

CAMB 608 -- Spring 2023
REGULATION OF EUKARYOTIC GENE EXPRESSION
Tuesday (3:00-5:00pm)
CRB 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 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 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.

Jan 10

Organizational meeting

Jan 17

Topic 1: How to read a paper

Student Presenter:

Faculty preceptor: Colin Conine/Doug Epstein

Paper: [Zygotic genome activation by the totipotency pioneer factor Nr5a2.](#)

Gassler J, Kobayashi W, Gáspár I, Ruangroengkulrith S, Mohanan A, Gómez Hernández L, Kravchenko P, Kümmecke M, Lalic A, Rifel N, Ashburn RJ, Zaczek M, Vallot A, Cuenca Rico L, Ladstätter S, Tachibana K. Science. 2022 Dec 23;378(6626):1305-1315.

Jan 24

Topic 2: Transcriptional condensates

Student Presenter: Gabriela Hayward-Lara

Faculty preceptor: Liling Wan

Paper: [Phase separation drives aberrant chromatin looping and cancer development.](#)

Ahn JH, Davis ES, Daugird TA, Zhao S, Quiroga IY, Uryu H, Li J, Storey AJ, Tsai YH, Keeley DP, Mackintosh SG, Edmondson RD, Byrum SD, Cai L, Tackett AJ, Zheng D, Legant WR, Phanstiel DH, Wang GG. Nature. 2021 Jul;595(7868):591-595.

Jan 31

Topic 3: Nuclear organization

Student Presenter: Liz Kraeutler

Faculty preceptor: Raj Jain

Paper: [H3K9me selectively blocks transcription factor activity and ensures differentiated tissue integrity.](#)

Methot SP, Padeken J, Brancati G, Zeller P, Delaney CE, Gaidatzis D, Kohler H, van Oudenaarden A, Großhans H, Gasser SM. Nat Cell Biol. 2021 Nov;23(11):1163-1175.

Feb 7

Topic 4: TAD dynamics

Student Presenter: Noel Buitrago

Faculty preceptor: Mustafa Mir

Paper: [Dynamics of CTCF- and cohesin-mediated chromatin looping revealed by live-cell imaging.](#) Gabriele M, Brandão HB, Grosse-Holz S, Jha A, Dailey GM, Cattoglio C, Hsieh TS, Mirny L, Zechner C, Hansen AS. Science. 2022 Apr 29;376(6592):496-501.

Feb 14

Topic 5: miRNAs and imprinting

Student Presenter: Avi Waldman

Faculty preceptor: Colin Conine

Paper: [Imprinted Maternally Expressed microRNAs Antagonize Paternally Driven Gene Programs in Neurons.](#) Whipple AJ, Breton-Provencher V, Jacobs HN, Chitta UK, Sur M, Sharp PA. Mol Cell. 2020 Apr 2;78(1):85-95.e8.

Feb 21

Topic 6: RNA modifications

Student Presenter: Annabel Sangree

Faculty preceptor: Alessandro Gardini

Paper: [Dynamic control of chromatin-associated m⁶A methylation regulates nascent RNA synthesis.](#) Xu W, He C, Kaye EG, Li J, Mu M, Nelson GM, Dong L, Wang J, Wu F, Shi YG, Adelman K, Lan F, Shi Y, Shen H. Mol Cell. 2022 Mar 17;82(6):1156-1168.e7.

Feb 28

Topic 7: Genome organization

Student Presenter: Claire Makowski

Faculty preceptor: Eric Joyce

Paper: [In vivo dissection of a clustered-CTCF domain boundary reveals developmental principles of regulatory insulation.](#) Anania C, Acemel RD, Jedamzick J, Bolondi A, Cova G, Brieske N, Kühn R, Wittler L, Real FM, Lupiáñez DG. Nat Genet. 2022 Jul;54(7):1026-1036.

March 7 (253 BRB)

Topic 8: Dosage compensation

Student Presenter: Lexie Schneider

Faculty preceptor: Montserrat Anguera

Paper: [Xist nucleates local protein gradients to propagate silencing across the X chromosome.](#) Markaki Y, Gan Chong J, Wang Y, Jacobson EC, Luong C, Tan SYX, Jachowicz JW, Strehle M, Maestrini D, Banerjee AK, Mistry BA, Dror I, Dossin F, Schöneberg J, Heard E, Guttman M, Chou T, Plath K. Cell. 2021 Dec 9;184(25):6174-6192.e32.

March 14

Topic 9: piRNAs and heterochromatin

Student Presenter: Lauren Reich

Faculty preceptor: Colin Conine

Paper: [Su\(var\)2-10 and the SUMO Pathway Link piRNA-Guided Target Recognition to Chromatin Silencing](#). Ninova M, Chen YA, Godneeva B, Rogers AK, Luo Y, Fejes Tóth K, Aravin AA. Mol Cell. 2020 Feb 6;77(3):556-570.e6.

March 21

Topic 10: Cryptic splicing and neurodegeneration

Student Presenter: Segovia Garcia

Faculty preceptor: Doug Epstein

Paper: [TDP-43 loss and ALS-risk SNPs drive mis-splicing and depletion of UNC13A](#). Brown AL, Wilkins OG, Keuss MJ, Hill SE, Zanovello M, Lee WC, Bampton A, Lee FCY, Masino L, Qi YA, Bryce-Smith S, Gatt A, Hallegger M, Fagegaltier D, Phatnani H; NYGC ALS Consortium, Newcombe J, Gustavsson EK, Seddighi S, Reyes JF, Coon SL, Ramos D, Schiavo G, Fisher EMC, Raj T, Secrier M, Lashley T, Ule J, Buratti E, Humphrey J, Ward ME, Fratta P. Nature. 2022 Mar;603(7899):131-137.

March 28

Topic 11: Transcriptional dynamics

Student Presenter: Kenneth Pham

Faculty preceptor: Mustafa Mir

Paper: [Transcriptional coupling of distant regulatory genes in living embryos](#). Levo M, Raimundo J, Bing XY, Sisco Z, Batut PJ, Ryabichko S, Gregor T, Levine MS. Nature. 2022 May;605(7911):754-760.

April 4

Topic 12: Nonsense mediated mRNA decay

Student Presenter: Nora Kiledjian

Faculty preceptor: Doug Epstein

Paper: [NMD is required for timely cell fate transitions by fine-tuning gene expression and regulating translation](#). Huth M, Santini L, Galimberti E, Ramesmayer J, Titz-Teixeira F, Sehlke R, Oberhuemer M, Stummer S, Herzog V, Garmhausen M, Romeike M, Chugunova A, Leesch F, Holcik L, Weipoltshammer K, Lackner A, Schoefer C, von Haeseler A, Buecker C, Pauli A, Ameres SL, Smith A, Beyer A, Leeb M. Genes Dev. 2022 Mar 1;36(5-6):348-367.

April 11

Topic 13: Endogenous retroviruses and tissue homeostasis

Student Presenter: Samantha Fallacaro

Faculty preceptor: Andrew Modzelewski

Paper: [Endogenous retroviruses promote homeostatic and inflammatory responses to the microbiota](#). Lima-Junior DS, Krishnamurthy SR, Bouladoux N, Collins N, Han SJ, Chen EY, Constantinides MG, Link VM, Lim AI, Enamorado M, Cataisson C, Gil L, Rao I, Farley TK, Koroleva G, Attig J, Yuspa SH, Fischbach MA, Kassiotis G, Belkaid Y.

April 18

Topic 14: TBD

Student Presenter: Rohan?

Faculty preceptor:

Paper: