BB484/584 – Chromatin and Epigenetics
Winter 2016

Time & Place:
Monday, Wednesday, Friday
9:00 - 9:50 am
2018 ALS Building (BB classroom)

Instructor:	Department	Phone:	e-mail:
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Welcome to BB484/584 – Chromatin and Epigenetics!

Purpose and learner outcomes:

This is a combined lecture and seminar course. The purpose of this course is to:

A) Introduce students to the basic concepts of epigenetics through interactive lectures and reading of the current primary literature. Selected examples of epigenetic phenomena will be discussed in detail; these will change from year to year depending on exciting new discoveries in the field.

B) Give access to background information and older seminal studies that were important in shaping our understanding of epigenetics as a field of research.

C) Provide a setting in which students are trained in critically evaluating original research results through questions and extended discussions.

D) Build a "research resource". Students will be exposed to various technologies and resources that "epigeneticists" utilize to conduct research. Their availability on campus will be discussed.

After attending this class, students will be able to:

A) Explain how heterochromatin and euchromatin differ from each other;

B) Explain how different chromatin regions are generated and maintained;

C) Describe what epigenetic modifications are and how they are controlled;

D) explain how certain epigenetic phenomena, such as genomic imprinting and X chromosome inactivation, are initiated;

E) Apply genetic, cytological and biochemical tools that can be used to investigate epigenetic phenomena.

Evaluations and grading:

Learner outcomes are measured by evaluation of a term paper (36%), group presentations (40%), and assignments based on readings for discussions during presentations (24%).

All students will submit a full-length term paper. Term papers can be prepared individually or by students in their assigned groups. To mimic grant proposal deadlines, students will receive a failing grade if the paper does not reach the instructor on time (*at the latest on March 4, 2016, 11:59 pm).* Submitting the manuscript by e-mail in MS Word format is preferable; students are encouraged to send papers in early. The paper counts for 36% of the grade. See "Paper Requirements" below and see the instructor if there are questions about this assignment.

All students will participate during class presentations ("journal club" style) in which they lead discussions of a recent or "classic" primary paper. Pre-assigned groups of up to four students will present each paper (*see schedule below and as separate file on Canvas*; each group will present on four occasions; each presentation is equivalent to 10% of the final grade. Lectures and discussion sessions are intended to foster interactions and critical thinking. You are always encouraged to ask questions and make comments and most of all, to enjoy engaging in scientific discussion.

Homework assignments (all individually graded) are based on papers that are required reading (total 24% of grade). Assignments are due *before* the relevant discussion starts, preferably submitted as an MS Word file.

Considerations for all participants in discussions:

Please be always prepared by at the very least reading the paper to be discussed. Read the supplementary information and try to understand the methods.

Considerations for discussion leaders:

Please know the background of the paper you discuss. Go back to the older literature that is referred to in the paper. Know the methods and be able to explain them, read the supplementary information and make it part of your presentation. Be critical, especially when it comes to the discussion ("Does the title match the findings?", "Do the authors over-interpret data?", "Are there other/better valid methods?"). Evaluate how well the paper is written (style, clarity, citations). Try to encourage questions and discussion.

Term paper requirements:

The paper should take the form of a short research proposal (10-page limit, single-spaced, Arial 11 pt) in an area of epigenetics research that interests you. Use the "Freitag_MRF" proposal on Canvas as example (note that this is a sweeping proposal – it may be better to focus more). Here are requirements:

1. The paper should have a paragraph each for summary, specific aims and significance.
2. Write an in-depth, critical introduction to the topic. Instead of "preliminary results", review the most recent data in the field and identify the most obvious next experiments that need to be carried out.
3. Formulate a testable hypothesis (at the most two) that will drive the field forward.
4. Propose experiments that will test your hypothesis. Support your choices (i.e., propose experiments that will give you answers that in turn allow you to derive a new testable hypothesis). Think of potential pitfalls.
5. The paper needs to have complete citations (i.e., all author names, dates, full journal names, paper titles). Grading will be on content (90%) but also on presentation (10%).

BB584 Additional Paper Critiques for Graduate Students:

Graduate students are required to submit 2-3 page-long critiques of each assigned paper (total score 120 for 12 reports). Papers can take the form of a written "journal club" presentation, in which the student presents a clear summary and critical analysis of the paper. For example, the following questions should be considered: Is the paper a significant contribution to knowledge? If so, why? Are experimental methods clearly described? Do the authors adequately consider alternative models? Are the experiments convincing? Are the conclusions drawn justified based on the reported results? What are the most important future directions for the work? *Please make sure to substantiate your opinions by citing from the literature as necessary.*

Contact Information:

If you have any questions or problems, feel free to contact me. My office is located on the second floor of the Agricultural and Life Sciences building (ALS2045), my laboratory is in ALS2035. My phone number is 737-4845 and my e-mail address is freitagm@oregonstate.edu.

