BIOLUN3193_001_2023_1 - STEM CELL BIOL & APPLICATIONS

Edit

Stem Cell Biology and Applications BIOL UN3193 and GR5193 Dr. D. Kalderon

Course Rationale

The course is designed to be of interest and value to Biology-related majors at Columbia (CC and GS) and Barnard, to undergraduate pre-medical students who are not pursuing a science major and to students in the Masters of Biotechnology program. All of these students should have sufficient background in Biology (three or more semesters), with College students likely to take the course in Junior or Senior years.

If you are an undergraduate you should register for UN3193. If you are a graduate student you should register for GR5193.

Curriculum:-

Three Credits.

Meets twice a week -75 min per class (T, R 4.10-5.25) plus a voluntary recitation or equivalent some weeks (mainly to prepare for presentations).

Location: 601B Fairchild (small room next to 601, access from corridor, not through 601)

Instructor: Dr. Daniel Kalderon ddk1@columbia.edu, 212-854-6469 Office hours by e-mail appointment.

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Summary

Dramatic advances in stem cell science have opened up a new landscape of potential future therapies. This course aims to teach fundamental principles, approaches and findings in stem cell biology, emphasizing the process of scientific discovery, the limits of current knowledge and key questions that remain to be explored. The central thread of pure science will provide the basis to explore potential medical applications. The two central themes will be (1) pluripotent stem cells and (2) adult stem cells.

Pluripotent stem cells (principally embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs)) can be amplified indefinitely and converted into any other cell type. Furthermore, iPSCs can be derived from more or less any cell (and hence personalized)

and they can be genetically modified in targeted ways. Those discoveries also inspired the realization that multiple cell types can be inter-converted directly without an iPS cell intermediate. These findings provide tremendous opportunities to learn more about developmental biology, to study disease processes, to search for ameliorating drugs and to produce cells that may beneficially be introduced into humans. The derivation, properties and potential uses of pluripotent stem cells will be discussed in the first half of this course.

Adult stem cells have the essential physiological function of maintaining tissues; they also may commonly be the cells that initially accumulate mutations that lead to cancer. Understanding how different adult stem cells function is therefore important in order to understand normal physiology, to contemplate using adult stem cells in cell therapies and potentially to find new ways to counter some cancers. Different adult stem cells, including the archetypal examples of mammalian hematopoietic stem cells and intestinal stem cells, will be explored in the second half of this course.

Course Goals

The learning goals are to

(i) become familiar with the fundamentals of stem cell biology and appreciate the current status and challenges,

(ii) understand how research progresses,

(iii) develop strong written and oral communication skills that emphasize reasoned argument and critical appraisal of evidence.

The plan is to achieve these goals through the content of lectures and classroom discussion, supplemented by reading selected primary research papers in detail, written homework assignments and classroom presentations.

Syllabus

This syllabus provides an overview of the course schedule (always subject to change if some topics demand more time than anticipated). The third column highlights written Assignments (graded or “fixed”, meaning completion earns full marks) that contribute to grades (date set- date due). Major issues within each Topic are listed below the schedule.

Documents linked below from 2021 will be replaced by 2023 documents over time.

	Tuesday		Thursday	Assignments
Week 1 1/17	Overview and T1 T1 Notes Actions T1&2 Slide pdf Actions T1&2 Slides Actions		T1. Mouse embryonic stem (es) cells	T1 references
Week 2 1/24	T2. Human embryonic stem (es) cells T2 Notes Actions		T3. Somatic Cell Nuclear Transfer (SCNT) T3 Notes Actions T3 Slides Actions T3 Slides.pdf Actions	Fixed Ass't 1 (1/24-1/31) T2 references T3 references
Week 3 1/31	T4. Mouse iPS cell derivation Research paper discussion		T4. Mouse iPS cell derivation Research paper discussion	Graded Ass't 1 (1/31-2/7) T4 references

	T4 Notes Actions		T4 Slides Actions T4 Slidespdf Actions	
Week 4 2/7	T5. Progress in iPS cell production. T5 Notes Actions T5 Slides Actions		T6. Differentiation of pluripotent stem cells T6 Notes Actions T6 Slides Actions	Prepare for presentations on 2/14 & 2/16
Week 5 2/14	Presentations Slides 1 Actions Slides 2. Actions Best IPSC generation methods Group B ref1 Actions ref2 Actions		Presentations slides3 Actions slides4 Actions . Zscan4 Actions Genetic integrity of hIPSCs reference HereLinks to an external site. ALS studies with iPSCs refs https://doi.org/10.1038/nn.4273Links to an external site.	Fixed Ass't 2 (2/14-2/21)

	ref3 Actions ref4 Actions Group C ref1 Actions http://dx.doi.org/10.5772/63202Links to an external site. Factor-free methods Reprogramming process		https://doi.org/10.1038/nn.3425Links to an external site.	
Week 6 2/21	T7. Potential iPSC applications in medicine & research T7 Notes Actions T7 Slides Actions	StemT7 Appl'n(2021).doc	T8. Direct conversion between cell types T8 Notes Actions T8 Slides Actions	Read paper to discuss 2/28
Week 7 2/28	Finishing Topic 7/8 plus research paper study exercise Extended pluripotent stem cells Actions		Best cell replacement strategy (organoids, matrices, differentiation methods for chosen tissues)	Prepare for Mid-term

