

BB484/584 – Chromatin and Epigenetics Winter 2017

**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 (34%), group presentations (30%), and assignments based on readings for discussions during presentations (36%).

All students will submit a full-length term paper in form of a research proposal. 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 10, 2017, 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 34% 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 three occasions; each presentation is equivalent to 10% of the final grade (individuals get group 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 36% 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 if necessary. 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 is better to be more focused).

Here are requirements:

1. The paper should have a paragraph each for summary, specific aims and significance. There will be different deadlines for sending these items in for review – we will discuss this in class.
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 that they are not presenters for (total score 120 for 9 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 2017:

Jan	9	Introduction to chromatin and epigenetics	Lecture 1
Jan	11	DNA and histone modifications	Lecture 2
Jan	13	<i>UHRF1 links histone and DNA methylation</i>	<i>Discussion 1</i>
Jan	16	<i>Martin Luther King Day</i>	No class
Jan	18	Chromatin remodeling	Lecture 3
Jan	20	<i>Histone Demethylation and Chromatin Remodeling</i>	<i>Discussion 2</i>
Jan	23	Assays for chromatin: ChIP and Hi-C	Lecture 4
Jan	25	<i>HiC in Neurospora</i>	<i>Discussion 3</i>
Jan	27	Post-transcriptional gene silencing, RNA interference	Lecture 5
Jan	30	<i>RNA-induced DNA methylation in plants</i>	<i>Discussion 4</i>
Feb	1	Position-effect variegation in flies and yeast	Lecture 6
Feb	3	<i>Fission yeast heterochromatin</i>	<i>Discussion 5</i>
Feb	6	Centromere chromatin structure	Lecture 7
Feb	8	<i>CENP-A and histone acetylation</i>	<i>Discussion 6</i>
Feb	10	Assembly of heterochromatin	Lecture 8
Feb	13	<i>Two complexes – neither called ACDC</i>	<i>Discussion 7</i>
Feb	15	Fighting invaders with heterochromatin: genome defense	Lecture 9
Feb	17	<i>DNA transposons adapted to form heterochromatin</i>	<i>Discussion 8</i>
Feb	20	Maintenance of heterochromatin	Lecture 10
Feb	22	<i>Inheritance of histone marks</i>	<i>Discussion 9</i>
Feb	24	Polycomb and Trithorax complexes: H3K27me and H3K4me	Lecture 11
Feb	27	<i>H3K27 methylation and non-coding RNA</i>	<i>Discussion 10</i>
Mar	1	Dosage compensation: One problem, three solutions	Lecture 12
Mar	3	X-chromosome inactivation	Lecture 13
Mar	6	<i>X-chromosome inactivation: battling RNAs</i>	<i>Discussion 11</i>
Mar	8	Genomic Imprinting	Lecture 14
Mar	10	<i>Imprinting of dormancy in plants</i>	<i>Discussion 12</i>
		TERM PAPER DUE (11:59 pm – no excuses)	
Mar	13	Epigenetics and Neo-Lamarckism – wrap up	Lecture 15
Mar	15	<i>and Mar 17 – Freitag at Fungal Genetics Conf</i>	<i>no class</i>

Reading for BB484 – Winter 2017

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. 13: 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 2 Jan. 20: Li C, Gu L, Gao L, Chen C, Wei CQ, Qiu Q, Chien CW, Wang S, Jiang L, Ai LF, Chen CY, Yang S, Nguyen V, Qi Y, Snyder MP, Burlingame AL, Kohalmi SE, Huang S, Cao X, Wang ZY, Wu K, Chen X, Cui Y. 2016. Concerted genomic targeting of H3K27 demethylase REF6 and chromatin-remodeling ATPase BRM in Arabidopsis. *Nature Genetics* 2016 Jun;48(6):687-93. doi: 10.1038/ng.3555
- Group 3 Jan. 25: Galazka JM, Klocko AD, Uesaka M, Honda S, Selker EU, Freitag M. 2016. Neurospora chromosomes are organized by blocks of importin alpha-dependent heterochromatin that are largely independent of H3K9me3. *Genome Res.* 26: 1069-80. doi: 10.1101/gr.203182.115.
- Group 4 Jan 29: Duan CG, Zhang H, Tang K, Zhu X, Qian W, Hou YJ, Wang B, Lang Z, Zhao Y, Wang X, Wang P, Zhou J, Liang G, Liu N, Wang C, Zhu JK. 2015. Specific but interdependent functions for Arabidopsis AGO4 and AGO6 in RNA-directed DNA methylation. *EMBO J.* 2015 Mar 4;34(5):581-92. doi: 10.15252/embj.201489453.
- Group 1 Feb 3 Zofall M, Smith DR, Mizuguchi T, Dhakshnamoorthy J, Grewal SI. 2016. Taz1-Shelterin Promotes Facultative Heterochromatin Assembly at Chromosome-Internal Sites Containing Late Replication Origins. *Mol Cell* 62: 862-74. doi: 10.1016/j.molcel.2016.04.034.
- Group 2 Feb 8 Shang WH, Hori T, Westhorpe FG, Godek KM, Toyoda A, Misu S, Monma N, Ikeo K, Carroll CW, Takami Y, Fujiyama A, Kimura H, Straight AF, Fukagawa T. 2016. Acetylation of histone H4 lysine 5 and 12 is required for CENP-A deposition into centromeres. *Nat Commun.* 7: 13465. doi: 10.1038/ncomms13465.
- Group 3 Feb. 13: Honda S, Bicocca VT, Gessaman JD, Rountree MR, Yokoyama A, Yu EY, Selker JM, Selker EU 2016. Dual chromatin recognition by the histone deacetylase complex HCHC is required for proper DNA methylation in *Neurospora crassa*. *Proc Natl Acad Sci U S A.* 2016 Oct 11;113(41):E6135-E6144.
- Group 4 Feb. 17: 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 1 Feb. 22: 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 2 Feb. 27: 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 3 Mar. 6: Vallot C, Patrat C, Collier AJ, Huret C, Casanova M, Liyakat Ali TM, Tosolini M, Frydman N, Heard E, Rugg-Gunn PJ, Rougeulle C. 2016. XACT Noncoding RNA Competes with XIST in the Control of X Chromosome Activity during Human Early Development. *Cell Stem Cell* pii: S1934-5909(16)30354-X. doi: 10.1016/j.stem.2016.10.014.
- Group 4 Mar. 10: Piskurewicz U, Iwasaki M, Susaki D, Megies C, Kinoshita T, Lopez-Molina L. 2016. Dormancy-specific imprinting underlies maternal inheritance of seed dormancy in *Arabidopsis thaliana*. *Elife* pii: e19573. doi: 10.7554/eLife.19573.