Syllabus

Bi 424/524 Advanced Molecular Genetics: Epigenetics Spring, 2012

Instructor: Eric Selker email: selker@uoregon.edu; office: 355D Streisinger; ph: 346-5193
Mondays and Wednesdays 16:00-17:20 (11 Pacific); office hours: Fridays 4-6PM and by appt.

April 2 (M) Lecture: **Epigenetics – overview**
Optional reading: Ptashne, M. (2007). On the use of the word epigenetic. Curr Biol 17, R233-236; Margueron and Reinberg (2010) Chromatin structure and the inheritance of epigenetic information. *Nat Rev Genet 11*: 285-96.

April 4 (W) Lecture: **Chromatin structure**
Review: Zhou et al. (2011) Charting histone modifications and the functional organization of mammalian genomes. Nat Rev Genet (2011) 12: 7-18

April 9 (M) Discussion of: **Hansen, K.H., Bracken, A.P., Pasini, D., Dietrich, N., Gehani, S.S., Monrad, A., Rappsilber, J., Lerdrup, M., and Helin, K. (2008). A model for transmission of the H3K27me3 epigenetic mark. Nat Cell Biol *10*, 1291-1300.**
Background: Schwartz, Y. B., and Pirrotta, V. (2007). Polycomb silencing mechanisms and the management of genomic programmes. Nat Rev Genet 8, 9-22.

April 11 (W) Lecture: **PEV (position effect variegation) in Drosophila**
Optional reading: Schotta, G.et al. (2003). Position-effect variegation and the genetic dissection of chromatin regulation in Drosophila. *Semin Cell Dev Biol 14*, 67-75. Vogel et al. (2009) High-resolution mapping of heterochromatin redistribution in a Drosophila position-effect variegation model. Epigenetics & chromatin 2: 1-18.

April 16 (M) Discussion of: **Dorer, D. R., and Henikoff, S. 1994. Expansions of transgene repeats cause heterochromatin formation and gene silencing in Drosophila. *Cell* 77: 993-1002.** Secondary discussion paper: Paredes et al. Ribosomal DNA deletions modulate genome-wide gene expression: "rDNA-sensitive" genes and natural variation. PLoS Genetics (2011) vol. 7 (4) pp. e1001376

April 18 (W) Lecture: **DNA methylation**
Optional reading: Li, E. and Bird, A. (2007) DNA methylation in mammals. *In:* "Epigenetics" edited by Allis et al. CSH Press pp.341-356. (on reserve); Fischle (2008) Talk is cheap--cross-talk in establishment, maintenance, and readout of chromatin modifications. *Genes & Dev. 22*: 3375-82; Law and Jacobsen. (2010) Establishing, maintaining and modifying DNA methylation patterns in plants and animals. Nat Rev Genet

April 23 (M) Discussion of: **Bourc'his, D. and T.H. Bestor. (2004) Meiotic catastrophe and retrotransposon reactivation in male germ cells lacking Dnmt3L. *Nature* 431: 96-9.**
***Required background paper:* Bourc'his, D., G.L. Xu, C.S. Lin, B. Bollman, and T.H. Bestor. (2001) Dnmt3L and the establishment of maternal genomic imprints. *Science* 294: 2536-9.**

April 25 (W) Lecture: **Gene silencing in filamentous fungi**
Optional reading: Allshire, R.C. & Selker, E. U. (2007) Fungal Models for Epigenetic Research: *Schizocaccharomyces pombe* and *Neurospora crassa*. *In:* "Epigenetics" edited by Allis, Jenuwein & Reinberg. CSH Press pp. 101-126; Galagan, J.E. and E.U. Selker (2004) RIP: The high cost of genome defense. *Trends in Genetics*, **20**: 417-423. Kelly and Aramayo. (2007) Meiotic silencing and the epigenetics of sex. Chromosome Res 15: 633-651

April 30 (M) Discussion of: **Shiu, P. K., Raju, N. B., Zickler, D., and Metzenberg, R. L. (2001) Meiotic silencing by unpaired DNA. Cell *107*, 905-16.** *Background paper*: Aramayo, R., and Metzenberg, R. L. (1996) Meiotic transvection in fungi. *Cell* **86**, 103-113.

May 2 (W) **Gene silencing in plants**
Optional reading: M. Matzke and O. Mittelsten Scheid (2007) Epigenetic Regulation in Plants. *In:* "Epigenetics" edited by Allis, Jenuwein & Reinberg. CSH Press pp. 167-189; Matzke et al. (2009) RNA-mediated chromatin-based silencing in plants. Curr. Opin. in Cell Biol. 21:1-10

May 7 (M) Discussion of: **Brzeska, K., Brzeski, J., Smith, J., and Chandler, V.L. (2010) Transgenic expression of CBBP, a CXC domain protein, establishes paramutation in maize. Proc Natl Acad Sci U S A**. 107: 5516-21.

