

CAMB 608 -- Fall 2021
REGULATION OF EUKARYOTIC GENE EXPRESSION
Tuesday (3:30-5:30pm)
CRB302 (in person)

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Format: This course is intended to bring students up to date on our understanding of gene regulation in eukaryotes. It is based on assigned topics and readings, formal presentations by individual class members, and the critical evaluation of primary data. Each student will be responsible for presenting one or two primary research papers. The course covers a variety of experimental systems and concepts.

Structure of presentation: Individual presentations should be organized as seminars, and include ~15 minutes of introduction. This introduction should supply sufficient background to place the paper in proper context within its field of study. It should also summarize the initial observations in the literature (original key publication(s)) that opened up this area of investigation. This introductory material should be derived from extensive additional reading, not just the assigned papers. After the introduction, the presentation (~50 minutes) will be devoted to a critical evaluation of the: 1) significance of the study (discuss major hypothesis being tested); 2) experimental design and methods (provide detailed description of new methods); 3) results (discuss their validity, reliability, replicability); 4) conclusions drawn from the study (not just the authors' but yours as well); and finally 5) a discussion of follow-up experiments (~20 minutes). Students should **not** simply give a blow-by-blow account of each experiment and the authors' conclusions. Engage your audience and promote discussion throughout the presentation by asking direct rather than open-ended questions. Engage your classmates early in the presentation by testing their knowledge of background material. Be sure to keep an eye on the clock and manage your time accordingly. The papers should be presented more as if they were the students' own work. It is possible, and often expected, that some of the figures in the highlighted paper will not be discussed in detail. The topics that we cover in this course build on one another, so as the course proceeds students should be able to relate and compare the data and conclusions of the papers being discussed to those of previous discussions, pointing out apparent consistencies and differences.

Preparation: At least one week prior to their presentation, students will discuss their assigned papers with their faculty preceptor (an outline and/or preliminary PowerPoint presentation is recommended). Email to make an appointment well in advance. This will allow sufficient time for feedback on the presentation and for the presenters to practice their deliveries. Students will post a review article covering a pertinent aspect of their topic on the Canvas course website a week before their presentation. Students are expected to read the review article before class in order to have a better appreciation for the field of study.

Class participation: Each class member will also critically evaluate the papers. Lively discussion involving all members of the class is expected. The papers should be treated as if they were being reviewed for publication in a journal—despite the fact that they're already published—and students should be prepared to discuss both a paper's strengths and weaknesses. A high level of discussion will not occur unless each participant thoroughly reads the papers and formulates questions. Accordingly, each student will be required to post one

question based on their reading of that week's paper on a shared google doc by Monday at 5pm prior to each class.

Grading scheme: Grades for the course will be based on students' presentations (~50%), weekly participation in the discussions (~40%), and quality of questions raised (~10%). The faculty will provide an evaluation of each student's presentation in a private setting immediately after the class. Students will also provide constructive feedback of each presentation by filling out an evaluation form prior to leaving the class. These forms will be given directly to the presenter at the end of class for his/her own use; they will not be read by the faculty. This peer review process will allow the presenters to obtain critical feedback on the style, clarity and content of their presentations.

August 24

Organizational meeting

September 14

Topic: Transcription condensates

Student Presenter:

Faculty preceptor: Doug Epstein

[RNA-Mediated Feedback Control of Transcriptional Condensates.](#)

Henninger JE, Oksuz O, Shrinivas K, Sagi I, LeRoy G, Zheng MM, Andrews JO, Zamudio AV, Lazaris C, Hannett NM, Lee TI, Sharp PA, Cissé II, Chakraborty AK, Young RA. Cell. 2021 Jan 7;184(1):207-225.e24.

September 21

Topic: Transcription initiation

Student Presenter:

Faculty preceptor: Alessandro Gardini

[A TBP-independent mechanism for RNA Polymerase II transcription](#)

James Z.J. Kwan, Thomas F. Nguyen, Marek A. Budzyński, Jieying Cui, Rachel M. Price, Sheila S. Teves

bioRxiv 2021.03.28.437425; doi: <https://doi.org/10.1101/2021.03.28.437425>

September 28

Topic: Transcription dynamics

Student Presenter:

Faculty preceptor: Shawn Little

[Single-molecule imaging of transcription dynamics in somatic stem cells.](#)

Wheat JC, Sella Y, Willcockson M, Skoultchi AI, Bergman A, Singer RH, Steidl U. Nature. 2020 Jul;583(7816):431-436.

October 5

Topic: Splicing dynamics

Student Presenter:

Faculty preceptor: Doug Epstein

[Dynamic imaging of nascent RNA reveals general principles of transcription dynamics and stochastic splice site selection.](#)

Wan Y, Anastasakis DG, Rodriguez J, Palangat M, Gudla P, Zaki G, Tandon M, Pegoraro G, Chow CC, Hafner M, Larson DR. Cell. 2021 May 27;184(11):2878-2895.e20.

