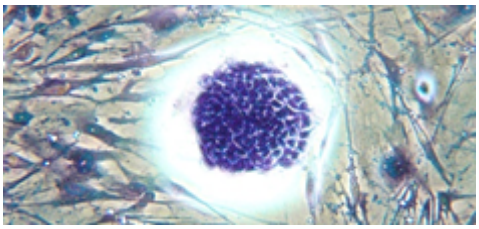


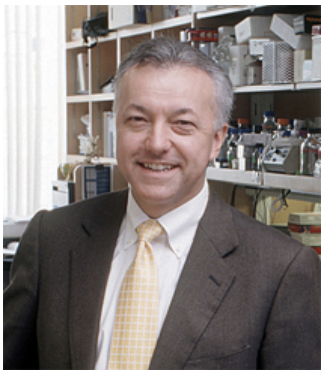
SCRB 167: Stem Cells and Regeneration in the Pathobiology and Treatment of Disease

spring term, 2015

Course description: *Stem cells are the basis for tissue maintenance and repair, and essential elements of normal organ and tissue physiology. Stem cells are also targets of numerous disease processes and through transplantation are important therapeutic agents. This course will allow advanced undergraduates to explore how stem cells and mechanisms of tissue homeostasis are affected in the course of human disease and how stem cells might be exploited to advance new therapies. In addition to lectures from prominent guest faculty, students will meet patients and their caregivers through in-class clinical sessions.*

Course website: http://isites.harvard.edu/k110009

Faculty:



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Course location: Tosteson Medical Education Center (TMEC), Room 227 on the Harvard Medical School campus
260 Longwood Avenue, Boston, MA 02115

Lecture: Tuesday: 2 hours, 2:00 p.m. to 4:00 p.m. involving presentations as follows:
• 1.0-1.5 hour interactive lecture by faculty with expertise in area under discussion.
• 0.5-1.0 hour interactive session with a patient visitor and/or clinician relevant to that week's subject.

• Each session requires reading one review article and two research papers—one scientific and one translational -- on the week's subject matter. The papers will be presented by students in Discussion Section right after class (see below under "Discussion Section"). Information from students regarding additional resources is very welcomed (*e.g.* websites, patient organizations, clinical databases, good online synopses, articles…).

Discussion section: Day and time: Tuesday 4:15 to 5:15 p.m. Location: Tuesday Sections convene in conference rooms 443, 445, and 446 of the Tosteson Medical Education Center (TMEC), 260 Longwood Avenue immediately after class. The class will be broken into sections, each with an assigned Teaching Fellow (TF), and will convene weekly for the entire course. Two students will present each week during this one-hour session. Each student will have 30 minutes to cover an assigned research or translational paper in a journal club format. Every student will give one research and one translational presentation over the course of the semester. Please see below, "**Tips on Student Presentations."**

Discussion section "Cold Call": In order to reinforce the importance of the assigned reading materials assigned each week, the teaching staff may randomly "cold call" students, who will be required to present the data from an individual figure from one of the papers. The student should briefly state the experimental hypothesis, approach used, and conclusions for the chosen figure. This ensures that all students will have done the reading every week.

Visits from patients: The lecture schedule will be complemented by the attendance of a patient and/or family members or caregivers who will provide an interactive, first-hand account of their specific condition, the challenges they face, and their expectations for future interventions and/or therapeutics. Feedback from previous offerings of this course indicates that these sessions are of considerable value to students and patients alike. It is obvious, but nevertheless must be pointed out, that the patients and their family members who visit this course will be communicating in a very personal and often poignant manner. These are not role-playing actors providing an interactive learning experience but are real people sharing their personal stories. It is important that students be active participants in these discussions, and to be considerate, thoughtful, and maintain the highest degree of respect and courtesy.

Patient privacy: On the first day of the course (January 27th) there will be a mandatory lecture for all students concerning patient privacy rights and the appropriate conduct of clinical staff in a hospital setting (per HIPAA regulations). This session must be attended (or the material reviewed with the course director) in order to register for the course.

