MCDB 191
Epigenetics
Winter 2022

Monday 12-1:50 Math Science 3915H
Starting on Zoom for at least the first two weeks. Please check your e-mail for a link to the zoom.

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The best way to contact me is via email

Volunteer Teaching Assistants:

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Course Materials

1. https://research.mcdb.ucla.edu/Jacobsen/LabWebSite/P_ClassEpigenetics.php is your home base, with links to everything you need, including papers that can be downloaded.

Course Description

Study of modern topics in epigenetic gene regulation. In last decade the field of epigenetics has exploded, identifying histone modifications and DNA methylation pathways as key regulators of gene expression. Through focus on primary literature, presentations, and group discussion, topics include reversible histone and DNA modifications, small RNA-based gene regulation pathways, imprinting, and cancer. Designed for students who have completed two upper-division biology courses.

Learning Outcomes for this Course

- Understand broad concepts in epigenetic gene regulation in a wide variety of eukaryotic organisms.
- Understand the basic techniques used in epigenetic research.
- Understand how epigenetics plays a role in processes underlying cancer.
- Understand how bioinformatics analyses are key to epigenetic research.

How to Succeed in this Course (Expectations for Students)

- Attend all classes and participate in discussion.
- Reading assigned papers before class.

- Working hard to make your presentation as clear and well thought out as possible.

Helping You Succeed & Creating an Inclusive Classroom Community (Instructor, TA, and Community Expectations)

If you need help understanding the material or with preparing your presentation, please contact the TA that is listed for the topic being covered. This is highly encouraged!

UCLA's Office for Equity, Diversity, and Inclusion provides resources, events, and information about current initiatives at UCLA to support equality for all members of the UCLA community. I hope that you will communicate with me or one of the TAs if you experience anything in this course that does not support an inclusive environment, and you can also report any incidents you may witness or experience on campus to the Office of Equity, Diversity, and Inclusion on their website.

How Your Learning Will Be Assessed (Grading Policy)

Grading will be based on participation and your presentation. This will be in five areas:

- Attendance (4 points per week).
- Reading the papers before the presentation is mandatory. Before the beginning of each class meeting, you complete a form in which you will provide a synopsis of the paper and a brief statement of which experiments you think would be the next logical step to take. This must be turned in at the very beginning of class on the day the paper is being presented. While we are online, please e-mail your evaluations to jaewonyun424@gmail.com. (5 points per week).
- Participation in the discussion of papers. Asking questions, making comments etc. (25 points total).
- Completing an evaluation of each presentation in order to provide feedback to the presenter. You must fill out these forms and turn them in at the very end of each class. Please put your name on the form so we can give you the points, and then we will remove your name and give an anonymous version to the presenter (1 point per week). Please e-mail these evaluations to jaewonyun424@gmail.com.
- Well thought out presentation with sufficient background information, and good visuals. This will require reading and understanding the paper to be presented in great detail, as well as reading supporting papers and reviews to put the paper into the context of the field as a whole. A TA will be available to help you with your presentation, and this is HIGHLY encouraged (25 points).
- Completing the course and instructor evaluation at the end of the quarter (20 points).

Grading Scale:

Letter	Grade Percentage
A+	97-100%
A	92%-96.9%
A-	88%-91.9%
B+	84%-87.9%
B	80%-83.9%
B-	76%-79.9%
C+	72%-75.9%
C	70%-71.9%
C-	64%-69.9%
D	60%-63.9%

F 0%-59.9%

Historically, most of the class has received a grade of A- or above. If needed, the flat scale may be adjusted in your favor. It is possible (and hoped for!) that everyone in the course receives an A.

Why I do not grade on a curve: In recent years, research has shown that grading on a curve can create unnecessarily competitive environments at UCLA and elsewhere. For this reason, your grade is not based on how you did in comparison to your peers. Scientific understanding and progress advance best through interaction and discussion. Therefore, I hope you will work with your classmates to enhance your own understanding of the material.

