

Fall 2017—Wednesday

PhD and MS Sessions: 3:00-5:00pm

Location: Broad CIRM Center 4th Floor Conference Room

Instructor: Denis Evseenko MD., PHD

Office: NRT 4503

Office Hours: Monday, 10:30-12:30PM

Contact Info: evseenko@usc.edu

Course Description

Often referred to as the next evolution of modern health care, regenerative medicine touches many disciplines - from clinical care and engineering to basic science. The topic for Fall 2017 will be "Essentials of Regenerative Medicine". This course provides students a foundation in this exciting field. The primary objective of the course is to provide a state-of-the-art review of various aspects of regenerative medicine including background material, the key scientific components of the field of regenerative medicine, stem cell research and other issues important to regenerative medicine. Seminars address the science behind regenerative medicine and its application to human disease. This journal club style course consists of an introductory lecture by the instructor, followed by the presentation of the primary literature by students in the form of PowerPoint presentations that include dynamic and detailed discussion by participants. The structure of the class will provide background to identify key gaps in knowledge, papers which have advanced the field and subsequent studies determining reproducibility of findings.

Guide for presentation (50 minutes)

1. Background 10 min
2. Present paper 20 min
3. Follow up work 10 min
4. Q&A 10 min throughout

Learning Objectives

The primary purpose of this course is to give students an in-depth view into the scientific process that developed a cutting-edge field of regenerative medicine. Specific objectives will include, but will be not limited to:

- To provide participants relevant biological, engineering and medical foundation and principles to understand the emerging field of regenerative medicine
- To become acquainted with topics from the broad spectrum that makes up regenerative medicine
- To learn about the technology and technique available for regenerative medicine research
- To springboard off this foundation into current, cutting-edge research

Students will learn how to identify important unsolved problems, to devise novel experimental methodology to make breakthroughs, and to critically evaluate interpretation of findings. A parallel learning objective is for students to improve their presentation skills by presenting and synthesizing the results of manuscripts within a small group setting.

Prerequisite(s): Principles of Developmental and Stem Cell Biology (DSR542)

Co-Requisite/Concurrent Enrollment: none

Recommended Preparation: none

Course Notes

None.

Technological Proficiency and Hardware/Software Required

None.

Required Readings and Supplementary Materials

Manuscripts for discussion each week are available on Blackboard as PDFs to all students.

Description and Assessment of Assignments

Students will present a primary manuscript to the class. Grading will be assessed based on clarity and succinctness of presentation, demonstration of abundant background reading, insightful introduction of and extension of the context to the paper, and ability to maintain a lively discussion. Students are also expected to read the primary manuscript each week and actively participate in discussions. At the end of the course, a written "Mini-Review" on a current manuscript (or pair of related manuscripts) will be required. This Mini-Review will be 2 pages maximum, not including references, and will include one small model figure. Format requirements are Arial 11 pt, 0.5" margins.

Grading Breakdown

How will students be graded overall, including the assignments detailed above. Participation should be no more than 15%, unless justified for a higher amount. All must total 100%.

Assignment	Points	% of Grade
Presentation	10	45
Written Mini-Review	10	40
Participation	15	15
TOTAL	35	100

Assignment Submission Policy

Presentations will be assigned at the beginning of the course. The written 3pg Mini-Review (journal preview style) is due at the last class and must be submitted as a PDF file to the instructor(s).

Additional Policies

Attendance and reading of the assigned manuscript prior to each class is mandatory. Students are chosen at random to lead the Q&A discussion.

	Topic	Instructor	Student
August 23 th	Introduction to the course.	Dr. Evseenko	
August 30 st	Stem cells and stem cell niche. Tissue regeneration and turnover.	Dr. Evseenko	TBD
September 6 th	Regenerative response in lower vertebrates.	Dr. Evseenko	TBD
September 13 th	Why some tissues do and other do not regenerate in mammals?	Dr. Evseenko	TBD
September 20 st	Regeneration and inflammation.	Dr. Evseenko	TBD
September 27 th	Regeneration and fibrosis.	Dr. Evseenko	TBD
October 4 th	Regeneration and cancer.	Dr. Evseenko	TBD
October 11 th	Regenerative response and aging.	Dr. Evseenko	TBD
October 18 th	Rejuvenation of the whole organism: myth or reality?	Dr. Evseenko	TBD
October 25 th	Organ and tissue transplantation and replacement.	Dr. Evseenko	TBD
November 1 nd	Biomaterials and scaffolds: guiding cells to build complex structures.	Dr. Evseenko	TBD
November 8 th	Ex vivo tissue engineering: can we really grow tissues for transplantation in the dish?	Dr. Evseenko	TBD
November 15 th	Activation of endogenous stem/progenitor cells.	Dr. Evseenko	TBD
November 22 rd	Thanksgiving break.	N/A	
November 29 th	Gene therapy.	Dr. Evseenko	TBD
December 6 th	Mini-review Final Exam Due.	Dr. Evseenko	TBD

