



254B Fall 2020

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Pluripotent Stem Cells

Dates: November 9 – December 15, 2020

Time for Instructor-Students meetings: 10:00am – 12:00pm on Tuesdays & Fridays
<https://uclahs.zoom.us/j/94414848658?pwd=eXYzcfppUUc1ZksyT0ViTG80ZkpwZz09>

Time for Students-only meetings: 10:00pm – 12:00pm on Mondays & Thursdays
<https://uclahs.zoom.us/j/92456974313?pwd=NHRUVzFuQlJFSWIXUm5Fb0prcTZndz09>

Note: For the first Students Only meeting (Monday, Nov 9), April and Kathrin will join for the first 30min to go over our class setup and expectations

Course Topic

We will introduce a broad range of current topics in stem cell research with a focus on the biology of pluripotent stem cells, including embryonic stem cells (ESCs) which are derived from pre-implantation embryos and induced pluripotent stem cells (iPSCs) obtained from somatic cells by expression of transcription factors. Pluripotent stem cells have the remarkable ability to differentiate into all cell types of the body. This unique feature of pluripotent stem cells together with the ability to generate these from adult cell types from patients has ushered in an era of personalized medicine and disease in a dish modeling, which has the potential to change how diseases are treated in the future. Our papers will discuss molecular features of pluripotent stem cells and differentiation processes, go over reprogramming processes to induce pluripotency, cover the use of pluripotent stem cells in disease modeling, their genetic manipulation, and also raise current limitations and challenges with regard to pluripotent stem cell biology and therapeutic applications.

Dates (dates shown in **red** = students only)

November **9** & 10: Introduction to our course with Drs. Pyle and Plath, and paper 1

November **12** & 13: paper 2

November **16** & 17: paper 3

November **19** & 20: paper 4

November **23** & 24: paper 5

November **30** & December 1: paper 6

December 3 & 4: paper 7
December 7 & 8: paper 8 and Q&A
December 15: turn in final exam

Course Materials

All discussion papers are available on the CCLE course site.

Useful Links for Accessing Papers Yourself:

PubMed: <http://www.ncbi.nlm.nih.gov/pubmed>

UCLA library system for e-publications: <http://www.ncbi.nlm.nih.gov/sites/entrez?tool=cdl&holding=uclalib&otool=cdlotool>

If you are using an off-campus computer, you will need to set up a VPN. Information can be found here at the UCLA Library's [WI+RE tutorial site](#). Recent papers from Elsevier (Cell, Molecular Cell) must be ordered from the library well ahead of your need for them due to the dispute between UC and the publisher. Go to the following Link https://ucelinks.cdlib.org/sfx_local/cgi/core/citation-linker.cgi. The [UCLA Interlibrary Loan Service](#) may also be helpful. One can also use [Sci Hub](#) to get PDFs, please use your own discretion when using this site. If you cannot get access – please email April and Kathrin – we will help!

Course Description

The MBIDP wants all of our graduate students to develop scientific thinking skills while working toward their Ph.D. We believe these skills are integral for your success in any scientific career. The 254 series is designed to strengthen your scientific thinking skills through practice and with guidance from faculty.

What is scientific thinking? We likely all have different ideas about what 'scientific thinking' means. For our purpose, we will define scientific thinking as the thought processes that are used in scientific inquiries, including formulating hypotheses, designing controlled experiments, and interpreting data.

How can we develop scientific thinking skills? We use scientific thinking in our own research, but we also apply it when we examine other people's research. As such, scientific thinking can and should be practiced by every scientist when they read primary literature or listen to a seminar. Evidence indicates that courses where students and instructors discuss primary literature can effectively couple the development of critical thinking skills with the communication of scientific thought and rationale. In addition, journal clubs provide venues for acquiring foundational knowledge and engaging in collaborative problem solving, both of which are preparation for diverse scientific careers.

The 254 courses are *centered around particular scientific themes* in order to 1) provide a consistent, knowledge-based anchor point for each course, and 2) provide exposure to methods and concepts that build understanding beyond each student's area of focus.

