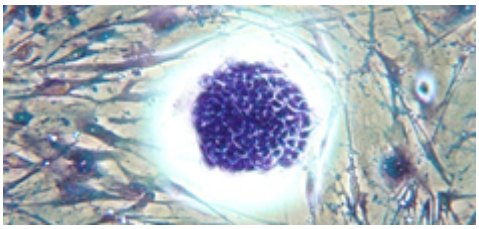

SCRB 167: Stem Cells and Regeneration in the Pathobiology and Treatment of Disease
Spring 2018

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: https://canvas.harvard.edu/courses/39827

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Course location: Tosteson Medical Education Center (TMEC), Room 209 (**TMEC 209**) on the Harvard Medical School campus 260 Longwood Avenue, Boston, MA 02115 (for 9 classes) or **Armenise 125** (for 4 classes, including the first 2). Course locations for each week are listed below.

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 a 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 immediately following class (see below under "Discussion Section").

Discussion Section: Tuesday 4:15 to 5:15 p.m.
Immediately following each lecture students will attend discussion section with their assigned Teaching Assistant (TA) in rooms 426, 443, and 445 in TMEC. 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. See more detail below.

Discussion Section "Cold Call": In order to reinforce the importance of the 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 objective, approach used, and conclusions for the chosen figure. This ensures that all students will have done the reading every week.

Visits from patients: One of the highlights of the course is opportunity for students to talk with patients and their family members or caregivers each week. We are very lucky that patients generously 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 years 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. While note taking is encouraged, please be respectful of the patients and **refrain from using your phones or computers during patient sessions**.

Patient privacy: On the first day of the course (January 23rd) 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, locations, and faculty presenters:

1/23	**Intro, patient privacy, iPS cells** (patient: sickle cell anemia), Len Zon, M.D. and David Breault, M.D., Ph.D. ***Armenise 125***
1/30	**Gut/Intestine** (patient: inflammatory bowel disease), David Breault, M.D., Ph.D. ***Armenise 125***
2/06	**Muscle development/disease** (patient: spinal muscular atrophy), Amy Wagers, Ph.D. ***TMEC 209***
2/13	**Diabetes** (patient: insulin dependent diabetes), Gordon Weir, M.D. ***TMEC 209***
2/20	**Bone Marrow Failure** (patient: Fanconi anemia), Len Zon, M.D. ***TMEC 209***
2/27	**Bone Marrow Transplantation** (patient: graft vs host disease), Jerry Ritz, M.D. ***Armenise 125***
2/27	**Midterm topic paragraph due**
3/06	**Lung Disease** (patient: Cystic Fibrosis), Carla Kim, Ph.D. ***Armenise 125***
3/09	**Midterm paper due**
3/13	***Spring Recess (no class)***
3/20	**Infertility/IVF** (patient: IVF/PGD), Catherine Racowsky, Ph.D. ***TMEC 209***
3/27	**Chronic Myeloid Leukemia** (patient: CML), George Daley, M.D., Ph.D. ***TMEC 209***
4/03	**Neurological disease/injury** (patient: spinal cord injury), Jeffrey Macklis, M.D., D. HST. ***TMEC 209***
4/10	**Heart Development and Repair** (patient: Barth syndrome), Bill Pu, M.D. ***TMEC 209***
4/17	**Mesenchyme**, (patient: bilateral knee replacement) Jenna Galloway, Ph.D. and April Craft, Ph.D. ***TMEC 209***
4/24	**Clinical translation,** George Daley, M.D., Ph.D. and Jerry Groopman, M.D. ***TMEC 209***
4/27	***Reading Period begins***
5/04	**Final paper due**

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, which will be discussed during Section on April 24. The course has a **limited number of copies** that can be borrowed for one week at a time so please plan accordingly (contact Elliott Hagedorn). 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 of 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; SCRB 10; MCB 52 or MCB 54
For advanced concentrator students only (seniors, qualified juniors, and the occasional sophomore).

Course grading: Students must register for a letter grade. **No P/F registration is allowed.**
Grades will be based upon:
- **Student presentations - 30% (15% x 2 presentations)**
- **Class participation - 10%**
- **Midterm paper (5 pages) - 20%**
- **Final paper (10 pages) - 40%**

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

• Each student will present two primary literature papers, which are categorized as either "research" or "translational." Students are responsible for putting the paper in context, providing specific and necessary background, identifying the main hypotheses tested, describing the important experiments and their conclusions, critiquing the study, and discussing the future directions and implications of the work. See more detail below.

• Class participation will be graded based on 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! Each week students must also submit two questions about the covered papers and identify the hypotheses of the two primary literature papers on Canvas. **Weekly submissions are due by 10PM on the night preceding class**.

• The culmination of the course will be a research proposal designed to test a novel hypothesis that the student designs in the field of stem cell biology. Each student will identify an unanswered or insufficiently probed question about the role of stem cells in human biology, disease or medicine, and develop a novel hypothesis that can be experimentally tested. In the **midterm,** students will develop the background that introduces this clearly defined hypothesis in 5 pages. In the **final,** students will build upon the midterm and propose experiments to test their hypothesis, discuss expected outcomes, alternative approaches, and implications in 10 pages. **A paragraph summarizing the topic and explicitly stating the hypothesis is due to TAs for feedback anytime before class on February 27th**. See more detail below.