ASSIGNED PAPERS:

1. **August 23. Introduction by Dr Evseenko. No paper.**
2. **August 30. Topic: Stem cells and stem cell niche. Tissue regeneration and turnover.**
Primary paper. Mesenchymal and haematopoietic stem cells form a unique bone marrow niche. Méndez-Ferrer et al. Nature 2010, 466(7308): 829–834. doi: 10.1038/nature09262.
Additional reading. The bone marrow niche for haematopoietic stem cells. Morrison SJ, Scadden DT. Nature. 2014 Jan 16;505(7483):327-34. doi: 10.1038/nature12984.
3. **September 6. Regenerative response in lower vertebrates.**
Primary paper. Mokalled MH et al. Injury-induced ctgfa directs glial bridging and spinal cord regeneration in zebrafish. Science. 2016 Nov 4;354(6312):630-634.
Additional reading. Godwin J et al. Macrophages are required for adult salamander limb regeneration. Proc Natl Acad Sci U S A. 2013 Jun 4;110(23):9415-20.

4. **September 13: Why some tissues do and other do not regenerate in mammals?**
Primary paper. Patterson M et al. Frequency of mononuclear diploid cardiomyocytes underlies natural variation in heart regeneration. *Nat Genet.* 2017 Aug 7. doi: 10.1038/ng.3929. [Epub ahead of print].
Additional reading. Kumar S et al. Sox9 Activation Highlights a Cellular Pathway of Renal Repair in the Acutely Injured Mammalian Kidney. *Cell Rep.* 2015 Aug 25;12(8):1325-38. doi: 10.1016/j.celrep.2015.07.034. Epub 2015 Aug 13.
Additional reading. Ausoni S, Sartore S. J Cell Biol. 2009 Feb 9;184(3):357-64. doi: 10.1083/jcb.200810094. From fish to amphibians to mammals: in search of novel strategies to optimize cardiac regeneration.

5. **September 20. Regeneration and inflammation.**
Primary paper. Taniguchi K et al. A gp130-Src-YAP module links inflammation to epithelial regeneration. *Nature.* 2015 Mar 5;519(7541):57-62. doi: 10.1038/nature14228.

6. **September 27. Regeneration and fibrosis.**
Primary paper. Kramann R et al. Perivascular Gli1+ progenitors are key contributors to injury-induced organ fibrosis. *Cell Stem Cell.* 2015 Jan 8;16(1):51-66. doi: 10.1016/j.stem.2014.11.004. Epub 2014 Nov 20.
Additional reading. Ding DC. Divergent angiocrine signals from vascular niche balance liver regeneration and fibrosis. *Nature.* 2014 Jan 2;505(7481):97-102. doi: 10.1038/nature12681. Epub 2013 Nov 20.

7. **October 4. Regeneration and cancer.**
Primary paper. Leuschke M. Lgr5-expressing chief cells drive epithelial regeneration and cancer in the oxyntic stomach. *Nat Cell Biol.* 2017 Jul;19(7):774-786. doi: 10.1038/ncb3541. Epub 2017 Jun 5.
Additional reading. Peter Friedl & Darren Gilmour. Collective cell migration in morphogenesis, regeneration and cancer. *Nature Reviews Molecular Cell Biology* **10**, 445-457 (July 2009) | doi:10.1038/nrm2720

8. **October 11. Regenerative response and aging.**
Primary paper. Brack et al. Increased Wnt signaling during aging alters muscle stem cell fate and increases fibrosis. *Science.* 2007 Aug 10;317(5839):807-10.
Additional reading. Blau H et al. The central role of muscle stem cells in regenerative failure with aging. *Nat Med.* 2015 Aug;21(8):854-62.

