

MCELLBI 38 Stem Cell Biology, Ethics and Societal Impact

Instructors

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Course Description

What are stem cells? How do they function normally in the body and how can we harness their potential for treating diseases? What are the biological, ethical and political barriers to genetically engineering stem cells for use in regenerative medicine? To address these questions, we will start with the fundamentals necessary to understand stem cell biology. We will explore how stem cell technologies can be advanced and used in novel medical therapies, with a particular focus on innovations for manipulating and engineering stem cells. Integral to these topics will be a thorough dialog of ethical implications and the controversies surrounding stem cell research.

Course Topics

Lectures #1 and #2: Introduction to Cells and Overview of Concepts in Stem Cell Biology

- Promise of stem cells in mitigating human disease, syndromes and injuries, modeling disease states, gene/cell therapies, tissue regeneration and bioengineering
- Definition of stem cell terminology, stem cells in embryonic and adult tissues
- Hierarchy of molecules-genes-cells-tissues-organisms
- Regulatory signals that alter gene expression, cell structure, function, differentiation and cell division

Reading: NIH website Stem Cell Basics I (<https://stemcells.nih.gov/info/basics/1.htm>)

Lectures #3, #4, and #5: Embryonic Stem Cells and Connections to Early Reproductive Processes

- Early steps in human reproduction (Zygote to blastocyst stage)
- Totipotent vs Pluripotent stem cells
- Embryonic stem cells: Sources, characterization and experimental manipulations
- Ethics of collecting stem cells from embryos vs adult tissue

Lectures #6, #7 and #8: Multipotent Stem Cells from Adult Tissues

- Multipotent stem cells from adult tissues and organ systems, stem cell niches,
- Advantages and disadvantages for use, characterization, experimental manipulations
- Immune markers and tissue/organ rejection
- Induced pluripotent stem cells (iPSC) and experimental differentiation into specific tissue types
- Experimental breakthroughs and limitations

Reading: Scudellari, Megan "A decade of iPSC cells" *Nature*, 534: 310-312.

Lectures #9, #10 and #11: Stem Cell Therapies: Hematopoietic and Bone Stem Cells

- Overview of blood cell types and functions, Hematopoietic stem cells, differentiation pathways
- Lymphoid vs myeloid cell pathways and stem cells
- Mesenchymal stem cells
- Current practices using patient's own cells for gene therapy
- Leukemia therapies with stem cells
- Ethics of gene therapy

Reading: Reardon, Sara "Leukaemia success heralds waves of gene-editing therapies" *Nature*, 527: 146-147.

Lectures #12, #13 and #14: Genetic Engineering of Stem Cells

- Molecular genetic strategies to regulate gene expression in stem cells
- Loss vs additional of expressed genes
- Replacing mutated genes with wild type versions
- Use of CRISPR/Cas9 genomic editing
- Ethics of gene editing and changing cell genotypes

Reading: Hall, Stephen "The first tinkering with human heredity may happen in the infertility clinic" *Scientific American*, Dec 2016.

Reading: Regalado, Antonio "Engineering the perfect baby" *MIT Technology Review*, March 5, 2015.

Lectures #15, #16, #17 and #18: Potential for Human Cloning: Reproductive Tissue Stem Cells

- Overview of human reproductive system and hormone control pathways
- Germline cell editing
- Mammary stem cells: Differentiation into specific tissue types
- Stem cells that give rise to spermatozoa and why men can keep making more sperm cells
- Ovarian stem cells: Role in oocyte development and why women cannot make more eggs
- Somatic cell nuclear transfer: Use of the oocyte to create a new organism (in animals).
- Ethics and politics of cloning animals and humans.

Reading: Weintraub, Karen "20 years after Dolly the sheep led the way – where is cloning now?" *Scientific American*, July 2016.

Lectures #19, #20 and #21: Tissue Regeneration and Bioengineering of Tissues and Organs

- Overview of regeneration and bioengineering of tissues
- Role of stem cells in controlling tissue regeneration
- Experimental strategies to bioengineer tissues and organs from cultured stem cells
- 3-D organoid cultures and tissue scaffolds
- Characterization of functional bioengineered organs
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Reading: Knoblich, Juergen "Building a brain in the lab" *Scientific American*, Jan 2017.

Reading: Bredenoord, AL, Clevers, H, Knoblich J (2017) "Human tissues in a dish: The research and ethical implications of organoid technology" *Science* 355.

Lectures #22, #23 and #24: Treating Injury and Degenerative Disease: Neuronal Stem Cells

- Overview of nervous system
- Location and function of Neuronal stem cells
- Isolation, generation and characterization of Neuronal stem cells
- Stem cell treatment for spinal cord injury
- Stem cell treatment for degenerative diseases: Parkinson's disease, stroke, multiple sclerosis, Alzheimer's disease
- Process of approving new stem cell treatments: Clinical trials for spinal cord injury and neurodegenerative diseases

Reading: Denworth, Lydia "Stem cells could repair Parkinson's brain damage" *Scientific American*, March 2015

Lectures #25, #26 and #27: Pancreatic Stem Cells and Potential Stem Cell therapies for Diabetes

- Overview of pancreatic beta islet cell function, insulin hormone action, regulation of blood glucose and diabetes
- Pancreatic stem cell locations, isolation and experimental manipulations
- Use and difficulties of employing engineered stem cells to treat Type I diabetes

Reading: Tang Q., Desai, TA "Approaching a cure for type 1 diabetes" *Nature Medicine* 22: 236-237.

Lectures #28, #29 and #30: Differentiation from Stem Cell Niches: Skin, Hair follicle and Intestinal Stem Cells

- Overview of skin and hair follicle cell biology and physiology
- Skin/hair stem cells and experimental manipulation to treat disorders
- Overview of intestinal organ structure, villi, intestinal cell locations and differentiation pathway.
- Relationship of intestinal stem cells to the normal microbiome and to physiological dysfunction such as bowel disorders.

