University of California, Department of Bioengineering
Course Number: BioE 113
Course Title: Stem Cell Technologies
Offered: Fall 2011: TuTh 2-330P, 106 STANLEY
Instructor: Irina Conboy (Office Hours: Tue/Th 3:45-4:45pm, B108B Stanley Hall)
Units: 4 units.
Final Exam Group: 5: TUESDAY, DECEMBER 13, 2011 8-11A
Course Format: three hours lecture and one hour discussion per week
Discussions: M 1-2P, 9 LEWIS; F 10-11A, 70 EVANS (attendance required to only one)
Prerequisites: Bio1A, BioE 10; or consent of instructor
Grading: Letter
GSIs: Haroldo Silva (hssilva@berkeley.edu); Joyce Bao (jxbao@berkeley.edu)
GSI Office Hours: W 11A-12P (Haroldo) and F 11A-12P (Joyce), B1 Atrium Stanley Hall

Course Description:

This course will teach the main concepts and current views on key attributes of embryonic stem cells (ESC), will introduce theory of their function in embryonic development, methods of ESC derivation, propagation and characterization and will discuss currently developing stem cell technologies.

The course will provide an overview of the genetic and epigenetic regulation of self-renewal and pluripotency of stem cells. Specific examples include selection of substrates and biomaterials for in vitro expansion and sustained pluripotency of ESC; ecto-, meso- and endoderm formation in 3D embryoid bodies, directed tissue-specific differentiation of hESCs, teratocarcinoma assays of pluripotency and clonal efficiency; nuclear transfer for creating syngeneic ESC lines for autologous tissue regeneration. The course will also discuss alternative methods for generating pluripotent stem cells that do not require destruction of human embryos; these will include lectures on de-differentiation of somatic cells into iPS cells suitable for autologous tissue transplantation, as well as cord blood and amniotic fluid stem cell derivation.

Important objectives of currently developing stem cell therapies will be introduced and discussed. Specific examples include biomaterial scaffolds and tissue-specific differentiation of ESC, microfulidics and micro-patterning single-cell platforms for characterization of ESC gene expression, engineering artificial niches for cell transplantation, and high throughput analysis in conjunction with computational biology and mathematical modeling for deciphering stem cell-specific signal transduction pathways. Particular emphasis is placed on the theoretical knowledge of the key attributes of ESC and novel technologies based on the use of ESC. Specific focus is given to applications for tissue engineering, cell replacement therapies and regenerative medicine.

Course Objectives & Policies:

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

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. Attendance will be taken at all discussion sections each week and it will be part of your class participation grade. In addition, there will be pop quizzes throughout the semester to check for lecture attendance and missing more than one may result in the reduction of your class participation grade. A mid-term examination on basic principles of stem cell engineering will be given in class (this exam will NOT include material from any journal articles).

Homeworks consist of in-class presentations of relevant published articles (from the assigned list below) describing the use of stem cell technologies in biomedicine or bioengineering. Each student is required to present two articles on separate topics of stem cell science (i.e. different dates) in groups composed of a maximum of four students. Each group is required to email a pdf version of their slide presentation to the GSIs at least 24 hours prior to their scheduled presentation date. The pdf files will be posted on the class bSpace website and will become part of the relevant course material for the final. A group that fails to email the presentation by the above deadline will have points deducted from the homework grade of all members in the group. Students are expected to finish selecting articles for presentation and thus finalizing their groups by the end of Week 5 (see Tentative Schedule below). Students shall email GSIs the top 4 articles they wish to present, in order of preference, and GSIs will assign students to their selections on a first-come first-served basis. A webpage on the class bSpace website will keep track of all student-selected articles and groups, but only GSIs will be able to edit it. This page will have a table with two columns: the first column will have the article's journal and title information and the second column will have the student's name and email for contact (same as used to contact GSIs unless requested otherwise).

The student presentations are a valuable asset to the course as they allow the students to participate in discussions of a number of highly relevant papers showing how the material learned in class is used for a plethora of applications ranging from basic research to clinical therapy. The final exam based on the fundamental principles of stem cell science and technology as these apply to key areas of bioengineering and regenerative medicine, as well as the assigned readings, will be given in class. All in-class examinations are open-book and open-notes, including but not limited to all assigned journal articles and their respective slide presentations.