Learning Outcomes for this 254 Course

Students will be able to

1. Identify and articulate the hypotheses being tested in primary research papers.
2. Develop and practice self-led discovery and curation of background info (literature searches).
3. Correlate the data and methods presented in a primary research paper with the authors' hypotheses and conclusions.
4. Evaluate the soundness of scientific arguments and conclusions presented in primary research papers.
5. Outline the logical flow of primary research papers and develop a generalized conception of logical scientific argumentation.
6. Correlate primary research findings with a larger body of work in the literature.
7. Understand experimental limitations.
8. Devise, plan, and propose 'next step' experiments that could follow on from primary research papers.
9. Increase level of comfort and skills in making presentations and discussing scientific concepts.

Course-specific Learning Outcomes:

1. Gain an appreciation for the classic and current research within field of pluripotent stem cell biology and early embryology.
2. Know key approaches in pluripotent stem cell field and utility in testing specific hypotheses.

Our Commitment to Inclusivity

We will work with you to create a learning environment that is inclusive and promotes learning. We expect you to generate a peer learning environment where everyone is included and all opinions and thoughts are welcome. The MBIDP is committed to making our community an inclusive environment where all scientists can succeed and achieve their goals. We encourage you to discuss with each other how your environment can be inclusive and to hold each other accountable for maintaining it. Concerns about inclusivity may also be discussed with us, with the 254 Overall Organizers: Dr. Kathrin Plath (kplath@mednet.ucla.edu) and/or Dr. Siobhan Braybrook (siobhanb@ucla.edu), or the MBIDP Director Dr. Hillary Collier (hcoller@ucla.edu).

UCLA's Office for Equity, Diversity, and Inclusion provides resources, events, and information about current initiatives at UCLA to support equality for all members of the UCLA community. We hope that you will communicate with us if you experience anything in this course that does not support an inclusive environment, and you can also report any incidents you may witness or experience on campus to the Office of Equity, Diversity, and Inclusion on [their website](#).

Course Structure

Student & Instructor Meetings: You are required to attend two meetings with us (instructors) per week (two hours each), for a total of five weeks. You will be expected to engage in discussions about the assigned research papers in these meetings. Rather than preparing to answer a set of questions for each paper that we will give you, students are expected to be ready to discuss the paper in its entirety.

All students are responsible for all aspects of the paper and topic, and all students should be prepared to answer any question that arises in the discussion with faculty. Students giving background information have the additional duty of presenting a short powerpoint on the background for the paper (see below).

For each paper, one (or a few students) should prepare the background information to be presented at the student/faculty meeting. The assignment will be done in the introductory session. The "background information" should be assembled in a PowerPoint presentation containing appropriate background slides for the paper to be discussed.

Background slides should:

- Define the major topic and question to be addressed in the paper
- Summarize relevant and important findings that led to these questions?
- Define approaches and terms that may not be known to everyone in the audience (assume that nobody is an expert in the field)

Student-only Meetings: You are also required to meet together twice a week; these group meetings can be deeply valuable in your learning, but they will be what you make them. Students are expected to read the papers, *including supplemental data*, and obtain appropriate background information to be able to adequately discuss the paper in the student/faculty sessions. One way to obtain background information is to read relevant review articles that can be found on Pubmed (see links above). Moreover, we can provide help in identifying useful background literature; please contact us if additional help/information is required. Also, remember that you are a team! Leverage each other's expertise and knowledge during your discussions.

In each student session, we expect you to work together to understand the background material, experimental approaches, results and conclusions for the paper discussion in the student/instructor session.

Please use the following questions as guides when reading, preparing, and discussing each paper – going over these questions will help you in the discussion with the instructors.

- What was the main question being addressed in the selected research paper?

- What were the relevant and important findings that led up to this paper?
- For each Figure/Section
 - What were the hypotheses being tested?
 - What experiments (and methods) were used to test the hypotheses? Were they appropriate?
 - Are there different approaches that you can think of?
 - What were the conclusions for each Figure/Section? Are they supported by the results presented?
 - What do you think of the statistics used?
- What were the overall conclusions from the paper and how do they address the initial question?
- What is a follow-up question that you have based on this paper?
 - What hypotheses would you propose to test?
 - How could you go about testing them?

First Student Meeting Description:

In your first student-only meeting of the course we will come for the first ~30min to discuss the course format and syllabus with you, including a discussion about utilizing the student-only sections fully. We will then discuss the utility of setting up group 'agreements' and work together to come up with your initial set. To facilitate this, we are providing a starting list of suggestions which we can use to get started; this list is based on workshops held by UCLA's Center for the Advancement of Teaching (CAT), our Center for Educational Innovation & Learning in the Life Sciences (CEILS) where they cite this work, and two labs within the MBIDP.