Lectures #31, #32 and #33: Use and Bioengineering of Cardiac and Muscle Stem Cells

- Overview of cardiac and muscle cell biology and physiology
- Cardiac stem cell markers, role in injury repair and potential use after heart attacks
- Reprogramming induced pluripotent stem cells to generate cardiomyocytes
- Treatment of heart injuries with normal or reprogrammed stem cell
- Skeletal muscle stem cells and involvement of satellite cells in generating new muscle fibers and building of stronger muscles.
- Stem cells and treatment of muscle disorders

Reading: Loike, John "Making human hamburgers: bioethics and the yuck factor" *Scientific American blog*, Sept 21, 2016.

Lectures #34, #35 and #36: Cancer Stem Cells

- Overview of human cancer and cell transformation, oncogenes and tumor suppressor genes
- Cancer cell mutations and enhanced or disrupted cell signaling pathways
- Cancer stem cell definitions
- Treatment complications due to therapy resistance
- Cancer stem cell signaling pathways in specific human cancer types (skin cancers, reproductive cancers, and others)
- Therapeutic targeting of cancer stem cells: Advances and difficulties

Lectures #37, #38, #39 and #40: Ethical, Political and Societal implications

- Commercialization of stem cell-based therapies
- Politics and Moral/ethical issues and public outreach
- Practicalities and feasibilities of using stem cells to treat human disease and injuries
- Access to healthcare and barriers to insurance coverage
- Pharmaceutical industry viewpoint
- De-extinction of animals and ecological implications
- Future innovations, trends and misconceptions of using human stem cells

Reading: Kolata, Gina “Stem cell therapies are still mostly theory, yet clinics are flourishing” *NY Times*, July 28, 2016.

Reading: Callaway, Ewen “Stem-cell plan aims to bring rhino back from brink of extinction” *Nature News*, May 3, 2016.

Reading assignments and resources

There is no textbook on this topic, so we will put all resources on bCourses. We will provide articles from a variety of sources (newspapers, National Institutes of Health, Scientific American, etc) for content and articulation to a non-scientific audience (see the course schedule).

Grades

Discussion section assignments: 20%

2 Midterms: 2 x 25% = 50%

Final: 30%

Discussion section assignments will be a combination of short answer questions and short discussion/analysis of published articles.

Course Policies

Safe, Supportive, and Inclusive Environment

Whenever a faculty member, staff member, post-doc, or GSI is responsible for the supervision of a student, a personal relationship between them of a romantic or sexual nature, even if consensual, is against university policy. Any such relationship jeopardizes the integrity of the educational process.

Although faculty and staff can act as excellent resources for students, you should be aware that they are required to report any violations of this campus policy. If you wish to have a confidential discussion on matters related to this policy, you may contact the Confidential Care Advocates on campus for support related to counseling or sensitive issues. Appointments can be made by calling (510) 642-1988.

The classroom, lab, and work place should be safe and inclusive environments for everyone. The Office for the Prevention of Harassment and Discrimination (OPHD) is responsible for ensuring the University provides an environment for faculty, staff and students that is free from discrimination and harassment on the basis of categories including race, color, national origin, age, sex, gender, gender identity, and sexual orientation. Questions or concerns? Call (510) 643-7985, email ask_ophd@berkeley.edu, or go to <http://survivorsupport.berkeley.edu/>.

Statement on Accommodation

If you need accommodations for any physical, psychological, or learning disability, or if you want me to have emergency medical information, please speak to me privately, either after class or during my office hours. For DSP students needing accommodations for the exams, please contact me at least two weeks prior to the midterm or final so that we can work out acceptable accommodations.

If there are any conflicts with the due dates of the exams or assignments for religious reasons, travel for campus sponsored extracurricular activities, medical and graduate school interviews, or for other reasons, please contact me.

Academic Honesty

We (Gary Firestone and Robin Ball) expect you to do your own work and to uphold the standards of intellectual integrity. If you are having trouble with an assignment or studying for an exam, or if you are uncertain about permissible and impermissible conduct or collaboration, please come see me with your questions. UC Berkeley's cheating policy (<http://bulletin.berkeley.edu/academic-policies/#studentconductappealstext>) will be followed.

Incomplete Policy

Under emergency/special circumstances, students may petition me to receive an incomplete grade. Please clearly state your reasoning in your comments to me.

Letters of Recommendation:

We are quite willing to provide letters of recommendation as needed for any of your applications (such as medical and graduate school and/or job opportunities). In addition to participating in the classroom discussions, please be sure to attend several of our course office hours. After the end of the course (even years later), please request an interview with one of us and bring a copy of your complete unofficial transcript, your CV and Personal Statement along with any recommendation forms that need to be filled in.

Additional Course Policies

- Be sure to pay close attention to deadlines.
- In consideration of other students, please turn off your cell phone during class time.
- Anyone eating in class must share their food with all other students.
- If you have a conflict with the midterm or due dates of assignments, please see me in advance.
- For unexpected emergencies, please email or phone me.
- You may discuss the general features of your discussion section assignments with other students, but the assignment that you submit must be completed on your own.

Evaluation of the Course

Please let us know how things are going during the course by email, in person or voice mail. Sometime during the middle of the semester we may solicit your feedback more formally on what is working well and what needs to be changed. Also, if you see either of us around campus (or at any sports events or other activities), feel free to introduce yourself and let us know how everything is going with the class and/or ask us any questions.

Fine Print

The course deadlines, assignments, exam times and material are subject to change at the whim of either instructor professor.