Dates, subjects, and faculty presenters:

1/27	**Intro, patient privacy, iPS cells** (patient: sickle cell anemia), George Daley, M.D., Ph.D.
2/03	**Bone Marrow Failure** (patient: Fanconi anemia), Len Zon, M.D.
2/10	**Chronic Myeloid Leukemia** (patient: CML), George Daley, M.D., Ph.D.
2/17	**Bone Marrow Transplantation** (patient: graft vs host disease), Jerry Ritz, M.D.
2/24	**Diabetes** (patient: insulin dependent diabetes), Gordon Weir, M.D.
3/03	**Muscle development/disease** (patient: Muscular dystrophy), Amy Wagers, Ph.D.
3/10	**Lung Disease** (patient: Cystic Fibrosis), Carla Kim, Ph.D.
3/17	***Spring recess (no class)***
3/24	**Infertility/IVF**, Catherine Racowsky, Ph.D. (patient TBD)
3/31	**Neurological disease/injury** (patient: spinal cord injury), Jeffrey Macklis, M.D., D. HST.
4/07	**Kidney Regeneration** (patient: kidney failure), Ben Humphreys, M.D., Ph.D.
4/14	**Gut/Intestine** (patient: inflammatory bowel disease), David Breault, M.D., Ph.D.
4/21	**Heart Development and Repair** (patient: heart failure), Richard Lee, M.D.
4/28	**Clinical translation**, George Daley, M.D. and Jerry Groopman
4/30	***Reading period begins***

Course auditing: Due to the sensitive nature of the patient visitor portion of the course, auditing without formal registration for a letter grade is not permitted.

Readings: The only book assigned for this class is Anatomy of Hope by Jerome Groopman. The book is available at the Coop, and there will be several copies that can be borrowed for one week at a time (contact Julie Perlin). The remainder of course readings will be assigned from the body of current, peer-reviewed scientific literature and uploaded to the course website. Directed reading will ensure in-depth exposure to what is known about the embryology of tissue formation, the ontogeny of cell development, maintenance, and regeneration within the tissue, anatomic pathology and pathophysiology for specific disease processes.

Prerequisites: LS1a, LS1b, MCB 52, (SCRB 10) or MCB 54
For advanced concentrator students only (seniors and qualified juniors).

Course grading: Students must register for a letter grade. **No P/F registration is allowed.**

Grades will be based upon:

- **Final Paper (10 pages) - 40%**
- **Student presentations - 30% (15% x 2 presentations)**
- **Midterm paper (5 pages) - 20%**
- **Class participation - 10%**

Each day a midterm or final paper is late leads to a full grade demerit.

• Class participation will be graded on two things: questions and overall engagement during lecture and section, including preparedness for cold calls during section. This course is most interesting for all when every student is actively engaged-- asking questions, providing insights during discussion sessions, and interacting with guests and visitors to the course. However, we encourage thoughtful participation; quality of input is far more valuable than quantity!

• Papers are to be in 12 point font, double-spaced, and should include citations from the primary literature. Please be mindful of the page limitations: 5 page midterm and 10 page final. Margins should not be smaller than 1 inch on any side.

• **The midterm paper is due the Friday before Spring Recess, March 13th, 2015 by 11:59 p.m. and the final paper is due Friday, May 8th, 2014 by 11:59 p.m.**

• The subject matter of these papers should reflect the student's individual interests and most often draw on material presented within the course. Occasionally students have offered papers on topics not presented during class, which is acceptable as long as they remain germane to our central theme. **Papers must be original works, and not excerpted from a student's thesis or research papers from previous classes.**

• The midterm paper should present a critical, analytical review of the literature concerning the use of stem cells for a specific human disease. Your paper should specifically indicate how stem cells play a role in the pathogenesis and/or clinical management of your chosen disorder. The analytical review should culminate in a specific, novel hypothesis that details how a new stem cell experiment or treatment could impact our understanding of the disease.