Group Agreements (to start from):

- To respect each other. The most basic human right. Separate the person from the actions.
- We are here to get it right, not to be right - there are 1000 different views and solutions!
- Make space, take space (or Step Up, Step Back) -
- To ask questions, and to find answers together
- Listen with as much care as you would want to be heard-
- Assume good intentions - give each other the benefit of the doubt
- Recognize and expand on other contributions -
- Speak from your experiences - intentionally avoid generalizations and speaking for others
- Try and show up as our best selves, and recognize that there is no final 'best'.
- Communicate, if and when we can, about our discomfort- call people in, not out.
- To hold ourselves accountable: when you know better, you do better.

After KP and AP leave, you will then launch into your first group discussion of the first paper, which you should have read before coming to this meeting.

Class attendance: Attendance for the full duration of all meetings is mandatory.

How to Succeed in this Course (Expectations we have of you)

What you put into this 254 is proportional to what you will gain. If you intentionally practice scientific thinking skills while you are reading the papers, discussing them in your student-only sessions, and in the instructor-student sessions you will succeed. We expect you to take ownership of your own learning and success, but also to practice care and help each other - this is a collaborative environment. Participation is key in this course. Identify points of interest and sticking points, both individually and as a group, and come to the Instructor led discussion ready to dig in. We expect that you will be resourceful in deciphering unfamiliar terminology and techniques, as individuals and as a group. We expect that you will work intentionally to help build an inclusive learning space for all.

How to Succeed in this Course (Expectations you can have of us)

Our primary goal is to facilitate the development and practice of scientific thinking. You can expect us to do this by guiding discussions, asking questions about your reasoning, and pushing you to engage fully with the material. Our secondary goal is to provide material that increases your background knowledge of the specific field/topic and methods used therein. You can expect us to guide your learning within the field, although the exposure will not be exhaustive, and provide expert critical information on experimental design as we work through the

material. You can also expect us to work to help build an inclusive discussion space, while acknowledging that all of us (even we) are learning.

How Your Learning Will Be Assessed (Grading Policy)

The distribution below delineates the letter-to-percentage ranges used in our class.

A:	90 - 100%
B:	80 - 89.9%
C:	70 - 79.9%
D:	60 - 69.9%
F:	0 - 59.9%

Grading Rubric

Participation in Discussion: 50%

Final Assignment: 35%

Presentation: 5%

Instructor Evaluated Improvement in Participation: 10%

Grading Breakdown

We will keep a record of your scored progress in the categories described below to aid in mid-course feedback and in understanding final grades, if requested.

Participating in Discussions: Participation will be evaluated based on the five aspects below. Each will be scored during each student/instructor meeting. These will be used for mid-course feedback to students.

1. Attendance. You must attend Student & Instructor and Student-only meetings consistently and arrive on time. Legitimate absences (e.g. physical illness, mental health, bereavement) can be made up by providing written answers to assigned questions (provided on CCLE or upon request). Please notify us or a fellow student (student-only meetings) if you are going to miss a meeting so discussions are not held in waiting. Please discuss with us if there is a reason why you will need to be consistently late (e.g. from the past includes cross-campus travel).

2. Communication. You should be able to succinctly and accurately describe experiments and explain figures. Practice, in your student-only sessions, identifying and articulating the hypotheses being tested, the methods used, the results shown, and your interpretation of the results.

3. Critical skills. You should be able to provide critical insight into the methodological soundness and significance of experiments, as they relate to the hypotheses being tested and the overall question being addressed. Develop and practice these skills together in your student-only sessions.

4. Synthesis and Forward Thinking. You should engage fully with the papers and provide insights into the experimental implications and unanswered questions that present to you, as an individual.

5. Inclusive Group Behavior. You should engage respectfully with each other in all meetings, according to your Group Agreements. This doesn't mean you can't disagree or challenge each other's thinking, but it does mean we all have to remember that everyone comes from a different place of experience and learning. We are together to get it right, not to be right.

Instructor Evaluated Improvement in Participation:

Following the mid-course feedback discussion with us, we expect you to work to improve your Participation in Discussion. This portion of your final grade will reflect our consensus evaluation of your honest attempts to improve on the constructive feedback you receive. Note that everyone has something they can improve on, even us!

