle 2: check-points, deliberate control and considerations

		in single cell analysis.
	10/01/20	Immune system1: cell transplantation technologies.
Week 7	10/06/20	Immune system2: rejection of non-self and considerations for tissue engineering.
	10/08/20	Engineering pluripotency and cell-fate switches. Safeguards and implications for regenerative medicine and understating human diseases.
Week 8	10/13/20	Protein engineering: Tim-barrel and directed protein evolution.
	10/15/20	**In class review prior to the Rolling Midterm;** Example presentation of a block of papers.
Week 9	10/20/20	**1. Directed reading and group presentation: Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. (https://www.ncbi.nlm.nih.gov/pubmed/16904174)**
	10/22/20	**2. Directed reading and group presentation: Designing Tim-barrel protein with atomic level accuracy. (https://www.nature.com/articles/nchembio.1966)**
Week 10	10/27/20	Use of micro-patterning and micro-fluidics for single cell analysis: implications for drug screening.
	10/29/20	**3. Directed reading and group presentation: A microfluidic processor for gene expression profiling of single human embryonic stem cells. (https://www.ncbi.nlm.nih.gov/pubmed/18094763)**
Week 11	11/03/20	**4. Directed reading and group presentation: Human iPSC-based cardiac microphysiological system for drug screening applications. (http://www.ncbi.nlm.nih.gov/pubmed/25748532)**

	11/05/20	In vivo cell imaging.
Week 12	11/10/20	**5. Directed reading and group presentation:** **MRI-based detection of alkaline phosphatase gene reporter activity using a porphyrin solubility switch.** **(https://www.ncbi.nlm.nih.gov/pubmed/24613020)** **6. Directed reading and group presentation:** **Comparison of reporter gene and iron particle labeling for tracking fate of human embryonic stem cells and differentiated endothelial cells in living subjects.** **(https://www.ncbi.nlm.nih.gov/pubmed/18218820)**
	11/12/20	Cell aging and rejuvenation.
Week 13	11/17/20	**7. Directed reading and group presentation:** **Rejuvenation of three germ layers tissues by exchanging old blood plasma with saline-albumin.** **(https://pubmed.ncbi.nlm.nih.gov/32474458/)** **8. Directed reading and group presentation**: **Human umbilical cord plasma proteins revitalize hippocampal function in aged mice** **(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5586222/)** .
	11/19/20	Ethical considerations and responsible conduct of research in Science and Technology.
Week 14	11/24/20	**9. Directed reading and group presentation** (concerns and retractions): **Patient-specific embryonic stem cells derived from human SCNT blastocysts.** **(https://www.ncbi.nlm.nih.gov/pubmed/15905366)** **10. Directed reading and group presentation:** **Stimulus-triggered fate conversion of somatic cells into pluripotency.** **(https://www.ncbi.nlm.nih.gov/pubmed/24476887)** Scientific and ethical evaluation of the retracted papers.
	11/26/20	Thanksgiving, no class

Week 15	12/01/20 12/03/20	Students present blocks of papers that address definition of high impact research.
FINALS: 12/15/2020, 8:00 – 11:00 AM		

Grading:

Class participation	10%
Midterm Exam (Paper presentation)	30%
Homework (Q&A group)	20%
Final Exam	40%
Total	100%

Course Summary:

Date	Details	Due
	Final Presentation (https://bcourses.berkeley.edu/courses/1496935/assignments/8200892)	
	Midterm Presentation (https://bcourses.berkeley.edu/courses/1496935/assignments/8185644)	
	Participation (https://bcourses.berkeley.edu/courses/1496935/assignments/8156539)	

Date	Details	Due
	Projected letter grade (https://bcourses.berkeley.edu/courses/1496935/assignments/8202377)	
	Q&A (Homework) (https://bcourses.berkeley.edu/courses/1496935/assignments/8196505)	