• The midterm paper can be thought of as a prelude to the final paper. You will receive feedback on the hypothesis proposed in the midterm and will expand upon it in the final. The final paper should describe how experimental approaches could be used to address your novel hypothesis, including relevant references. The best papers have a novel hypothesis, offer innovative insights, and generate a readable synthesis of key points and concepts. Revised text from your midterm should be incorporated into your final paper as background and introduction. If you choose a new topic for the 10 page final the new topic needs to be approved by your TF. Please see, "**Advice for the Midterm and Final Papers**."

Attendance: Attendance is mandatory. Up to one excused absence is permitted per term. If a student expects to be absent for more than one session per term (such as for graduate or medical school interviews), they should not register for the course. Excused absences may be made-up by completing a two-page paper on the missed session's topic.

Accommodations for students with disabilities: Students needing academic adjustments or accommodations because of a documented disability must present their Faculty Letter from the Accessible Education Office (AEO) (http://www.aeo.fas.harvard.edu/) and speak with the professor by the end of the second week of the term which is **February 7, 2014**. Failure to do so may result in the Course Head's inability to respond in a timely manner. All discussions will remain confidential, although Faculty are invited to contact AEO to discuss appropriate implementation.

Academic integrity: Students are encouraged to discuss the course with one another. That said, intellectual integrity must always be maintained and every student is expected to do their own work. Each of the assigned term papers, mid-term and final, are to be the sole work of the submitting student. Additionally, term papers must be ORIGINAL works and not previously offered for a grade in another course, or be substantially derived from work to be submitted for a thesis. Papers are additionally required to properly cite the work, ideas, and comments of others, published or otherwise. PowerPoint presentation should incorporate original materials and text, and properly cite sources of any materials (pictures, data, etc.) drawn from the internet. Proper attribution is not only a cornerstone of academic integrity, but also contributes significantly to a person's reputation as a well-versed and generous colleague. Regarding student presentations offered during discussion section, though two students will present in each section, these talks are to be individually given, not offered as a combined effort.

Details on course Location and commuting to the Longwood Medical Area:

The Tosteson Medical Education Center (TMEC) is part of the Harvard Medical School campus and is located at 260 Longwood Avenue in Boston. The area is easily accessible via the M2 shuttle running between Harvard Square and the Longwood Medical Area. The HMS stop is the "end of the line" at Vanderbilt Hall at the intersection of Avenue Louis Pasteur and Longwood Avenue directly across from the Harvard Medical School quad. As an alternative, MBTA routes include the "D" (Longwood Medical Area stop) and "E" (Longwood stop) trains of the Green Line subway, the CT2 Ruggles bus from Kendall Square at MIT, or the #47 bus from Central Square in Cambridge. The CT2 and #47 buses stop quite close to TMEC on Longwood Avenue but each of the green-line trains will require 5-15 minutes of additional travel time to reach TMEC.

TMEC Building

Tips on Student Presentations…

Each student will present twice per term during Section: once on an assigned translational research paper and then again on an assigned experimental research publication from the current scientific literature. These presentations are most often provided in PowerPoint format. Students should prepare no more than 20 minutes of material in order to provide ample opportunity for Q+A and group discussion. Your TA/TF is available to discuss your presentation plans in advance as are course faculty depending on their schedules. Do not hesitate to contact them!

Translational paper presentations:

The goal of this presentation is to foster discussion regarding translational research as it pertains to the subject material and potentially the patient presentation from that week's class. A good presenter will describe the clinical and translational relevance of the paper, and be prepared to lead a discussion, including asking thoughtful questions of the other students and being prepared to thoroughly analyze and evaluate comments and questions asked by their colleagues. In general, this presentation will offer a review of the translational and/or clinical nature of the week's subject matter through the lens of the assigned paper and explore how regenerative potential is part of the picture. Note: there tend to be a great many patient-oriented groups/websites catering to specific conditions which may offer good images and information.

Research paper presentations:

The goal of this presentation to familiarize you with the process of reading a paper, distilling the main story and how it is demonstrated experimentally, and then conveying that story to your peers. Throughout the talk you should try to include questions or other ways to engage your classmates. Don't forget to leave time for discussion during your presentation!