What constitutes a good presentation?

- Shoot for a 10-minute introduction and 20-30-minute explanation of the paper. This leaves plenty of time for discussion and questions. You don't have to explain every figure of the paper in great detail. Best is to spend more time on the figures that really demonstrate the main point of the paper, and spend less time on less important figures. The art is knowing how to convey the main message of the paper concisely, while critically analyzing the validity of the data presented. You should however look carefully at all of the figures during your preparation so that you can field questions about the entire paper. Similarly, try to understand the materials and methods so you can field questions, but you don't need to get bogged down in presenting every detail of the techniques used.
- Use material from other papers and reviews on the reading list, or other papers that you might find on your own, to provide a summary of the field that you are presenting, and to make it clear how the paper fits into that field.
- Try to end with a statement of the main findings of the paper, and what would be the next logical questions to ask in this field.
- Visuals. Please use Powerpoint (or equivalent software) for presentations.

TOPICS

Week 1 January 3 **Introduction and Background Lectures** Epigenetics overview – Ranjith Papareddy. Preparation of presentations: - an example by Brandon Boone.
Discussion
Loss of Karma transposon methylation underlies the mantled somaclonal variant of oil palm. (2015) M. Ong-Abdulla, N. Jiang *et al.* **Nature**, 525: 533-537.
Related papers and reviews
The alternative role of DNA methylation in splicing regulation. (2015) Galit L. Maor, Ahuvi Yearim, Gil Ast. **Trends Genet.**, 31: 274-280.

Week 2 January 10 **DNA Methylation**
Discussion
UHRF1 Plays a Role in Maintaining DNA Methylation in Mammalian Cells. (2007) Magnolia Bostick, Jong Kyong Kim, Pierre-Olivier Estève, Amander Clark, Sriharsa Pradhan, Steven E. Jacobsen. **Science**, 317:1760-1764. Jaewon TA/Sofia Luengo-Woods

Highly Integrated Single-Base Resolution Maps of the Epigenome in Arabidopsis. (2008) Lister, R. et al. **Cell**, 133:523-536. Ranj TA/Matt Soldano
Related papers and reviews
Eukaryotic Cytosine Methyltransferases. (2005) Mary Grace Goll and Timothy H. Bestor **Annu. Rev. Biochem**, 74:481–514.
Cytosine Methylation: Remaining Faithful. (2008) Steen K.T. Ooi and Timothy H. Bestor. **Current Biology**, 18:R174-R176.
Establishing, maintaining and modifying DNA methylation patterns in plants and animals. (2010) Julie A. Law and Steven E. Jacobsen. **Nature Reviews Genetics**, 11:204-220.
Transcription factors as readers and effectors of DNA methylation. (2016) Heng Zhu, Guohua Wang and Jiang Qian. **Nature Review Genetics**, 17:551-565.

Week 3 January 24 **Histone methylation and demethylation**
Discussion
Methylation of Histone H3 lysine 9 creates a binding site for HP1 proteins. (2001) Monika Lachner, Dónal O'Carroll, Stephen Rea, Karl Mechtler and Thomas Jenuwein. **Nature**, 410:116-120. Lucia TA/Rimsha Hussaini
JHDM2A, a JmjC-Containing H3K9 Demethylase, Facilitates Transcription Activation by Androgen Receptor. (2006) Kenichi Yamane, Charalambos Toumazou, Yu-ichi Tsukada, Heiye Erdjument-Bromage, Paul Tempst, Jiemin Wong, Yi Zhang. **Cell**, 125(3):483-495. Zhenhui TA/Jonathan Omens
Related papers and reviews
Regulation of chromatin structure by site-specific hisone H3 methyltransferases. (2000) Stephen Rea, Frank Eisenhaber, Dolnal O'Carroll, Brian D. Strahl, Zu-Wen Sun, Manfred Schmid, Susanne Opravil, Karl Mechtler, Chris P. Ponting, C. David Allis, and Thomas Jenuwein. **Nature**, 406:593-599.
HP1: a functionally multifaceted protein. (2008) Laura Fanti and Sergio Pimpinelli. **Current Opinions in Genetics and Development**, 18:169-174.
Regulation of Histone methylation by demethylimination and demethylation (2007) Robert Klose and Yi Zhang. **Nature Reviews Molecular Cell Bio**, 8.4:307-18.

