

CAMB 608 -- FALL 2019
REGULATION OF EUKARYOTIC GENE EXPRESSION
Tuesday (3-5pm) CRB Room 302

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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 one topic supported by one or two primary papers. The course covers a variety of experimental systems and concepts.

Structure of presentation: Individual presentations should be organized as seminars, and include ~20 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 by asking direct rather than open-ended questions. 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: ~Two weeks prior to their presentation, students will discuss their assigned papers with their faculty preceptor (an outline and/or preliminary PowerPoint presentation is recommended). Call or 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 the pdf of their paper, supplemental figures, as well as a review article covering their topic on the Canvas course website a week before their presentation. The Friday before their presentation, students will meet with Doug Epstein to discuss strategies for enhancing class discussion.

Class participation: Each class member will read and critically evaluate the papers. Lively discussion and debate 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 prepare at least one question from each of the assigned papers prior to 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.

Aug. 27

Organizational meeting

Sep. 10

Topic: Promoter repression

Student Presenter:

Faculty preceptor: Doug Epstein

[Direct Promoter Repression by BCL11A Controls the Fetal to Adult Hemoglobin Switch.](#)

Liu N, Hargreaves VV, Zhu Q, Kurland JV, Hong J, Kim W, Sher F, Macias-Trevino C, Rogers JM, Kurita R, Nakamura Y, Yuan GC, Bauer DE, Xu J, Bulyk ML, **Orkin SH.** Cell. 2018 Apr 5;173(2):430-442.e17.

Sep. 17

Topic: Alternative Polyadenylation

Student Presenter:

Faculty preceptor: Doug Epstein

[Nudt21 Controls Cell Fate by Connecting Alternative Polyadenylation to Chromatin Signaling.](#)

Brumbaugh J, Di Stefano B, Wang X, Borkent M, Forouzmand E, Clowers KJ, Ji F, Schwarz BA, Kalocsay M, Elledge SJ, Chen Y, Sadreyev RI, Gygi SP, Hu G, Shi Y, Hochedlinger K
Cell. 2018 Jan 11;172(1-2):106-120.

Sep. 24

Topic: Role of Architectural Boundaries in gene regulation

Student Presenter:

Faculty preceptor: Eric Joyce

[Functional dissection of the Sox9-Kcnj2 locus identifies nonessential and instructive roles of TAD architecture.](#)

Despang A, Schöpflin R, Franke M, Ali S, Jerković I, Paliou C, Chan WL, Timmermann B, Wittler L, Vingron M, Mundlos S, Ibrahim DM.
Nat Genet. 2019 Aug;51(8)

Oct. 1

Topic: How enhancers get activated

Student Presenter:

Faculty preceptor: Alessandro Gardini

[Enhancer Reprogramming Promotes Pancreatic Cancer Metastasis.](#)

Jae-Seok Roe, Chang-Il Hwang, Tim D.D. Somerville, Joseph P. Milazzo, Eun Jung Lee, Brandon Da Silva, Laura Maiorino, Hervé Tiriatic, Chris Vakoc
Cell, Vol. 170, Issue 5, p875–888 2017

Oct. 8

Topic: Enhancer-promoter interactions

Student Presenter:

Faculty preceptor: Eric Joyce

[Live-cell imaging reveals enhancer-dependent Sox2 transcription in the absence of enhancer proximity.](#)

Alexander JM, Guan J, Li B, Maliskova L, Song M, Shen Y, Huang B, Lomvardas S, Weiner OD. *Elife*. 2019 May 24;8.

Oct. 15

Topic: Transcriptional bursting

Student Presenter:

Faculty preceptor: Shawn Little

[Intrinsic Dynamics of a Human Gene Reveal the Basis of Expression Heterogeneity.](#)

Rodriguez J, Ren G, Day CR, Zhao K, Chow CC, Larson DR.

Cell. 2019 Jan 10;176(1-2):213-226.

Oct. 22

Topic: Promoter pausing

Student Presenter:

Faculty preceptor: Shawn Little

[Dynamic turnover of paused Pol II complexes at human promoters.](#)

Erickson B, Sheridan RM, Cortazar M, Bentley DL.