Feedback

In the third week (mid-course), we will provide you with concrete feedback with respect to the Participation criteria above: what is going well and where you could lean in. Feedback will be delivered in an individual meeting with one of us, and you are expected to summarize afterwards and submit your action items for leaning in to us.

The Final

Exams are meant to show yourself and us what you've learned with respect to the course Learning Outcomes. As such, the final exam will be a written assignment based on a paper chosen from an instructor provided previously un-discussed paper. Each final will be evaluated independently by the two instructors and a consensus score will be given. We will provide you with written feedback on your finals, within 1 week of their receipt.

Written assignment details

The format will be a discussion of the paper. Be sure to use proper citations for literature. The report should be no more than 2 pages, 1.5 or 2 line spacing, 1 inch page margins, font Arial & size 11. It should cover the following:

Section 1: Paper Discussion (80 pts)

- (1) Summarize the relevant finding(s) that lead to the work (10 pts).
- (2) Summarize the main question(s) addressed in this paper (10 pts).
- (3) Describe the key hypotheses being tested and the key experiments and finding(s) supporting the major conclusion(s) of the paper (40 pts).
- (4) Describe any conclusions that do not agree with the data shown, if applicable. (10 pts).
- (5) Identify a follow-on Question that interests you based on your reading of the paper you chose. (10 pts).

The report should be submitted by email to the instructors by email on the last day of the class.

Course Content (dates shown in red = students only)

Week 1

November 9 & 10: Discussion of our course with Drs. Pyle and Plath (~ 30 min)

paper 1: Blastocyst-like structures generated solely from stem cells. Rivron NC, Frias-Aldeguer J, Vrij EJ, Boisset JC, Korving J, Vivié J, Truckenmüller RK, van Oudenaarden A, van Blitterswijk CA, Geijsen N. *Nature*. 2018 May;557(7703):106-111. doi: 10.1038/s41586-018-0051-0. PMID: 29720634

November 12 & 13: **paper 2:** Derivation of pluripotent epiblast stem cells from mammalian embryos. Brons IG, Smithers LE, Trotter MW, Rugg-Gunn P, Sun B, Chuva de Sousa Lopes SM, Howlett SK, Clarkson A, Ahrlund-Richter L, Pedersen RA, Vallier L. *Nature*. 2007 Jul 12;448(7150):191-5. doi: 10.1038/nature05950. PMID: 17597762

Week 2

November 16 & 17: **paper 3.** Genome editing reveals a role for OCT4 in human embryogenesis. Fogarty NME, McCarthy A, Snijders KE, Powell BE, Kubikova N, Blakeley P, Lea R, Elder K, Wamaita SE, Kim D, Maciulyte V, Kleinjung J, Kim JS, Wells D, Vallier L, Bertero A, Turner JMA, Niakan KK. *Nature*. 2017 Oct 5;550(7674):67-73. doi: 10.1038/nature24033. PMID: 28953884

November 19 & 20: **paper 4:** Systematic identification of culture conditions for induction and maintenance of naive human pluripotency. Theunissen TW, Powell BE, Wang H, Mitalipova M, Faddah DA, Reddy J, Fan ZP, Maetzel D, Ganz K, Shi L, Lungjangwa T, Imsoonthornruksa S,

Stelzer Y, Rangarajan S, D'Alessio A, Zhang J, Gao Q, Dawlaty MM, Young RA, Gray NS, Jaenisch R. *Cell Stem Cell*. 2014 Oct 2;15(4):471-487. doi: 10.1016/j.stem.2014.07.002. PMID: 25090446

Week 3

November 23 & 24: [paper 5](#): Charting cellular identity during human in vitro beta-cell differentiation. Veres A, Faust AL, Bushnell HL, Engquist EN, Kenty JH, Harb G, Poh YC, Sintov E, Gürtler M, Pagliuca FW, Peterson QP, Melton DA. *Nature*. 2019 May;569(7756):368-373. doi: 10.1038/s41586-019-1168-5. PMID: 31068696