Week 4 January 31 **Polycomb**
Discussion
Role of Histone H3 Lysine 27 Methylation in Polycomb-Group Silencing. (2002) Ru Cao, Liangjun Wang, Hengbin Wang, Li Xia, Hediye Erdjument-Bromage, Paul Tempst, Richard S. Jones, and Yi Zhang. **Science**, 298:1039-1043. Lucia TA/Yilin Piao
Chromatin Compaction by a Polycomb Group Protein Complex. (2004) Nicole J. Francis, Robert E. Kingston, and Christopher L. Woodcock. **Science**, 306:1574-1577.-Ranj TA/Kim Chen
Related papers and reviews
Transcriptional regulation by Polycomb group proteins. (2013) Luciano Di Croce and Kristian Helin. **Nature Structural & Molecular Biology**, 20:1147-1155.
A new world of Polycombs: unexpected partnerships and emerging functions. (2013) Yuri B. Schwartz and Vincenzo Pirrotta. **Nature Reviews Genetics**, 14:853-864.

PCGF3/5-PRC1 initiates Polycomb Recruitment in X chromosome inactivation. (2017) Mafalda Almeida, Greta Pintacuda, Osamu Masui, Yoko Koseki, et al. **Science**, 356:1081-1084.

Week 5 February 7 **RNA-directed Silencing + DNA demethylation.**
RNA-directed Silencing - Discussion
Discrete small RNA-generating loci as master regulators of transposon activity in Drosophila. (2007) Brennecke J, Aravin AA, Stark A, Dus M, Kellis M, Sachidanandam R, Hannon GJ. **Cell**, 128(6):1089-103. Ranj TA/Sean Cheah
RNA-directed Silencing - Related papers and reviews
Review: RNA-mediated epigenetic regulation of gene expression. (2015) Holoch D, Moazed D. **Nature reviews Genetics**, 16(2):71.
Small silencing RNAs: an expanding universe. (2009) Ghildiyal M, Zamore PD. **Nature reviews Genetics**, 10(2):94.

DNA demethylation - Discussion
Genome-Wide Demethylation of *Arabidopsis* Endosperm. (2009) Tzung-Fu Hsieh, et al., **Science**, 324: 1451-1454. Jaewon TA/Cynthia Dang
DNA demethylation - Related papers and reviews
DEMETER, a DNA Glycosylase Domain Protein, Is Required for Endosperm Gene Imprinting and Seed Viability in *Arabidopsis.* (2002) Yeonhee Choi, Mary Gehring, Lianna Johnson, Mike Hannon, John J. Harada, Robert B. Goldberg, Steven E. Jacobsen, and Robert L. Fischer. **Cell**, 110: 33-42**.**
The evolving functions of DNA methylation. (2008) Daniel Zilberman. **Current Opinion in Plant Biology**, 11:554-559.
DEMETER DNA Glycosylase Establishes MEDEA Polycomb Gene Self-Imprinting by Allele-Specific Demethylation (2006). Gehring et al., Cell 124, 495.
Reversing DNA Methylation: Mechanisms, Genomics, and Biological Functions. (2014) Hao Wu and Yi Zhang. **Cell**, 156: 45-68