May 9 (W) Lecture: **Gene silencing in yeasts (Guest lecture by Dr. Andrew Klocko)**
Optional reading: Rusche, L.N., A.L. Kirchmaier, and J. Rine. (2003) The establishment, inheritance, and function of silenced chromatin in *Saccharomyces cerevisiae*. *Annu Rev Biochem* **72**: 481-516; Grewal. (2010) RNAi-dependent formation of heterochromatin and its diverse functions. Current Opinion in Genetics & Development. 20: 134-41

May14 (M) Discussion of: **Bayne et al. (2010) Stc1: A Critical Link between RNAi and Chromatin Modification Required for Heterochromatin Integrity. *Cell 140*: 666-677.**

May 16 (W) Lecture: **Imprinting and X-inactivation**
Optional reading: D. P. Barlow and M. S. Bartolomei (2007) Genomic Imprinting in Mammals *In:* "Epigenetics" edited by Allis et al. CSH Press pp. 357-375; Bartolomei (2009) Genomic imprinting: employing and avoiding epigenetic processes. *Genes & Development 23*: 2124-33; N. Brockdorff and B. M. Turner (2007) Dosage Compensation in Mammals. *In:* "Epigenetics" edited by Allis et al. CSH Press pp. 321-339. Nora and Heard. (2009) X chromosome inactivation: when dosage counts. Cell 139: 865-7.

May 21 (M) Discussion of: **Tian et al. (2010) The Long Noncoding RNA, Jpx, Is a Molecular Switch for X Chromosome Inactivation. Cell 143: 390-403.**

May 23 (W) Lecture: **Epigenetics and Human Disease (Guest lecture by Dr. Michael Rountree)**
Optional reading: Mund and Lyko. (2010) Epigenetic cancer therapy: Proof of concept and remaining challenges. Bioessays 32: 949-57; Zoghbi, H.Y. & Beaudet, A.L Epigenetics and Human Disease (2007) *In:* "Epigenetics" edited by Allis, Jenuwein & Reinberg. CSH Press. pp. 435-456; Baylin, S.B. & Jones, P.A. Epigenetic Determinants of Cancer (2007) *In:* "Epigenetics" edited by Allis, Jenuwein & Reinberg. CSH Press. pp. 457-476.

May 28 (M) Memorial Day Holiday

May 30 (W) Student talks

June 4(M) Student talks

June 6 (W) Student talks

June 11 (M) Term papers due at noon. *It must be **emailed** on time* to **selker@uoregon.edu**; please also deliver hard copy to Selker's office or to his mailbox in Kla75.

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Course objectives, format, requirements and grading: The purpose of the course is to provide for in-depth study of advanced topics in genetics. Lectures will serve primarily to introduce topics. About one third of class meetings will be used for organized discussions on readings from the primary scientific literature. Students will serve as leaders for the corresponding discussion. Written responses to questions on the readings will be due at the beginning of each of the discussion periods. There will be occasional quizzes but no final exam. A term paper in the form of a research proposal related to a topic of the course will be due at noon on Monday of finals week (June 11). **Please submit it both by email and as a hard copy.** In the final several class meetings, each student will give a brief (8-10 min.) oral presentation to the class on the subject of their term paper. The course will be only offered on a graded basis. Grading will be based on instructor's assessment of individual achievements in the following areas and will be weighted as indicated:

problem sets	35%
oral presentations and discussions	20%
written research proposal (term paper)	30%
quizzes	15%

Readings: There will be no textbook. The primary discussion papers (required reading), as well as some extra materials (some required reading; some optional), will be made available on Departmental server (http://biology.uoregon.edu/classes/bi424s12/) and copies will also be placed in the reading room in Streisinger Hall.

Discussions and problem set logistics:
-Discussion leaders must arrange a meeting ("pre-discussion") *with the instructor, e.g. on Friday before the Monday discussion.*
-Problem sets will normally be handed out in the class period before the associated Discussion and will be due at start of the Discussion period; no credit will be given for late assignments.

Term paper and related oral presentation: This is similar to the research proposal part of a typical graduate student "comprehensive exam" (we can discuss this) but it should be 2000 words or less. The primary purpose of writing this research proposal is to gain experience identifying an interesting biological problem, proposing hypotheses or models to explain or solve the problem and designing experiments to test the hypotheses. Any topic discussed or related to those in the course is acceptable; you are encouraged to email the instructor a brief (few sentence) description of your proposed project. Please note that the term paper is not only a scientific exercise; it is a writing exercise as well. Think carefully about what you want to say; say it logically and concisely. After you are satisfied with your paper, put it down (e.g. 1-2 days) and then reread it critically and see if you can improve it. You should put it through at least two drafts. The final copy should be printed double-spaced. Grading will be principally on the scientific merits of your ideas but writing quality will "count" as well, much as it does when a paper is being reviewed for publication or when a grant is being reviewed for possible funding. Both the proposal and the oral talk about the proposed research should include background to put the proposed work in context.