October 12**Topic:** Noncoding RNAs**Student Presenter:****Faculty preceptor:** Colin Conine[A Network of Noncoding Regulatory RNAs Acts in the Mammalian Brain.](#)

Kleaveland B, Shi CY, Stefano J, Bartel DP. Cell. 2018 Jul 12;174(2):350-362.e17.

October 19**Topic:** Nuclear positioning**Student Presenter:****Faculty preceptor:** Raj Jain[Active chromatin marks drive spatial sequestration of heterochromatin in C. elegans nuclei.](#)

Cabianca DS, Muñoz-Jiménez C, Kalck V, Gaidatzis D, Padeken J, Seeber A, Askjaer P, Gasser SM. Nature. 2019 May;569(7758):734-739.

October 26**Topic:** Epigenetic silencing**Student Presenter:****Faculty preceptor:** Golnaz Vahedi[Epigenetic silencing by SETDB1 suppresses tumour intrinsic immunogenicity.](#)

Griffin GK, Wu J, Iracheta-Vellve A, Patti JC, Hsu J, Davis T, Dele-Oni D, Du PP, Halawi AG, Ishizuka JJ, Kim SY, Klaeger S, Knudsen NH, Miller BC, Nguyen TH, Olander KE, Papanastasiou M, Rachimi S, Robitschek EJ, Schneider EM, Yeary MD, Zimmer MD, Jaffe JD, Carr SA, Doench JG, Haining WN, Yates KB, Manguso RT, Bernstein BE. Nature. 2021 Jul;595(7866):309-314.

November 2**Topic:** RNA interference**Student Presenter:****Faculty preceptor:** Colin Conine[An isoform of Dicer protects mammalian stem cells against multiple RNA viruses.](#)

Poirier EZ, Buck MD, Chakravarty P, Carvalho J, Frederico B, Cardoso A, Healy L, Ulferts R, Beale R, Reis E Sousa C. Science. 2021 Jul 9;373(6551):231-236.

November 9**Topic:** Transcriptional noise**Student Presenter:****Faculty preceptor:** Shawn Little[A DNA-repair pathway can affect transcriptional noise to promote cell fate transitions.](#)

Desai RV, Chen X, Martin B, Chaturvedi S, Hwang DW, Li W, Yu C, Ding S, Thomson M, Singer RH, Coleman RA, Hansen MMK, Weinberger LS. Science. 2021 Jul 22:eabc6506.

November 16

Topic: RNA modifications

Student Presenter:

Faculty preceptor: Colin Conine

[A Unified Model for the Function of YTHDF Proteins in Regulating m⁶A-Modified mRNA.](#)

Zaccara S, Jaffrey SR. Cell. 2020 Jun 25;181(7):1582-1595.e18.

November 23

Topic: Enhancer-promoter interactions

Student Presenter:

Faculty preceptor: Eric Joyce

[Enhancer release and retargeting activates disease-susceptibility genes.](#)

Oh S, Shao J, Mitra J, Xiong F, D'Antonio M, Wang R, Garcia-Bassets I, Ma Q, Zhu X, Lee JH, Nair SJ, Yang F, Ohgi K, Frazer KA, Zhang ZD, Li W, Rosenfeld MG. Nature. 2021 Jul;595(7869):735-740.

November 30

Topic: Genome architecture

Student Presenter:

Faculty preceptor: Doug Epstein

[Cis-regulatory chromatin loops arise before TADs and gene activation, and are independent of cell fate during early Drosophila development.](#)

Espinola SM, Götz M, Bellec M, Messina O, Fiche JB, Houbbron C, Dejean M, Reim I, Cardozo Gizzi AM, Lagha M, Nollmann M.

December 7

Topic: X-inactivation

Student Presenter:

Faculty preceptor: Montserrat Anguera

[Spn links RNA-mediated endogenous retrovirus silencing and X chromosome inactivation.](#)

Carter AC, Xu J, Nakamoto MY, Wei Y, Zarnegar BJ, Shi Q, Broughton JP, Ransom RC, Salhotra A, Nagaraja SD, Li R, Dou DR, Yost KE, Cho SW, Mistry A, Longaker MT, Khavari PA, Batey RT, Wuttke DS, Chang HY. Elife. 2020 May 7;9:e54508.

December 14

Topic: Noncoding variants and human disease

Student Presenter:

Faculty preceptor: Doug Epstein

[Extensive pleiotropism and allelic heterogeneity mediate metabolic effects of *IRX3* and *IRX5*.](#)

Sobreira DR, Joslin AC, Zhang Q, Williamson I, Hansen GT, Farris KM, Sakabe NJ, Sinnott-Armstrong N, Bozek G, Jensen-Cody SO, Flippo KH, Ober C, Bickmore WA, Potthoff M, Chen M, Claussnitzer M, Aneas I, Nóbrega MA. Science. 2021 Jun 4;372(6546):1085-1091.