• **The midterm paper is due Friday, March 9th, 2018 by 11:59 p.m. and the final paper is due Friday, May 4th, 2018 by 11:59 p.m. Papers must be original works, and not excerpted from a student's thesis or research papers from previous classes.** Students are strongly encouraged to begin working on their midterm and final papers well in advance of the due dates. This will allow adequate time to seek help, if needed – do not procrastinate!

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 one of the primary research papers from the class. This two-page paper can be organized as if the student were presenting the paper to the class. Please consult with your TA before writing the paper.

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 Dr. Zon by the end of the second week of the term which is **February 2, 2018**. 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) and Armenise building are part of the Harvard Medical School campus and are located at 260 Longwood Avenue and 210 Longwood Avenue, respectively, 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/Armenise on Longwood Avenue but each of the green-line trains will require 5-15 minutes of additional travel time.

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 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. The presenter should both ask thoughtful questions to engage their classmates and be 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 tends to be a great many patient-oriented groups/websites catering to specific conditions that may offer good images and information.

Research paper presentations:

The goal of this presentation is to familiarize you with the process of reading a basic science 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!

Both types of paper 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. Students are encouraged to dedicate time to critically evaluating the work – highlighting flaws in experimental design, limitations of the work or potential alternative interpretations. 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 and future directions. Students should challenge themselves to come up with their own ideas about what experiments should be done next in addition to stating those mentioned by the authors or in companion commentary pieces. 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 paper and be prepared to give a brief description of the background, experimental approach, and conclusions of any single figure.

Advice for Midterm and Final Papers…

These assignments let you demonstrate your understanding of the material presented in class and your ability to 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. Your TA 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. 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. 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. In addition, your paper should specifically indicate how stem cells play a role in the pathogenesis and/or clinical management of your chosen disorder or human biology. 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 or underlying biology.

An "A" midterm paper will achieve the following:

- Identify an unanswered or insufficiently probed **question** about the role of stem cells in development, homeostasis, disease, or medicine
- Provide a clearly-stated, novel testable **hypothesis** that addresses this question
- 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 or holes

Of note, although detailed experiments should not be proposed in the midterm, it will be important that students are already considering what the basic framework of their experimental approaches will be (e.g. whether a specific model organism might be used or what general experimental techniques might be employed).

In the **final paper** most students will expand on the hypothesis developed in the midterm. You will receive feedback on the proposed hypothesis, which should help guide preparation of the final paper. You may change topics between your midterm and final, but your TA must approve the new topic of your 10 page final paper. Please do so ***well in advance*** of the final paper deadline. Revised text from your midterm can be incorporated into your final paper as background and introduction. The final paper will build upon the midterm in the form of a grant proposal. The proposal will expand upon the hypothesis of the midterm, outline detailed experiments to test the hypothesis, discuss expected outcomes, alternative approaches, and implications. The best papers have a novel and testable hypothesis, offer creative and innovative insights and approaches, and generate a readable synthesis of key points and concepts. The proposal should be organized with a logical progression, clearly presenting a concise argument, and free of grammatical errors.

An "A" final paper will additionally achieve the following:

- Incorporate feedback from the midterm and improve on all that was expected of the midterm
- Propose a feasible **experimental outline** to determine whether the hypothesis is valid

The following is an example of a good structure for a final paper, with subheadings included for each section:

- Introduction/Background: comprised of mostly revised text from the midterm, unless you choose a new topic
- Specific Aims: a typical NIH grant proposal will include 2-3 Specific Aims. For the final paper you might have two *independent* aims, at most, each of which might include the following subsections:
  - Rationale: presents the justification and logic for the proposed experiments

        - Methodology/Approach: describes in detail the experiments that will be performed to test the hypothesis. Here you might have sub-aims to help organize your experiments, perhaps two sub-aims for each main Specific Aim.
        - Expected results: discusses anticipated experimental outcomes
        - Potential pitfalls and alternative approaches: evaluates limitations of the proposed experiments and discusses what additional experiments could be done in the event of a failed experiment or unexpected experimental outcome
        - Implications: frames the potential findings of the work within the context of the current field
    - Include a summary at the end that restates the central thesis and proposed experimental approach

Important for both midterm and final:

- Provide a relevant and current bibliography including additional works not presented/assigned during class
- It is critical to thoroughly edit for readability and to present a coherent argument

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

- 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 and frequent typos

Papers are to be in 12 point Times New Roman font, double-spaced, with margins that are not smaller than 1 inch on any side. Please be mindful of the page limitations: 5 page midterm and 10 page final (including any figures).

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 experiments to test 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.

Students are encouraged to seek help from the Harvard College Writing Center (https://writingcenter.fas.harvard.edu). This can be particularly important for non-native English speakers or for students that have limited experience with scientific writing. Additionally, students may seek help from the Harvard College Bureau of Study Counsel (https://bsc.harvard.edu/).