University Policies – A reminder:

Please note: "Students with documented disabilities who may need accommodations, who have any emergency medical information the instructor should know, or who need special arrangements in the event of evacuation, should make an appointment with the instructor as early as possible, no later than the first week of the term. In order to arrange alternative testing, the student should make the request at least one week in advance of the test. Students seeking accommodations should be registered with the Office of Services for Students with Disabilities."

The University rules on civility and honesty can be found at: http://oregonstate.edu/admin/stucon/regs.html

Cheating or plagiarism by students is subject to the disciplinary process outlined in the Student Conduct Regulations. Students are expected to be honest and ethical in their academic work. Academic dishonesty is defined as an intentional act of deception in one of the following areas:

- Cheating-use or attempted use of unauthorized materials, information or study aids
- Fabrication-falsification or invention of any information
- Assisting-helping another commit an act of academic dishonesty
- Tampering-altering or interfering with evaluation instruments and documents
- Plagiarism-representing the words or ideas of another person as one's own

Behaviors disruptive to the learning environment will not be tolerated and will be referred to the Office of Student Conduct for disciplinary action.

Use of cellular phone call, texting, messaging and twitter functions is not permitted in the classroom during lectures. Feel free, however, to use phones to look up information during class.

"The goal of Oregon State University is to provide students with the knowledge, skill and wisdom they need to contribute to society. Our rules are formulated to guarantee each student's freedom to learn and to protect the fundamental rights of others. People must treat each other with dignity and respect in order for scholarship to thrive. Behaviors that are disruptive to teaching and learning will not be tolerated, and will be referred to the Student Conduct Program for disciplinary action. Behaviors that create a hostile, offensive or intimidating environment based on gender, race, ethnicity, color, religion, age, disability, marital status or sexual orientation will be referred to the Affirmative Action Office."

Prerequisites and Co-requisites

DESIRED PREREQUISITES: BB451; BB492/592; MCB554 (can be waived with instructor consent)

Schedule Winter 2016:

Jan	4	Introduction to epigenetics	Lecture 1
Jan	6	Histones, nucleosomes, histone modifications	Lecture 2
Jan	*8*	*SILAC and nucleosome-interacting proteins*	*Discussion 1*
Jan	11	Chromatin remodeling	Lecture 3
Jan	*13*	*Regulation of ISWI*	*Discussion 2*
Jan	15	Epigenetics of *Saccharomycetes*: SIR proteins	Lecture 4
Jan	18	*Martin Luther King Day*	No class
Jan	20	Proteins involved in methylation of DNA and histones	Lecture 5
Jan	*22*	*UHRF1 links histone and DNA methylation*	*Discussion 3*
Jan	25	Post-transcriptional gene silencing in plants	Lecture 6
Jan	27	RNA interference in fission yeast and worms	Lecture 7
Jan	*29*	*RNA-induced DNA methylation in plants*	*Discussion 4*
Feb	1	Position-effect variegation in flies and yeast	Lecture 8
Feb	*3*	*HAATI chromosome ends*	*Discussion 5*
Feb	5	Assembly of heterochromatin	Lecture 9
Feb	*8*	*Two complexes – neither called ACDC*	*Discussion 6*
Feb	10	Fighting invaders with heterochromatin: genome defense	Lecture 10
Feb	*12*	*DNA transposons adapted to form heterochromatin*	*Discussion 7*
Feb	15	Maintenance of heterochromatin	Lecture 11
Feb	*17*	*Inheritance of histone marks*	*Discussion – 8*
Feb	19	Polycomb and Trithorax complexes: H3K27me and H3K4me	Lecture 12
Feb	22	*H3K27 methylation and non-coding RNA*	*Discussion 9*
Feb	24	Dosage compensation: One problem, three solutions	Lecture 13
Feb	26	X-chromosome inactivation	Lecture 14
Feb	*29*	*X-chromosome inactivation: RNA and histones*	*Discussion 10*
Mar	2	Genomic Imprinting	Lecture 15
Mar	*4*	*Airn and small RNA involved in imprinting*	*Discussion 11*
		TERM PAPER DUE (11:59 pm – no excuses)	
Mar	7	Epigenetics and Neo-Lamarckism?	Lecture 16
Mar	*9*	*Epigenetics and behavior*	*Discussion 12*
Mar	*11*	*Freitag at Neurospora Information Conference*	*No class*

Reading for BB484 – Winter 2016

1. All background reading is posted on Canvas in the folder for each lecture. This includes chapters from "Epigenetics, 2nd edition" or reviews that complement the lecture discussions.