Week 6 February 14 **Enhancers**

Discussion
Histone modifications at human enhancers reflect Global cell-type-specific gene expression. (2009) Nathaniel D Heintzman, Gary C Hon, R David Hawkins, Pouya Kheradpour, Alexander Stark, Lindsey F Harp, Zhen Ye, Leonard K Lee, Rhona K Stuart, Christina W Ching, Keith A Ching, Jessica E Antosiewicz-Bourget, Hui Liu, Xinmin Zhang, Roland D Green, Victor V Lobanenkov, Ron Stewart, James A Thomson, Gregory E Crawford, Manolis Kellis, Bing Ren. **Nature**, 459:108-112. Zhenhui TA/Vishvak Subramanyam

Enhancer Divergence and *cis*-Regulatory Evolution in the Human and Chimp Neural Crest. (2015) Prescott SL, Srinivasan R, Marchetto MC, Grishina I, Narvaiza I, Selleri L, Gage FH, Swigut T, Wysocka J. **Cell**, 163(1):68-83. Brandon TA/Alex Dunkwu
Related papers and reviews
Modification of Enhancer Chromatin: What, How, and Why? Calo E, Wysocka J. (2013) **Mol. Cell**, 49(5):825-37.

Week 7 Feb 28 **Targeted Epigenetics + 3D chromatin architecture**
Targeted Epigenetics - Discussion
Genome-wide programmable transcriptional memory by CRISPR-based epigenome editing. (2021) Nunez, et al., *Cell* 184, 2503-2519. Brandon TA/ Thomas Lai
Targeted Epigenetics - Related papers and reviews
Editing DNA Methylation in the Mammalian Genome. (2016) X. Shawn Liu, Hao Wu, Xiong Ji, Yonatan Stelzer, Xuebing Wu, Szymon Czauderna, Jian Shu, Daniel Dadon, Richard A. Young, Rudolf Jaenisch. **Cell**, 167: 233-247.
The epigenome editors: How tools such as CRISPR offer new details about epigenetics. (2017) Cassandra Willyard. **Nature Medicine**, 23:900-903.
Targeted DNA demethylation in vivo using dCas9-peptide repeat and scFv-TET1 catalytic domain fusions. (2016) Sumiyo Morita, Hirofumi Noguchi, Takuro Horii, Kazuhiko Nakabayashi, Mika Kimura, Kohji Okamura, Atsuhiko Sakai, Hideyuki Nakashima, Kenichiro Hata, Kinichi Nakashima & Izuho Hatada. **Nature Biotechnology**, 34(10):1060-1065.
Epigenome editing by a CRISPR-Cas9-based acetyltransferase activates genes from promoters and enhancers. (2015) Isaac B Hilton, Anthony M D'Ippolito, Christopher M Vockley, Pratiksha I Thakore, Gregory E Crawford, Timothy E Reddy & Charles A Gersbach. **Nature Biotechnology**, 33(5):510–517.

3D chromatin architecture - Discussion
Comprehensive mapping of long-range interactions reveals folding principles of the human genome. (2009) Lieberman-Aiden, E. et al. **Science**, 326:289–293. Zhenhui TA/Emma Raffman
3D chromatin architecture - Related papers and reviews
Chromosome territories, nuclear architecture and gene regulation in mammalian cells. (2001) Cremer, T. & Cremer, C. **Nature Reviews Genetics**, 2:292-301.
Exploring the three-dimensional organization of genomes: interpreting chromatin interaction data. (2013) Dekker J, Marti-Renom MA, Mirny LA. **Nature reviews Genetics**, 14(6):390.

Week 8 March 7 **Phase separation and Epigenetics.**
Discussion
Liquid droplet formation by HP1a suggests a role for phase separation in heterochromatin. (2017) Larson, A. G. et al. **Nature**, 547: 236-240. Brandon TA/Isabel Bellon

Transcription Factors Activate Genes through the Phase-Separation Capacity of Their Activation Domains. (2018). Boija et al., 2018, **Cell** 175, 1842–1855. Lucia TA/Naira Margarian
Related papers and reviews
Phase Separation Model for Transcriptional Control. (2017) Hnish, D., et al. **Cell**, 169: 13-23.
Evaluating phase separation in live cells: diagnosis, caveats, and functional consequences. (2019). McSwiggen et al. **Genes & Development** 33:1–16.

