Biology 568: Advanced Topics in Molecular Genetics - Epigenetics (Spring, 2021)

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Introduction

"Epigenetics" refers to mechanisms of gene expression and cellular differentiation that alter chromatin structure but do not involve changes in the DNA sequence. Examples include covalent modifications of DNA (methylation), covalent modifications of histones (methylation, acetylation, phosphorylation, etc), plus additional aspects of chromatin structure such the programmed deployment of histone variants, noncoding RNAs, chromatin remodeling and higher order chromatin structures. These aspects of chromatin structure can be rather stable and may be inherited by daughter cells during cell division, or in some cases from one generation to the next (parent to offspring). Epigenetic factors play key roles in virtually all biological processes, including development, stem cell biology, cancer, behavior, drug addiction, learning and memory. In this course, we will focus on primarily on epigenetic factors in animals and animal cells.

Contact Information

Course meets: Wednesdays at 4:30 - 7:10 pm, online. Log into the Blackboard course website, click on the "Tools" menu (left panel, below "assessments"), then click on "Blackboard Collaborate Ultra" tool, then click on the "unlocked course room" icon (near the top left of the window).

Office hours: Fridays, 2:00 pm – 4:00 pm online via Zoom:
https://gmu.zoom.us/j/7931936280?pwd=RWV1OC9oVmRpQUNQb3Y5czhURG91UT09#success

E-mail: kfryxell@gmu.edu *(Must include "BIOL 568" in the subject line of your e-mails)*

Telephone: 703-993-1069 *(Calls to my office phone are forwarded via the internet. Please leave a detailed message including your name, class number callback phone number, and dates/times when you are available for me to call you back.*

Course web site: GMU Blackboard web site - includes lecture notes, study questions, and other materials.

Readings

There is one required text for this class: *Epigenetics (2nd edition)* edited by C. D. Allis et al. (2015), Cold Spring Harbor Laboratory Press. Copies are available in the Science & Technology campus bookstore, plus one copy in the Mercer Library on 2 hour reserve. Most of the reading will be assigned from this text. A few additional readings will be assigned from the primary research literature (listed below) are available from the GMU library e-journals website. Study questions based on the assigned readings will be posted weekly, along with lecture notes, on Blackboard.

Grading summary: 45% midterm + 45% final exam + 10% participation.

Participation grades are based on a combination of attendance and participation in discussions during class (which is strongly encouraged). Midterm and final examinations will consist of short-answer and short essay questions, modeled on the study questions that are posted weekly.

Course Schedule

Introductory course meeting. Wednesday, January 27.

Lecture 1. Wednesday, February 3 - A survey of epigenetic marks.
Text chapter 3, pp. 47-76.
Filion, GJ et al. (2010) Systematic protein location mapping reveals five principal chromatin types in *Drosophila* cells. *Cell* **143**, 212-224.

Lecture 2. Wednesday, February 10 - Gene regulation at the epigenetic level.
text, pp. 21-23; pp. 76-86.
Ernst, J. et al. (2011) Mapping and analysis of chromatin state dynamics in nine human cell types. *Nature* **473**, 43-49.

Sartorelli, V. and S. M. Lauberth (2020) Enhancer RNAs are an important regulatory layer of the epigenome. *Nat. Struct. Mol. Biol.* **27(6)**, 521-528.

Lecture 3. Wednesday, February 17 – Chromosome looping and higher order structures.

Text chapter 19, pp. 507-528.

Ong CT and Corces VG (2014) CTCF: an architectural protein bridging genome topology and function. *Nat. Rev. Genet.* **15**, 234-246.

Hnisz, D. et al. (2017) A phase separation model for transcriptional control. *Cell* **169**, 13-23.

Lecture 4. Wednesday, February 24 - DNA methylation.

Text chapter 15, pp. 423-443.

Zhu, H. (2016) Transcription factors as readers and effectors of DNA methylation. *Nat. Rev. Genet.* **17(9)**, 551-565.

Tillotson, R. and A. Bird (2020) The molecular basis of MeCP2 function in the brain. *J. Mol. Biol.* **432**, 1602-1623.

Lecture 5. Wednesday, March 3 - Histone variants and histone chaperones.

Text chapter 20, pp. 529-549; chapter 22, pp. 575-597.

Hammond, CM et al. (2017) Histone chaperone networks shaping chromatin function. *Nat. Rev. Mol. Cell Biol.* 18, 141-158.

Lecture 6. Wednesday, March 10 - Regulation of gene expression by Polycomb and Trithorax.

Text chapter 17, pp. 463-488; chapter 18, pp. 489-506.

Ferrari, KJ et al. (2014) Polycomb-dependent H3K27me1 and H3K27me2 regulate active transcription and enhancer fidelity. *Mol. Cell* 53, 49-62.

Wednesday, March 17 - Midterm Exam (covers lectures 1-6)

Lecture 7. Wednesday, March 24 – Nucleosome remodeling.

Text chapter 21, pp. 555-573.

Petty E, Pillus L (2013) Balancing chromatin remodeling and histone modifications in transcription. *Trends Genet.* 29, 621-629.

Lecture 8. Wednesday, March 31 - X chromosome inactivation

Text chapter 3, pp. 86-88.

Text chapter 25, pp. 641-665.

Jeon Y, Sarma K, Lee JT (2012) New and Xisting regulatory mechanisms of X chromosome inactivation. *Curr. Opin. Genet. Dev.* 22: 62-71.

Lecture 9. Wednesday, April 7 - Genomic imprinting in mammals.

Text chapter 26, pp. 667-686.

Bian C, Yu X (2014) PGC7 suppresses TET3 for protecting DNA methylation. *Nucl. Acids Res.* 42, 2893-2905.

Lecture 10. Wednesday, April 14 - Chromatin remodeling in stem cells.

Text chapter 27, pp. 687-709.

Beagan, J. A. et al. (2017) YY1 and CTCF orchestrate a 3D chromatin looping switch during early neural lineage commitment. *Genome Res.* **27**, 1139-1152.

Lecture 11. Wednesday, April 21 - Epigenetic control of immunity.

Text chapter 29, pp. 737-762.

Guo C et al. (2011) CTCF-binding elements mediate control of V(D)J recombination. Nature 477, 424-430.

Lecture 12. Wednesday, April 28 - Epigenetic control of the nervous system.

Text chapter 32, pp. 807-830.

Marshall, O. J. and A. H. Brand (2017) Chromatin state changes during neural development revealed by *in vivo* cell-type specific profiling. *Nat. Commun.* **8**, 2271.

Saturday, May 1 – Reading day

Wednesday, May 5 – Final exam (covers lectures 7-12), online, 4:30 pm – 7:10 pm.