GRADING:

Class participation	10%
Midterm Exam	30%
Homeworks	20%
Final Exam	40%
Total	100%

Tentative Schedule:

Week 1	
8/25/11	Introductory lecture
Week 2	
8/30/11	Basic principles of stem cell science; overview
9/1/11	Strategies for differential gene expression in animal embryos
Week 3	
9/6/11	Basic principles of embryonic development
9/8/11	Deciphering and modeling core transcription regulatory circuitry in ESC and their progeny.
Week 4	
9/13/11	Epigenetics and ES cell fate: Polycomb complexes and chromatin states.
9/15/11	Signal transduction networks regulating "stemness" and tissue-specific differentiation: synthetic networks for cell fate programming and

	reprogramming
Week 5	
9/20/11	Regulation of cell cycle progression: comparison between somatic, ES cells and cancer cells.
9/22/11	Meiosis, oogenesis and SCNT
Week 6	
9/27/11	Immune system and rejection of non-self: considerations for tissue engineering.
9/29/11	Strategies for manufacturing and replacing tissues using stem cells; biomaterials and scaffolds in ex-vivo organogenesis.
Week 7	
10/4/11	Derivation and culture of hESCs: Synthetic, animal-free, and chemically defined conditions Nat Biotechnol. 2010 Jun;28(6):611-5. Long-term self-renewal of human pluripotent stem cells on human recombinant laminin-511. Biomaterials. 2010 Jul;31(19):5137-42. Defined high protein content surfaces for stem cell culture. Biomaterials. 2011 Oct;32(29):6912-9. Engineered polymer-media interfaces for the long-term self-renewal of human embryonic stem cells.
10/6/11	Alternative strategies for hESC derivation that do not require the destruction of human embryo: de-differentiation of somatic cells into iPS cells Cell. 2006 Aug 25;126(4):663-76. Epub 2006 Aug 10. Comment in: Cell. 2006 Aug 25;126(4):652-5. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. PLoS One. 2010 Dec 30;5(12):e14397. Activation of pluripotency genes in human fibroblast cells by a novel mRNA based approach. Nat Cell Biol. 2011 May;13(5):541-9. Incomplete DNA methylation underlies a transcriptional memory of somatic cells in human iPS cells.
Week 8	
10/11/11	Alternative strategies for hESC/progenitor cell derivation that do not require the destruction of human embryo Blood. 2011 May 5;117(18):4773-7. Hematopoietic stem/progenitor cells, generation of induced pluripotent stem cells, and isolation of endothelial progenitors from 21- to 23.5-year cryopreserved cord blood. Exp Cell Res. 2011 Aug 1;317(13):1895-903 Selection of alkaline phosphatase-positive induced pluripotent stem cells from human amniotic fluid-derived cells by feeder-free system. Nature. 2006 Jan 12;439(7073):212-5. Generation of nuclear transfer-derived pluripotent ES cells from cloned Cdx2-deficient blastocysts.
10/13/11	**In class open-book Midterm exam**

Week 9	
10/18/11	Strategies for directed differentiation of ES cells: neurons Cell Stem Cell. 2011 Jul 27. Direct Reprogramming of Adult Human Fibroblasts to Functional Neurons under Defined Conditions. PLoS One. 2011 Apr 29;6(4):e18992. Transplantation of adult mouse iPS cell-derived photoreceptor precursors restores retinal structure and function in degenerative mice. Nat Med. 2006 Nov;12(11):1259-68. Functional engraftment of human ES cell-derived dopaminergic neurons enriched by coculture with telomerase-immortalized midbrain astrocytes.
10/20/11	Strategies for directed differentiation of ES cells: adult islet cells Nat Biotechnol. 2008 Apr;26(4):443-52. Epub Pancreatic endoderm derived from human embryonic stem cells generates glucose-responsive insulin-secreting cells in vivo. PLoS ONE. 2008 Jan 16;3(1):e1451 Islet-like clusters derived from mesenchymal stem cells in Wharton's Jelly of the human umbilical cord for transplantation to control type 1 diabetes. Proc Natl Acad Sci U S A. 2010 Jul 27;107(30):13426-31 Reversal of hyperglycemia in diabetic mouse models using induced-pluripotent stem (iPS)-derived pancreatic beta-like cells.
Week 10	
10/25/11	Strategies for directed differentiation of ES cells: T cells; immune response Stem Cells Dev. 2011 Jul;20(7):1131-42 Induced pluripotent stem cells expressing elevated levels of sox-2, oct-4, and klf-4 are severely reduced in their differentiation from mesodermal to hematopoietic progenitor cells. Stem Cell Rev. 2011 Sep;7(3):736-47. Development of Feeder-Free Culture Systems for Generation of ckit+sca1+ Progenitors from Mouse iPS Cells. Nat Immunol. 2004 Apr;5(4):410-7. Induction of T cell development and establishment of T cell competence from embryonic stem cells differentiated in vitro.
10/27/11	Strategies for directed differentiation of ES cells: liver, cardio-vascular, Hepatol Int. 2011 Feb 6. PMID:21484132 Direct differentiation of hepatic cells from human induced pluripotent stem cells using a limited number of cytokines. Cell. 2010 Aug 6;142(3):375-86. Direct reprogramming of fibroblasts into functional cardiomyocytes by defined factors. Biomaterials. 2008 Mar;29(7):844-56. The effect of cyclic strain on embryonic stem cell-derived cardiomyocytes.
Week 11	