Last paper on 3D chromatin architecture

3D chromatin architecture - Discussion
Targeted Degradation of CTCF Decouples Local Insulation of Chromosome Domains from Genomic Compartmentalization. (2017) Nora, et al. **Cell**, 169:930–944. Lucia TA/Abe Horrillo
3D chromatin architecture - Related papers and reviews
Chromosome territories, nuclear architecture and gene regulation in mammalian cells. (2001) Cremer, T. & Cremer, C. **Nature Reviews Genetics**, 2:292-301.
Exploring the three-dimensional organization of genomes: interpreting chromatin interaction data. (2013) Dekker J, Marti-Renom MA, Mirny LA. **Nature reviews Genetics**, 14(6):390.

Student Resources for Support and Learning

Providing feedback to me and to your TAs: I encourage your feedback at any time throughout the quarter about things that are helping you learn, or things that aren't helping. Please communicate with me or with your TA if there are ways that we can improve the course.

Personal Problems: Sometimes, factors out of our control make it difficult to focus on schoolwork. If you are having a personal problem that affects your participation, please talk to me so we can create a plan. If you are not comfortable speaking with me directly, please utilize the other student resources provided below in order to understand how to best approach success in this course given your personal needs. Please do not wait until the end of the quarter to share any challenges that have negatively impacted you. The sooner we meet, the more options we will have to support your overall academic success.

Academic Accommodations Based on a Disability: Students needing academic accommodations based on a disability should contact the UCLA Center for Accessible Education (CAE) at (310)825-1501 or in person at Murphy Hall A255. When possible, students should contact the CAE within the first two weeks of the term as reasonable notice is needed to coordinate accommodations.

Campus Resources and Support Services around UCLA Available to Students:

- **Students in Crisis**: From the Office of the Dean of Students: Faculty and Staff 911 Guide for Students, commonly known as the "Red Folder." This tool is intended to provide you with quick access to important resources for assisting students in need.
- **Bruin Resource Center**: Includes services for transfer students, undocumented students, veterans, and students with dependents. http://www.brc.ucla.edu/
- **Counseling and Psychological Services Wooden Center West**: (310) 825-0768 www.caps.ucla.edu
- **Letters & Science Counseling Service: A316 Murphy Hall**: (310) 825-1965 www.college.ucla.edu
- **Academics in the Commons at Covel Commons**: (310) 825-9315 free workshops on a wide variety of issues relating to academic & personal success www.orl.ucla.edu (click on "academics")

● **Lesbian, Gay, Bisexual and Transgender Resource Center Student Activities Center, B36**: (310) 206- 3628 www.lgbt.ucla.edu
● **Center for Accessible Education (Formerly Office for Students with Disabilities)**: A255 Murphy Hall: (310) 825-1501, TDD (310) 206-6083; www.cae.ucla.edu
Dashew Center for International Students and Scholars 106 Bradley Hall: (310) 825-1681 www.internationalcenter.ucla.edu
● **Student Legal Services; A239 Murphy Hall**: (310) 825-9894; www.studentlegal.ucla.edu
● **Dean of Students Office; 1206 Murphy Hall**: (310) 825-3871; www.deanofstudents.ucla.edu

Additional Course Policies and UCLA Policies

Use of Laptops, Tablets or Phones in Class: You can decide if you want to use your laptop, tablet or phone in class. However, research finds that laptop multitasking is likely to hinder not only your own learning, but also the learning of anyone who can see your laptop. For the sake of your peers' learning, I therefore ask that if you use an electronic device during class, either only have lecture notes showing, or sit in the back row.