M254A: Molecular Biology of the Genome and Chromatin (2020)
Faculty: Thomas Vondriska & Siavash Kurdistani
Course Web Site: https://ccle.ucla.edu/course/view/17F-MOLBIO254A-1

All meeting of this course will take place via Zoom in Fall 2020.

Students-only meetings: **10:00 am – 12:00 pm on Mondays & Thursdays**

Faculty-Student meetings: **10:00 am – 12:00 pm on Tuesdays & Fridays**

FINAL EXAM: Date, Time and Locations TBD

Short Description:

This course will focus on research articles that utilize molecular, biochemical or structural approaches to gain mechanistic insight into function and regulation of DNA and chromatin. Topics include transcriptional and epigenetic regulation, DNA replication and repair, and protein translation. This section emphasizes self-driven learning based on primary literature.

Section Format

There will be 9 paired meetings (student-only and faculty-student sessions) where different topics will be discussed. Six of these meetings will involve the discussion of a primary research article while the other three meetings will center on student presentations that further explore topics that come up during the research article meetings. Each of the nine meetings will have a "Student Leader" who will be in charge of the (mandatory) student-only class and be MC of the faculty-student class.

Research Article Meetings

In the student session, the class will go over the paper and decide how to evenly distribute the presentation in the faculty session. Everyone should have carefully read the paper prior to this class and be prepared for a joint discussion. You should also talk about additional relevant information that would be appropriate to present (or might be asked by the faculty the next day!).

In general, there will be a background/introduction section that the leader may present in the faculty session. However, in some cases there may be more extensive background needed, which may utilize material from an earlier paper that sets up the present work; this could be the responsibility of another student. The leader is in charge of assigning tasks to rest of the class that will be determined at the student meeting, obtaining ppt slides from students prior to faculty class, assembling/ordering the final ppt presentation for the faculty class discussion, and ensuring smooth transitions between student presentations. It will be best if rendered PyMol files, movies, etc. are also ready to go on the computer used for the presentation. The leader will also give a final summary/wrap-up. The goal is to divide up the work/presentation equally, with the leader having a significant organizational role for that presentation. The leader is responsible for uploading the ppt presentation to the class web site at least 30 min prior to the faculty class, and then emailing within a day after class a final ppt containing any modifications/corrections that are made from the class discussion (as appropriate). The

powerpoint file should be small enough or divided into small enough files that it will not cause problems with email (<10 MB / email).

Each student will prepare a short presentation on a particular aspect of the paper. This will usually involve a small number of ppt slides (usually no more than 3-4) showing data figures from the paper and additional material to aid in the presentation. Each ppt slide should have the name of the person who prepared it (e.g., on a corner of the slide). It is often best to separate panels from composite figures to organize/focus the presentation and so that they are large and easily seen when projected. Use of the white board is also encouraged. Each presenter should plan for a ~5 min (absolutely no longer than 10 min) presentation so there is adequate time for discussion. Practice/rehearse your oral presentation before class! In general, most if not all parts of the paper should be covered, including parts of the text where there is no corresponding data figure or table. However, less time can/should be spent on tangential or redundant points; the faculty member in charge of the particular paper can give guidance on this if needed. As we will need to cover everything in the 2 h faculty-student time block, the presentations must be focused and concise. Although you will only be responsible for presenting a single aspect of the paper in class, it is critical that you have a firm understanding of the entire paper and participate in the discussions surrounding each presentation.

Note: Explaining what the figure shows (results) and how the authors interpret it (their discussion) is the first component of any presentation. The second and equally important component is your independent evaluation of the data for its thoroughness, use of appropriate controls, and implications regarding the authors' hypothesis. It is fine to say you agree with the authors' interpretation—although this certainly need not always be the case—but you must state why you agree or disagree and identify limitations or alternative explanations.

Student Presentation Meetings

There will be three student presentation sessions interspersed between primary research article discussions in which students will explore issues that were raised in previously sessions in order to practice "self-directed learning". For the student-only discussion, topics / questions will be discussed / refined collectively and then distributed to individual students. In the faculty-student session, each student will prepare a short presentation that centers on their assigned question / topic. Similar to what was described earlier, this will involve a small number of ppt slides (usually no more than 3-4) that introduce the question and cover the relevant concepts. It should also include a critical experiment / figure from a primary research article that illustrates the key concept / idea. In addition, presenters are expected to be proficient in their assigned topic and be able to cite key publications from the literature.

We will try to arrange a meeting with the class at some time towards the end of boot camp week to discuss the overall course format and identify student leaders for each of the 9 meetings. Think about which topics / papers you would choose to lead and email us beforehand with your top three choices. We will do our best to accommodate your preferences.

By the end of this module we hope that you will have become:

- Proficient at reading primary research papers in biochemistry
- Proficient at looking up information (self learning)
- Proficient at oral presentations and critical discussion of experimental approaches and data
- Confident with independently critiquing original, published work

We emphasize that students are responsible for all the material covered in the faculty class discussion, not just the specific topic they presented. All aspects of the papers and discussions are fair game for exam questions.

Grading: 50% of the final grade will be determined from the quality of the student presentations and discussions in each of the 9 sessions and 50% will be from the final exam. Details regarding the format of the final exam will be discussed in class.

Dates and Primary Papers

October 5: Chromatin regulatory mechanisms
Cancer-Specific Retargeting of BAF Complexes by a Prion-like Domain. Boulay et al. *Cell* 171, 163–178, PMID: 28844694.

October 12: A fluorescent RNA aptamer
Warner KD, Chen MC, Song W, Strack RL, Thorn A, Jaffrey SR, Ferré-D'Amaré AR. Structural basis for activity of highly efficient RNA mimics of green fluorescent protein. *Nat Struct Mol Biol.* 2014 Aug;21(8):658-63. doi: 10.1038/nsmb.2865. Epub 2014 Jul 15. PubMed PMID: 25026079; PubMed Central PMCID: PMC4143336.

October 19: Structural model the PIC
Structure of promoter-bound TFIID and model of human pre-initiation complex assembly. Louder RK, He Y, López-Blanco JR, Fang J, Chacón P, Nogales E. *Nature*. 2016 Mar 31;531(7596):604-9. doi: 10.1038/nature17394. Epub 2016 Mar 23.

October 26: In vitro reconstitution of yeast DNA replication
Yeeles JT, Deegan TD, Janska A, Early A, Diffley JF. Regulated eukaryotic DNA replication origin firing with purified proteins. *Nature.* 2015 Mar 26;519(7544):431-5. doi: 10.1038/nature14285. Epub 2015 Mar 4. PubMed PMID: 25739503; PubMed Central PMCID: PMC4874468.

November 2: Transcriptional regulatory landscape at single cell level
Integrated Single-Cell Analysis Maps the Continuous Regulatory Landscape of Human Hematopoietic Differentiation**.** Buenrostro JD, Corces MR, Lareau CA, Wu B, Schep AN, Aryee MJ, Majeti R, Chang HY, Greenleaf WJ. *Cell*. 2018 May 31;173(6):1535-1548. PMCID: PMC5989727

November 9: Protein Translation
Kostova KK, Hickey KL, Osuna BA, Hussmann JA, Frost A, Weinberg DE, Weissman JS. CAT-tailing as a fail-safe mechanism for efficient degradation of stalled nascent polypeptides. *Science*. 2017 Jul 28;357(6349):414-417. doi: 10.1126/science.aam7787. PubMed PMID: 28751611.