11/1/11	Strategies for directed differentiation of ES cells: gametes PLoS One. 2011;6(7):e22413. Stage-Specific Germ-Cell Marker Genes Are Expressed in All Mouse Pluripotent Cell Types and Emerge Early during Induced Pluripotency. Dev Cell. 2006 Jul;11(1):125-32.In vitro-differentiated embryonic stem cells give rise to male gametes that can generate offspring mice. Nature. 2008 Nov 20;456(7220):344-9. Generation of pluripotent stem cells from adult human testis.
11/3/11	Use of micro-patterning and micro-fluidics for deciphering and controlling stem cell fate Lab Chip. 2008 Jan;8(1):68-74. A microfluidic processor for gene expression profiling of single human embryonic stem cells. PLoS One. 2010 Sep 23;5(9):e12921. Abrogation of E-cadherin-mediated cellular aggregation allows proliferation of pluripotent mouse embryonic stem cells in shake flask bioreactors. Biomaterials. 2010 Jul;31(21):5526-35 The enhancement of human embryonic stem cell osteogenic differentiation with nano-fibrous scaffolding.
Week 12	
11/8/11	In vivo imaging techniques for stem cell technologies Stem Cells Dev. 2011 Apr 27. In Vitro Imaging of Angiogenesis Using Embryonic Stem Cell-Derived Endothelial Cells. Dev Biol. 2010 Oct 1;346(1):90-101. Survival and death of epiblast cells during embryonic stem cell derivation revealed by long-term live-cell imaging with an Oct4 reporter system. 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.
11/10/11	Mice cloned from olfactory sensory neurons, iPS derived from B-cells : understanding embryonic development through stem cell technologies Nature. 2004 Mar 4;428(6978):44-9. Mice cloned from olfactory sensory neurons. Cell. 2008 Apr 18;133(2):250-64 Erratum in:Cell. 2008 Jul 25;134(2):365. Direct reprogramming of terminally differentiated mature B lymphocytes to pluripotency. Nat Biotechnol. 2008 Aug;26(8):916-24. Epub 2008 Jul 1. A drug-inducible transgenic system for direct reprogramming of multiple somatic cell types.
Week 13	
11/15/11	Primate SCNT Nature. 2007 Nov 22;450(7169):497-502. Producing primate embryonic stem

	cells by somatic cell nuclear transfer. Stem Cells. 2008 Feb;26(2):485-93. Development of human cloned blastocysts following somatic cell nuclear transfer with adult fibroblasts. Dev Biol. 2004 Dec 15;276(2):237-52. Erratum in:Dev Biol. 2005 Feb 15;278(2):619. Embryogenesis and blastocyst development after somatic cell nuclear transfer in nonhuman primates: overcoming defects caused by meiotic spindle extraction.
11/17/11	Using stem cell technologies to understand human diseases PLoS Biol. 2011 Jul;9(7):e1001099. Epub 2011 Jul 12. Generation of Healthy Mice from Gene-Corrected Disease-Specific Induced Pluripotent Stem Cells. Circ Res. 2011 Jul 28. Cardiomyocytes Obtained From Induced Pluripotent Stem Cells With Long-QT Syndrome 3 Recapitulate Typical Disease-Specific Features In Vitro. Nature 2010; 464:292–296. Telomere elongation in induced pluripotent stem cells from dyskeratosis congenita patients.
Week 14	
11/22/11	Adult pluripotent stem cells in planaria and mammals. Continuation of embryonic organogenesis during tissue repair in adults? Science. 2011 May 13;332(6031):811-6. Clonogenic neoblasts are pluripotent adult stem cells that underlie planarian regeneration. Science. 2011 May 13;332(6031):852-5. Polarized notum activation at wounds inhibits Wnt function to promote planarian head regeneration. Leukemia. 2010 Aug;24(8):1450-61. Epub 2010 May 27. Molecular signature of adult bone marrow-purified very small embryonic-like stem cells supports their developmental epiblast/germ line origin.
11/24/11	Ethical considerations, public opinion and regulation of stem cell science and technology Bioethics. 2011 Jul 4. doi: 10.1111/j.1467-8519.2011.01896.x.PMID:21726264 UNCERTAIN TRANSLATION, UNCERTAIN BENEFIT AND UNCERTAIN RISK: ETHICAL CHALLENGES FACING FIRST-IN-HUMAN TRIALS OF INDUCED PLURIPOTENT STEM (IPS) CELLS. Science. 2005 Jun 17;308(5729):1777-83. (+concerns and retractions). Patient-specific embryonic stem cells derived from human SCNT blastocysts: scientific and ethical evaluation of the retracted paper. Why the integrity of stem cell science and science in general is so important.
Week 15	
11/29/11	Stem cell-based technologies: from lab to start-up (invited speaker). TBA
12/1/11	UC Berkeley SSSCR (invited speaker). TBA

Week 16	
12/6/11	Overview of the course material
12/13/11	**In class open book Final Exam.**