BioE 361/MatSci 381: Biomaterials in Regenerative Medicine
Winter 2009-2010
T/Th 11:00 – 12:15; Clark Center S361

Instructors: Prof. Sarah Heilshorn  
heilshorn@stanford.edu  
Office hours: Tuesdays 2-3 pm*  
McCullough 246
Prof. Jennifer Cochran  
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Office hours: Fridays 1-2 pm*  
Clark W250A

*Instructors are available for additional office hours by appointment.

TAs: Widya Mulyasasmita and Andreina Parisi-Amon (BIOE361@gmail.com)
Office hours: Monday and Wednesday 4-5 pm, McCullough 211

Grading: 15% In-class discussion and problem solving  
(6 total, 1 absence allowed, 3% per assignment, graded pass/fail)  
50% Problem sets (6 total)  
5% Final project: Midterm update (due Thurs, Feb 4; graded pass/fail)  
30% Final project: Independent research proposal (due Fri, March 12)

Course Goals:
At the end of this course, students are expected to be able to:
• Describe the differences and similarities of various stem and progenitor cell populations.
• Quantitatively analyze the critical materials properties that can influence cell behavior.
• Select the appropriate, quantitative experimental protocols for a specific biomaterials study and describe the advantages and limitations of these protocols.
• Select the appropriate materials for a specific regenerative medicine study and describe the advantages and limitations of these materials.
• Converse at an advanced level about the current key topics of investigation in the field of biomaterials for regenerative medicine.

Pre-Requisites:
This course is designed for graduate students and upper-level undergraduate students. All enrolled students are expected to have a background in undergraduate-level engineering calculus, Newtonian physics, general chemistry, and biology or biochemistry. Undergraduate students are strongly encouraged to complete ENGR 50 or ENGR 50M and BIO 41 or 42 before enrolling in this course.

Course Format:
Four types of activities will be used to achieve the course goals: interactive class lectures on selected topics by experts in the field (14 lectures), reading and quantitative analysis of data from peer-reviewed research manuscripts (6 problem sets), in-class discussions and problem-solving sessions (6 discussions), and a final project written in the style of an independent research proposal.
Supplemental Course Activities:
Due to the interdisciplinary nature of the course material and the diversity of the students enrolled, this course will require substantial independent reading by each student. In addition to the required reading assignments that are peer-reviewed research manuscripts and review articles, supplemental reading from undergraduate-level textbooks will be suggested for each topic. While the supplemental readings are not required, all students are expected to understand the background information provided in these selected texts and should choose to complete these assignments as appropriate given their background knowledge. For example, a Materials Science and Engineering student may elect to complete the supplemental reading on the cell cycle, while a Bioengineering student may elect to complete the supplemental reading on material elasticity.

The course includes seven guest lectures by experts in the field of biomaterials and/or regenerative medicine. Depending on the availability of guest speakers, students are invited to sign up to attend lunch with the speakers. Sign up sheets will be available in class one week before each scheduled guest lecture on a first-come, first-served basis.

Textbooks for Supplemental Reading (on reserve at Terman Library):

Homework Policy:
Students are welcome to work in groups to complete the homework sets; however, each student must turn in an individual set of answers. Homework is due on the date stated on the syllabus at the beginning of class. There is a 10% penalty per day for late homework. No extensions for late homework will be given, and assignments more than 7 days late will not be accepted. For all homework grading questions, see the course TAs first.

Coursework:
Course information including homework assignments, homework solutions, links to required and supplemental reading, and course schedule and syllabus will be available online at the Stanford Coursework website.

To access manuscripts using Stanford site licenses, you must access the website through a Stanford IP address or set up a proxy server on your computer.
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<th>Date</th>
<th>Lecture</th>
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<tr>
<td>Jan 5 T</td>
<td>Course Introduction: overview of tissue engineering/regenerative medicine – historical and future perspectives</td>
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<td>Jan 19 T</td>
<td>Discussion 2: Mechanotransduction and Differentiation</td>
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<td>Problem Set 3 due: TBA</td>
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<td>Jan 21 Th</td>
<td>Sanjay Kumar, UC Berkeley: Cell Mechanics</td>
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<td>Jan 26 T</td>
<td>Helen Blau, Stanford: Stem Cell Niches</td>
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<td>Jan 28 Th</td>
<td>Discussion 3: Cell-Binding Ligands</td>
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<td>Feb 2 T</td>
<td>Jennifer Cochran: Natural Materials</td>
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<td>Feb 4 T</td>
<td>Sarah Heilshorn: Synthetic Materials</td>
<td>Final Proposal Midterm Update due</td>
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<td>Feb 9 T</td>
<td>Discussion 4: Material-Directed Differentiation</td>
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<td>Problem Set 4 due: TBA</td>
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<td>Feb 11 Th</td>
<td>Jennifer Cochran: Growth Factor Engineering and Delivery</td>
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<td>Feb 16 T</td>
<td>Seung-Wuk Lee, UC Berkeley: Nanoscale Biomaterials</td>
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<td>Feb 18 Th</td>
<td>Discussion 5: Drug Delivery</td>
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<td>Problem Set 5 due: TBA</td>
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<td>Feb 23 T</td>
<td>Karen Christman, UC San Diego: Discovery to Clinical Therapy</td>
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<td>Feb 25 Th</td>
<td>Discussion 6: Scaffold Remodeling and Adaptive Biomaterials</td>
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<td>Problem Set 6 due: TBA</td>
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<td>Mar 2 T</td>
<td>Fan Yang, Stanford: High-Throughput Biomaterials Analysis</td>
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<td>Mar 4 Th</td>
<td>Sarah Heilshorn: Engineered Peptides and Proteins</td>
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<td>Mar 9 T</td>
<td>Jennifer Cochran: Extracellular Matrix Mimics</td>
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<td>Mar 11 Th</td>
<td>Sarah Heilshorn: Inorganic Materials</td>
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<td>Mar 12 Fri</td>
<td>Final Papers Due by 10:00 pm</td>
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BIOE361/MATSCI 381 Final Project: Independent Research Proposal

The format for the final project will follow that of a standard (but shortened) NIH fellowship application for a research project that can be completed by one person in three years.

