

CAMB 608 -- Spring 2024
REGULATION OF EUKARYOTIC GENE EXPRESSION
Tuesday (3:00-5:00pm)
Stemmler 105

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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 (~15 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 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 12pm 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.

Jan 9

Organizational meeting

Jan 16

Topic 1: How to read a paper

Student Presenter:

Faculty preceptor: Colin Conine/Doug Epstein

Paper: [Reorganization of lamina-associated domains in early mouse embryos is regulated by RNA polymerase II activity.](#) Pal M, Altamirano-Pacheco L, Schauer T, Torres-Padilla ME. Genes Dev. 2023 Oct 1;37(19-20):901-912.

Jan 23

Topic 2: Transgenerational epigenetic inheritance

Student Presenter: Joanatta Shapiro

Faculty preceptor: Colin Conine

Paper: [Transgenerational inheritance of acquired epigenetic signatures at CpG islands in mice.](#) Takahashi Y, Morales Valencia M, Yu Y, Ouchi Y, Takahashi K, Shokhirev MN, Lande K, Williams AE, Fresia C, Kurita M, Hishida T, Shojima K, Hatanaka F, Nuñez-Delicado E, Esteban CR, Izpisua Belmonte JC. Cell. 2023 Feb 16;186(4):715-731.e19.

Jan 30

Topic 3: Enhancer specificity

Student Presenter: William Gao

Faculty preceptor: Doug Epstein

Paper: [Cell type directed design of synthetic enhancers.](#)

Taskiran II, Spanier KI, Dickmanken H, Kempynck N, Pančíková A, Ekşi EC, Hulselmans G, Ismail JN, Theunis K, Vandepoel R, Christiaens V, Mauduit D, Aerts S. Nature. 2023 Dec 12. doi: 10.1038/s41586-023-06936-2.

Feb 6

Topic 4: Promoter pausing

Student Presenter: Sena Sarikaya

Faculty preceptor: Priya Sivaramakrishnan

Paper: [Lola-I is a promoter pioneer factor that establishes de novo Pol II pausing during development.](#) Ramalingam V, Yu X, Slaughter BD, Unruh JR, Brennan KJ, Onyshchenko A, Lange JJ, Natarajan M, Buck M, Zeitlinger J. Nat Commun. 2023 Sep 21;14(1):5862.

Feb 13

Topic 5: Epigenetic memory

Student Presenter: Miles Arnett

Faculty preceptor: Raj Jain

Paper: [Single-cell chromatin state transitions during epigenetic memory formation.](#) Fujimori T, Rios-Martinez C, Thurm AR, Hinks MM, Doughty BR, Sinha J, Le D, Hafner A, Greenleaf WJ, Boettiger AN, Bintu L. bioRxiv. 2023 Oct 5:2023.10.03.560616.

Feb 20

Topic 6: X-inactivation

Student Presenter: Kelsey Leach

Faculty preceptor: Montserrat Anguera

Paper: [Polycomb repressive complexes 1 and 2 are each essential for maintenance of X inactivation in extra-embryonic lineages.](#)

Masui O, Corbel C, Nagao K, Endo TA, Kezuka F, Diabangouaya P, Nakayama M, Kumon M, Koseki Y, Obuse C, Koseki H, Heard E. Nat Cell Biol. 2023 Jan;25(1):134-144.

Feb 27

Topic 7: Epigenetic silencing

Student Presenter: Arushi Sahay

Faculty preceptor: Andrew Modzelewski

Paper: [TNRC18 engages H3K9me3 to mediate silencing of endogenous retrotransposons.](#) Zhao S, Lu J, Pan B, Fan H, Byrum SD, Xu C, Kim A, Guo Y, Kanchi KL, Gong W, Sun T, Storey AJ, Burkholder NT, Mackintosh SG, Kuhlers PC, Edmondson RD, Strahl BD, Diao Y, Tackett AJ, Raab JR, Cai L, Song J, Wang GG. Nature. 2023 Nov;623(7987):633-642.