The presentations should include both an introduction to the topic in general (e.g., figures from reviews or textbooks) and enough background to put the paper into the context of the field (e.g., a related figure from an earlier paper laying the groundwork for the current study). You will then lead your classmates through the paper, making sure to emphasize important experiments and point out any holes you find in their logic or their experimental approach. It is not necessary to include every figure from the paper in your slides; choose those figures which you feel are most relevant and important to the story that the paper is trying to tell. Occasionally, figures from the online supplemental materials accompanying the main article will provide added emphasis to important points so be sure to check whether or not supplementary materials are available. Conclude your talk with a discussion of what you think the implications of the paper are/were on the scientific field, as well as what future directions are suggested by the research you have presented. The demonstration of critical thinking is a very important part of the presentation.

Cold call:

Each week, students will be selected at random to present a figure from one of that week's assigned literature articles. No student will be cold called on the same week that they are giving either the translational or research paper presentations. For this reason, every student is urged to pay close attention to each research paper and be prepared to give a brief description of the background, experimental approach, and conclusions of any single figure.

Advice for the Midterm and Final Papers…

These assignments let you demonstrate your understanding of the material presented in class and, for the final, independently apply it to a current problem in the field of stem cell biology that you find intriguing. As you hear lectures and read the literature for the course, make notes on which topics interest you and record any creative or novel ideas you come up with along the way. These ideas will seed your research and help you write original, thought-provoking papers. As for your presentations, your TA/TF is available to discuss your term paper plans in advance as are course faculty depending on their schedules. Do not hesitate to contact them!

The midterm paper is a chance for you to become intimately familiar with the literature surrounding a topic of your choice. Your paper will be graded on its critical analysis of the state of current research in the field, including major controversies and any important unanswered questions relating to a disease. Your midterm should conclude with a novel hypothesis at the end of the document which you have developed. Most students will develop and expand on this hypothesis in the final paper. You may change topics between your midterm and final but the new topic of your 10 page paper must be approved by your TF.

An "A" final paper will achieve the following:

- Identify an unanswered or insufficiently probed **question** about the role of stem cells in human biology, disease, or medicine
- Provide a clearly-stated, novel **hypothesis** that addresses your thesis within the first paragraph of the paper (is likely the conclusion of your midterm)
- Provide **background** on the history of the issue and why it is important
- Describe the **current state of research** in the field and any controversies
- Propose a feasible **experimental outline** to determine whether the hypothesis is valid
- Include a summary at the end that restates the central thesis and findings of the paper
- Provide a relevant bibliography including additional works not presented/assigned during class

A paper with the following characteristics will receive a poor grade:

- Is written like a book report, with lots of description but little original thought
- Fails to explain clearly the question being addressed or the proposed hypothesis
- Ignores a major viewpoint or area of research relevant to the question
- Is poorly organized, lacks a logical progression, or contains grammatical errors

Recommendations on sources: Balance your sources between review and primary research articles. At the beginning of the research process, review articles can provide useful breadth and perspective. As you learn more about the topic, reading primary literature will help you to understand the current state of research and the experimental tools of the field that may be useful in proposing a test for your hypothesis. As with any research paper, your final bibliography should not over-rely on reviews compared to citations from the primary literature.

Three useful resources for accessing primary and review articles:

1. PubMed Full Text (enter through the library's website: https://www.countway.harvard.edu/index.html). This is the most authoritative source for up-to-date papers. Click through to the purple buttons that say "Find at Harvard" to get to the actual PDFs.

2. Web of Science (enter through the same library website). This is a useful tool because it indexes which papers have been cited by which other papers. This lets you search for the most heavily cited papers or get quick access to everything cited by a single paper (such as a review). There is often a few months' lag time between publication and when papers appear on Web of Science.

3. PubGet (enter at pubget.com). This is similar to PubMed, but after you enter your HUID once, all of the PDFs show up more quickly. This is a good way to look through a lot of papers in a short amount of time, for example if you were searching for a particular type of figure. This also has a publication delay compared to PubMed and fewer search parameters.