You are encouraged to speak to and share ideas among your classmates, TAs, and the course instructors. However, you must not propose something from your own lab’s research, research that has already been published, or ideas that you find on someone else’s lab website.

Each student must choose one of the selected medical topics and one of the selected biomaterials topics from the pre-approved list below for their independent research proposal.

**Medical Topics:** Cardiovascular Regeneration, Neural Regeneration, Cartilage Regeneration, Liver Regeneration, Cornea Regeneration, Wound Healing

**Biomaterials Topics:** Mechanotransduction, Cell Receptor-Ligand Interactions, Development of New Biomaterials, Design of Artificial Stem Cell Niches, Drug Delivery

**Note:** Students can propose alternative topics to those listed before January 28. Students performing research in the field of biomaterials and/or regenerative medicine are expected to choose topics that are not the same as their research projects.

**Midterm Update:** Due Thursday, February 4, in class.

One page maximum description of chosen medical topic and chosen biomaterials topic. Include a discussion of possible research ideas with a minimum of six (6) references (not included in the page limit). State your hypothesis concisely; one or two sentences should suffice. The midterm updates will be graded pass/fail only. No late updates will be accepted.

**Research Proposal:** Due Friday, March 12, 10:00 pm.

Submit by email as a single PDF file to: BIOE361@gmail.com.

**Tips:**
To convince a reviewer that your proposal is worth funding, you need to write clearly and concisely, with logical and well-organized paragraphs. Strive to make the title and specific aims precise with verbs like: “identify, elucidate, determine, measure, quantify”. Avoid vague language like: “characterize, study, investigate”. Do not assume that your reviewers have an in-depth knowledge of the research area. Your overarching goal is to convince the reviewer that this topic is interesting and important and that you have the right experimental system and expertise to successfully complete the research. Use figures (schematics, flow charts, sample data, etc) to explain difficult concepts.
GUIDELINES FOR THE FINAL RESEARCH PROPOSAL:

Format:
4 to 6 pages including figures, single spaced, 1” margins, 12 point Arial font. References do not count towards the page limits.
(FYI: a real NIH fellowship application is 10 pages, single spaced, including figures)

A. Project Title: (not to exceed 60 characters).

B. Specific Aims: (0.5-1 page maximum)
This section should serve as an outline for your experimental design and include 2-3 aims that your proposal will address.
   a) Clearly state the problem/questions being investigated
   b) Specify the hypotheses being tested and/or technology being developed
   c) Concisely describe the key experiments

C. Background (1-2 pages maximum)
Critically evaluate existing knowledge in the field and identify gaps and unanswered questions that your proposal intends to fill. This section is not meant to be a complete review of the field, but an overview of the information directly related to the proposed research.

D. Experimental Design
This section is the bulk of the proposal upon which a lot of emphasis and thought should be placed. The experiments should be focused and well thought-out.

Describe the experimental design and methods to be used to accomplish the specific aims of the proposal. Follow the order and organization of the specific aims in section B. Put most of your emphasis on outlining the logic of the proposed experiments rather than the nitty-gritty details. State which specific aim or hypothesis is being tested with each experiment. If possible, discuss possible outcomes and interpretations and include any necessary experimental controls. It is important to include potential pitfalls and obstacles that may be encountered and how you will address them. Sometimes it is valuable to propose several alternative approaches for attacking one specific question rather than addressing multiple questions superficially.

It is beneficial to include a time-line of when the experiments will be performed in relation to the three-year proposal, and how long the proposed experiments will take.

E. Significance (0.5-1 page maximum)
Why are these experiments important and why should they be funded? Why is the system you have proposed the best? Assume that the reviewer does not know or care about the subject as much as you do and try to convince them that you have a winning proposal.

F. Literature Cited: No more than 35 references should be used. References do not count in the page limit. Include all author names, article title, journal title, year, volume, and page numbers.
Criteria for grading:
1) Specific aims: Are the goals of the research project clearly stated? Note: The goal of the project can be to test a specific hypothesis and/or to develop a new technology.

2) Background: What is currently known about this particular topic? What other approaches have been used to study these questions? What is still not well understood?

Experimental design:
3) Experimental controls: Are the proposed experiments appropriate and well defined? Have any necessary positive and negative controls been included?

4) Feasibility: Is the proposal too ambitious- do you propose to do too many experiments or experiments that are impractical? Are you not ambitious enough- proposing trivial extensions of things that have already been done? Have you identified potential problems and alternative approaches that could be taken?

5) Experimental interpretation: What results do you expect to obtain from your experiments? Are these results quantitative? What types of statistical analyses do you expect to perform on your data? How will you interpret these results as supporting or rejecting your hypotheses?

6) Significance: Have you demonstrated that your proposed research will address an important clinical problem or basic science need? How will your specific results potentially affect future research directions, scientific understanding, or clinical protocols?

Grading breakdown:

- 20% Specific Aims
- 25% Background
- 10% Experimental Design
- 15% Experimental Controls
- 15% Feasibility
- 15% Experimental Interpretation
- 15% Significance
- 100% Total