2. Papers for discussions (absolutely required reading for all students):

Group 1	Jan. 8:	Till Bartke, Michiel Vermeulen, Blerta Xhemalce, Samuel C. Robson, Matthias Mann, Tony Kouzarides (2010) Nucleosome-Interacting Proteins Regulated by DNA and Histone Methylation. Cell 143: 470–484.
Group 2	Jan. 13:	Clapier CR, Cairns BR. 2012. Regulation of ISWI involves inhibitory modules antagonized by nucleosomal epitopes. Nature 492: 280-4. doi: 10.1038/nature11625.
Group 3	Jan. 22:	Rothbart SB, Krajewski K, Nady N, Tempel W, Xue S, Badeaux AI, Barsyte-Lovejoy D, Martinez JY, Bedford MT, Fuchs SM, Arrowsmith CH, Strahl BD. 2012. Association of UHRF1 with methylated H3K9 directs the maintenance of DNA methylation. Nat Struct Mol Biol. 19: 1155-60. doi: 10.1038/nsmb.2391.
Group 1	Jan 29:	Blevins T, Podicheti R, Mishra V, Marasco M, Tang H, Pikaard CS.2015. Identification of Pol IV and RDR2-dependent precursors of 24 nt siRNAs guiding de novo DNA methylation in Arabidopsis. Elife. 2015 Oct 2;4. pii: e09591. doi: 10.7554/eLife.09591.
Group 2	Feb 3	Jain D, Hebden AK, Nakamura TM, Miller KM, Cooper JP. 2010. HAATI survivors replace canonical telomeres with blocks of generic heterochromatin. Nature 467: 223-7. doi: 10.1038/nature09374.
Group 3	Feb 8	Honda S, Lewis ZA, Shimada K, Fischle W, Sack R, Selker EU. 2012 Heterochromatin protein 1 forms distinct complexes to direct histone deacetylation and DNA methylation. Nat Struct Mol Biol. 19: 471-7, S1. doi: 10.1038/nsmb.2274.
Group 1	Feb. 12:	Cam HP, Noma K, Ebina H, Levin HL, Grewal SI (2008) Host genome surveillance for retrotransposons by transposon-derived proteins. Nature 451: 431-436.
Group 2	Feb. 17:	Petruk S, Sedkov Y, Johnston DM, Hodgson JW, Black KL, Kovermann SK, Beck S, Canaani E, Brock HW, Mazo A. 2012. TrxG and PcG proteins but not methylated histones remain associated with DNA through replication. Cell 150: 922-33. doi: 10.1016/j.cell.2012.06.046.
Group 3	Feb. 22:	Kaneko S, Li G, Son J, Xu CF, Margueron R, Neubert TA, Reinberg D. 2010. Phosphorylation of the PRC2 component Ezh2 is cell cycle-regulated and up-regulates its binding to ncRNA. Genes Dev. 24: 2615-20. doi: 10.1101/gad.1983810.
Group 1	Feb. 29:	Sarkar MK, Gayen S, Kumar S, Maclary E, Buttigieg E, Hinten M, Kumari A, Harris C, Sado T, Kalantry S. 2015. An Xist-activating antisense RNA required for X-chromosome inactivation. Nat Commun. 2015 Oct 19;6:8564. doi: 10.1038/ncomms9564.
Group 2	Mar. 4:	Takashi Nagano, Jennifer A. Mitchell, Lionel A. Sanz, Florian M. Pauler, Anne C. Ferguson-Smith, Robert Feil, Peter Fraser (2008) The Air Noncoding RNA Epigenetically Silences Transcription by Targeting G9a to Chromatin. Science 322: 1717-1720.
Group 3	Mar. 9:	Weaver IC, Hellstrom IC, Brown SE, Andrews SD, Dymov S, Diorio J, Zhang TY, Szyf M, Meaney MJ. 2014. The methylated-DNA binding protein MBD2 enhances NGFI-A (egr-1)-mediated transcriptional activation of the glucocorticoid receptor. Philos Trans R Soc Lond B Biol Sci. 2014 Sep 26;369(1652). pii: 20130513. doi: 10.1098/rstb.2013.0513.