9. **October 18. Rejuvenation of the whole organism: myth or reality?**
Primary paper. Ocampo et al. In Vivo Amelioration of Age-Associated Hallmarks by Partial Reprogramming. *Cell.* 2016 Dec 15;167(7):1719-1733.e12. doi: 10.1016/j.cell.2016.11.052.

10. **October 25. Organ and tissue transplantation and replacement.**
Primary paper. Bernhardt WM et al. Donor treatment with a PHD-inhibitor activating HIFs prevents graft injury and prolongs survival in an allogeneic kidney transplant model. *Proc Natl Acad Sci U S A.* 2009 Dec 15;106(50):21276-81. doi: 10.1073/pnas.0903978106.

11. **November 1. Biomaterials and scaffolds: guiding cells to build complex structures.**
Primary paper. Jakus A et al. Hyperelastic "bone": A highly versatile, growth factor-free, osteoregenerative, scalable, and surgically friendly biomaterial. *Science Translational Medicine*, 2016; 8 (358): 358ra127 DOI: 10.1126/scitranslmed.aaf7704.
Additional reading. 3D bioprinting of tissues and organs. Sean V Murphy & Anthony Atala *Nature Biotechnology* 32, 773–785 (2014) doi:10.1038/nbt.2958.

12. **November 8. Ex vivo tissue engineering: can we really grow tissues for transplantation in the dish?**

Primary paper. Atala et al. Tissue-engineered autologous bladders for patients needing cystoplasty. Lancet. 2006 Apr 15;367(9518):1241-6.

13. **November 15. Activation of endogenous stem/progenitor cells.**

Primary paper. Flores et al. Lactate dehydrogenase activity drives hair follicle stem cell activation. Nature Cell Biology. 2017 Epub ahead of print August 14.

14. **November 22. Thanksgiving break.**

15. **November 29. Gene therapy for tissue regeneration.**

Primary paper. Bez M et al. In situ bone tissue engineering via ultrasound-mediated gene delivery to endogenous progenitor cells in mini-pigs. Sci Transl Med. 2017 May 17;9(390). pii: eaal3128. doi: 10.1126/scitranslmed.aal3128.

16. **December 6th. Final Exam**

Instructions for paper presentation

At each meeting a primary paper from the list will be presented and discussed. The primary paper should be introduced and contextualized using seminal papers in the field in a few slides. Presenters should address all figures and supplementary data from the primary paper with critical review and promote class discussion. Afterward, discussion on reproducibility (if appropriate) and field advances will be shown in a few slides. PhD students will present individually and MS students will present in small groups. For the final exam, PhD students will write a mini-review on the topic they present.

Statement on Academic Conduct and Support Systems

Academic Conduct

Plagiarism – presenting someone else’s ideas as your own, either verbatim or recast in your own words – is a serious academic offense with serious consequences. Please familiarize yourself with the discussion of plagiarism in *SCampus* in Section 11, *Behavior Violating University Standards* <https://scampus.usc.edu/1100-behavior-violating-university-standards-and-appropriate-sanctions/>. Other forms of academic dishonesty are equally unacceptable. See additional information in *SCampus* and university policies on scientific misconduct, <http://policy.usc.edu/scientific-misconduct/>.

Discrimination, sexual assault, and harassment are not tolerated by the university. You are encouraged to report any incidents to the *Office of Equity and Diversity* <http://equity.usc.edu/> or to the *Department of Public Safety* <http://capsnet.usc.edu/department/department-public-safety/online-forms/contact-us>. This is important for the safety whole USC community. Another member of the university community – such as a friend, classmate, advisor, or faculty member – can help initiate the report, or can initiate the report on behalf of another person. *The Center for Women and Men* <http://www.usc.edu/student-affairs/cwm/> provides 24/7 confidential support, and the sexual assault resource center webpage sarc@usc.edu describes reporting options and other resources.

Support Systems

A number of USC’s schools provide support for students who need help with scholarly writing. Check with your advisor or program staff to find out more. Students whose primary language is not English should check with the *American Language Institute* <http://dornsife.usc.edu/ali>, which sponsors courses and workshops specifically for international graduate students. *The Office of Disability Services and Programs* http://sait.usc.edu/academicsupport/centerprograms/dsp/home_index.html provides certification for students with disabilities and helps arrange the relevant accommodations. If an officially declared emergency makes travel to campus infeasible, *USC Emergency Information* <http://emergency.usc.edu/> will provide safety and other updates, including ways in which instruction will be continued by means of blackboard, teleconferencing, and other technology.