March 5

Topic 8: Chromatin dynamics

Student Presenter: Emma Welter

Faculty preceptor: Mustafa Mir

Paper: [Cohesin and CTCF control the dynamics of chromosome folding.](#)

Mach P, Kos PI, Zhan Y, Cramard J, Gaudin S, Tünnermann J, Marchi E, Eglinger J, Zuin J, Kryzhanovska M, Smallwood S, Gelman L, Roth G, Nora EP, Tiana G, Giorgetti L. Nat Genet. 2022 Dec;54(12):1907-1918.

March 12

Topic 9: Target-directed miRNA degradation

Student Presenter: Diego Mendez

Faculty preceptor: Colin Conine

Paper: [Target-directed microRNA degradation regulates developmental microRNA expression and embryonic growth in mammals.](#) Jones BT, Han J, Zhang H, Hammer RE, Evers BM, Rakheja D, Acharya A, Mendell JT. Genes Dev. 2023 Jul 1;37(13-14):661-674.

March 19

Topic 10: RNA surveillance

Student Presenter: Nicole DeBruyne

Faculty preceptor: Doug Epstein

Paper: [Oncogenic CDK13 mutations impede nuclear RNA surveillance.](#)

Insko ML, Abraham BJ, Dubbury SJ, Kaltheuner IH, Dust S, Wu C, Chen KY, Liu D, Bellaousov S, Cox AM, Martin BJE, Zhang T, Ludwig CG, Fabo T, Modhurima R, Esgdaille DE, Henriques T, Brown KM, Chanock SJ, Geyer M, Adelman K, Sharp PA, Young RA, Boutz PL, Zon LI. Science. 2023 Apr 21;380(6642):eabn7625.

March 26

Topic 11: 3D genome folding

Student Presenter: Mingjia Li

Faculty preceptor: Eric Joyce

Paper: [WAPL functions as a rheostat of Protocadherin isoform diversity that controls neural wiring.](#)

Kiefer L, Chiosso A, Langen J, Buckley A, Gaudin S, Rajkumar SM, Servito GIF, Cha ES, Vijay A, Yeung A, Horta A, Mui MH, Canzio D. Science. 2023 Jun 23;380(6651):eadf8440.

April 2

Topic 12: Transcription factor target search

Student Presenter:

Faculty preceptor: Mustafa Mir

Paper: [Chromatin organization drives the search mechanism of nuclear factors.](#)

Mazzocca M, Loffreda A, Colombo E, Fillot T, Gnani D, Falletta P, Monteleone E, Capozzi S, Bertrand E, Legube G, Lavagnino Z, Tacchetti C, Mazza D. Nat Commun. 2023 Oct 13;14(1):6433.

April 9

Topic 13: Transcriptional condensates

Student Presenter: Johnny Doherty

Faculty preceptor: Liling Wan

Paper: [A chaperone-like function of FUS ensures TAZ condensate dynamics and transcriptional activation.](#)

Shao Y, Shu X, Lu Y, Zhu W, Li R, Fu H, Li C, Sun W, Li Z, Zhang Y, Cao X, Ye X, Ajiboye E, Zhao B, Zhang L, Wu H, Feng XH, Yang B, Lu H. Nat Cell Biol. 2024 Jan 3. doi: 10.1038/s41556-023-01309-3.

April 16

Topic 14: Enhancer hubs

Student Presenter:

Faculty preceptor: Colin Conine

Paper: [RNA-mediated symmetry breaking enables singular olfactory receptor choice.](#)

Pourmorady AD, Bashkirova EV, Chiariello AM, Belagzhal H, Kodra A, Duffié R, Kahiapo J, Monahan K, Pulupa J, Schieren I, Osterhoudt A, Dekker J, Nicodemi M, Lomvardas S. Nature. 2023 Dec 20. doi: 10.1038/s41586-023-06845-4.