Week 4

November 30 & December 1: [paper 6](#): Identification of SARS-CoV-2 Inhibitors using Lung and Colonic Organoids. Han Y, Duan X, Yang L, Nilsson-Payant BE, Wang P, Duan F, Tang X, Yaron TM, Zhang T, Uhl S, Bram Y, Richardson C, Zhu J, Zhao Z, Redmond D, Houghton S, Nguyen DT, Xu D, Wang X, Jessurun J, Borczuk A, Huang Y, Johnson JL, Liu Y, Xiang J, Wang H, Cantley LC, tenOever BR, Ho DD, Pan FC, Evans T, Chen HJ, Schwartz RE, Chen S. *Nature*. 2020 Oct 28. doi: 10.1038/s41586-020-2901-9. PMID: 33116299

December 3 & 4: [paper 7](#): iPSC Modeling of RBM20-Deficient DCM Identifies Upregulation of RBM20 as a Therapeutic Strategy. Briganti F, Sun H, Wei W, Wu J, Zhu C, Liss M, Karakikes I, Rego S, Cipriano A, Snyder M, Meder B, Xu Z, Millat G, Gotthardt M, Mercola M, Steinmetz LM. *Cell Rep*. 2020 Sep 8;32(10):108117. doi: 10.1016/j.celrep.2020.108117. PMID: 32905764

Week 5

December 7 & 8: [paper 8](#): Pre-clinical study of induced pluripotent stem cell-derived dopaminergic progenitor cells for Parkinson's disease. Doi D, Magotani H, Kikuchi T, Ikeda M, Hiramatsu S, Yoshida K, Amano N, Nomura M, Umekage M, Morizane A, Takahashi J. *Nat Commun*. 2020 Jul 6;11(1):3369. doi: 10.1038/s41467-020-17165-w. PMID: 32632153

Q&A

Week 6

December 15: turn in final exam

Additional Course Policies and UCLA Policies

Student Resources with Respect to Harassment:

Harassment and discrimination based on: race, ethnicity, ancestry, color; sex, gender, gender identity, gender expression, sexual orientation; national origin, citizenship status; religion; disability, pregnancy, medical condition, genetic predisposition; domestic partnership/marital status; age; or veteran status is not acceptable within our community, may violate UCLA regulations, and will be addressed. Information on how to obtain redress or counseling if you are subjected to such harassment or discrimination can be found at <https://equity.ucla.edu/report-anincident/>.

UCLA is bound by Title IX, a federal law that applies to any education program receiving federal assistance. Title IX prohibits gender discrimination, including sexual harassment, domestic and dating violence, sexual assault, and stalking. Students who have experienced sexual harassment or sexual violence can receive confidential support and advocacy at the CARE Advocacy Office for Sexual and Gender-Based Violence, 1st Floor Wooden Center West, CAREadvocate@caps.ucla.edu, (310) 206-2465. You can also report sexual violence or sexual harassment directly to the University's Title IX Coordinator, 2241 Murphy Hall, titleix@conet.ucla.edu, (310) 206-3417.

Student Mental Health Resources:

Stress is a part of all of our daily lives and it is normal for students to feel stress about courses and course work. We often also feel stress with respect to our lives and the world we live in. If you feel negative stress, that which impacts your ability to function and/or your mental health, there are many resources on campus for students that can help you gather insight and tools to intentionally manage your mental health, including: UCLA Behavioral Wellness Center For Graduate Students (<https://medschool.ucla.edu/bwc>), a student mental health center primary for GPB graduate students, medical students, and medical residents; UCLA's Counselling and Psychological Services center (<https://www.counseling.ucla.edu/>), a mental health resource for students at UCLA; and The Bruin Resource Center (<http://www.brc.ucla.edu/>).

Support for Undocumented Students:

The MBIDP supports our undocumented students and recognizes you as an important member of our community. UCLA provides many resources to support undocumented students and information can be found on the following websites: UCLA's Undocumented Students Program (<https://www.usp.ucla.edu/>) and UCLA's Office of Equity, Diversity, and Inclusion (<https://equity.ucla.edu/know/immigration/>).

Academic Accommodations Based on a Disability:

If you need academic accommodations based on a disability you should contact the Center for Accessible Education (CAE) at (310)825-1501 or in person at Murphy Hall A255. When possible, you should contact the CAE within the first two weeks of the term as reasonable notice is needed to coordinate accommodations. For more information visit www.cae.ucla.edu. If you require accommodations from us during meetings, please let us know so we can develop a plan together.