Genes Dev. 2018 Sep 1;32(17-18):1215-1225.

Oct. 29

Topic: Regulating transcription at its core: Pol2 and its partners

Student Presenter:

Faculty preceptor: Alessandro Gardini

[The Histone Deacetylase SIRT6 Restrains Transcription Elongation via Promoter-Proximal Pausing](#)

Jean-Pierre Etchegaray, Lei Zhong, Catherine Li, Telmo Henriques, Eileen Ablondi, Tomoyoshi Nakadai, Capucine Van Rechem, Christina Ferrer, Raul Mostoslavsky
Molecular Cell, published online August 6, 2019

Nov. 5

Topic: Phase separation and gene regulation

Student Presenter:

Faculty preceptor: Melike Lakadamyali

[Coactivator condensation at super-enhancers links phase separation and gene control.](#)

Sabari, B. R., Dall'Agnese, A., Boija, A., Klein, I. A., Coffey, E. L., Shrinivas, K., Abraham, B. J., Hannett, N. M., Zamudio, A. V., Manteiga, J. C., Li, C. H., Guo, Y. E., Day, D. S., Schuijers, J., Vasile, E., Malik, S., Hnisz, D., Lee, T. I., Cisse, II, Roeder, R. G., Sharp, P. A., Chakraborty, A. K. & Young, R. A. *Science* **361** (2018).

Nov. 12

Topic: Dosage compensation

Student Presenter:

Faculty preceptor: Doug Epstein

[The Implication of Early Chromatin Changes in X Chromosome Inactivation.](#)

Żylicz JJ, Bousard A, Žumer K, Dossin F, Mohammad E, da Rocha ST, Schwalb B, Syx L, Dingli F, Loew D, Cramer P, Heard E. *Cell*. 2019 Jan 10;176(1-2):182-197

Nov. 19

Topic: Imaging TADs in single cells

Student Presenter:

Faculty preceptor: Melike Lakadamyali

[Super-resolution chromatin tracing reveals domains and cooperative interactions in single cells.](#)

Bintu, B., Mateo, L. J., Su, J. H., Sinnott-Armstrong, N. A., Parker, M., Kinrot, S., Yamaya, K., Boettiger, A. N. & Zhuang, X. *Science* **362** (2018).

Nov. 26

Topic: Lamina associated domains

Student Presenter:

Faculty preceptor: Raj Jain

[Promoter-Intrinsic and Local Chromatin Features Determine Gene Repression in LADs.](#)

Leemans C, van der Zwalm MCH, Brueckner L, Comoglio F, van Schaik T, Pagie L, van Arensbergen J, van Steensel B. *Cell*. 2019 May 2;177(4):852-864.

Dec. 3

Topic: Nuclear organization and cell fate

Student Presenter:

Faculty preceptor: Doug Epstein

[CARM1 and Paraspeckles Regulate Pre-implantation Mouse Embryo Development.](#)

Hupalowska A, Jedrusik A, Zhu M, Bedford MT, Glover DM, Zernicka-Goetz M. *Cell*. 2018 Dec 13;175(7):1902-1916.

Dec. 10

Topic: LncRNAs, cardiovascular risk, iPSC disease modeling

Student Presenter:

Faculty preceptor: Doug Epstein

[Unveiling the Role of the Most Impactful Cardiovascular Risk Locus through Haplotype Editing.](#)

Lo Sardo V, Chubukov P, Ferguson W, Kumar A, Teng EL, Duran M, Zhang L, Cost G, Engler AJ, Urnov F, Topol EJ, Torkamani A, **Baldwin KK**. *Cell*. 2018 Dec 13;175(7):1796-1810.

Dec. 17

Topic: Neuronal activity dependent transcription

Student Presenter:

Faculty preceptor: Jenn Cremins

[Sensory experience remodels genome architecture in neural circuit to drive motor learning.](#)

Yamada T, Yang Y, Valnegri P, Juric I, Abnoui A, Markwalter KH, Guthrie AN, Godec A, Oldenborg A, Hu M, Holy TE, Bonni A. *Nature*. 2019 May;569(7758):708-713.