	Slides Actions		03022023 Organoid class.pptx Actions Cardiac organoids paper.pdf Actions	
Week 8 3/7	Mid-term exam		Adult Stem Cells Introduction Intro Notes Actions Intro Slides Actions	
3/14 Spring Break				
Week 9 3/21	T10. Blood cell biology: hematopoietic stem cells (HSCs) T10R Notes Actions T10R Slides Actions		Discussion of HSC heterogeneity, including Dykstra Actions	Prepare for presentations 3/28

Week 10 3/28	HSC replication presentations Foudi Actions and Bernitz Actions		T10. HSC biology niches	Prepare for presentations/discussions next week
Week 11 4/4	T10. More HSC biology native hematopoiesis		Native hematopoiesis papers (presentations & discussions)	Graded Ass't 2 (due 4/13)
Week 12 4/11	T10. HSC biology niches		T12. Intestinal stem cell biology Lgr5 paper T12 Notes Actions T12 Slides Actions	Fixed Ass't 3 (due 4/20)
Week 13 4/18	T12. Intestinal stem cell biology Population Asymmetry paper Actions		T12. Intestinal stem cell biology More than one stem cell?	Plan Final paper: pick a topic & develop an outline by 5/1
Week 14 4/25	New stem cell possibilities. Resolution of all findings for intestinal stem cells.		Discussion of outstanding adult stem cell issues	

Week 15 5/2	Work on final paper EWFinal Actions Thy1Paper Actions Thy1Supp Actions Greco Actions Review Actions		Work on final paper	Meetings to discuss final paper
Week 16 5/9	Exam Week		Final paper Due	

Topic 1

Major concepts in developmental biology

Tissue culture

Capturing a pluripotent state in tissue culture- Embryonic Stem (ES) cells

Uses of mouse ESCs

Topic 2

Human ES cells

Potential uses of human ES cells

Topic 3

Reversing development- Somatic Cell Nuclear Transfer (SCNT)

SCNT in humans

Potential uses of animal and human SCNT

Imprinted genes

Topic 4

Mouse iPSC derivation

Detailed study of a landmark research paper (class discussion)

Topic 5

Improvements on mouse iPSC derivation

Human iPSCs

Naïve and primed pluripotent states

Topic 6

Differentiation of pluripotent stem cells in vitro

Integrating differentiated cells into tissues

Presentations

1 & 2. Reprogramming methods suitable for iPSC clinical and other applications

3 & 4. Quality control (genetic & epigenetic) and alternatives to self-iPSCs

Topic 7

Potential applications of iPSCs in medicine and research

Progress towards selected applications

Topic 8

Direct reprogramming of one cell type to another

Comparisons (in vitro, in vivo and via iPSCs)

Topic 9

Current ESC/iPSC applications

Presentations:

5 & 6. Chosen from Diabetes (islet cell replacement), heart muscle, organoid applications, progress towards synthetic tissues.

Adult Stem Cell Introduction

Key concepts and case study regarding definition of stem cells

Topic 10

Hematopoietic Stem Cells (HSCs)

Inferences from transplantation

Re-evaluating strict lineage hierarchy & uniformity of HSCs

HSC niches

Presentations 7 &8: HSC papers about heterogeneity and replicative lifespan

Topic 11 (incorporated briefly into Topic 10)

HSC applications in medicine

Topic 12

Intestinal Stem Cells

Discovery paper- Lgr5 marker (class discussion)

Population Asymmetry paper (class discussion)

More than one type of stem cell (discussion of group of papers)

Last Class: Outstanding questions in adult stem cell biology

Final Assignment: In-depth analysis of one of a selection of topics, including a proposal for next steps.

Not included (insufficient time but notes available on request & possible topics for outstanding questions):

Topic 13

Stem Cell origin of (some) cancers

- gut

- blood

Topic 14

Cancer Stem Cells (propagating cancers)

Expectations for students (Grading)

There will be three graded written homework assignments (for 24% of the final grade), two homework assignments to hand in for fixed rewards (for 16% of final grade), one mid-term exam (20%), a final paper (20%, in place of a final exam), and evaluation of participation (20%), which includes contributions to class discussions and presentations. Students will generally have 7 days to complete each graded homework assignment.

Academic Integrity: Standard University policies. Details concerning plagiarism and collaboration will be spelled out carefully.

Specifically,

1. In written homework assignments each student's words must be their own. Any short quotations from published sources must be indicated as such and attributed (there should be no long quotations). Discussion among students will be encouraged but the final products submitted by each student should not have common sentences or, for longer sections of writing, near-identical flows of thoughts, arguments or explanations. Referencing the published source for specific prior scientific findings and conclusions should be done to the best of each student's ability. However, it is not expected (by a long way) that every statement will be justified in this way.
2. During in-class examinations that are closed-book it is expected that students will not try to confer with each other or any other source. This also applies to any situation where the timing of an examination is altered for a particular student.