

## BISC 403 FALL 2014 ADVANCED MOLECULAR BIOLOGY

Lectures: TTh 12:30 – 1:50, THH 208 Discussion: Tue 4-5:50 ZHS 360, Weds 2-3:50 VKC157

### Professors:

Prof. Susan Forsburg, Office: RRI 104C Office hours: Tues 2-3, and by appointment Tel/vox: (213) 740-7342, email: <a href="mailto:forsburg@usc.edu">forsburg@usc.edu</a>	Prof. John Tower Office: RRI 219C Office hours: Tues 10-12 and by appointment. Tel/vox: (213) 740-5384 email: <a href="mailto:jtower@usc.edu">jtower@usc.edu</a>	TA: Tara Mastro lab: RRI 108 Office ours TBA Tel/vox 213-740-5558 <a href="mailto:mastro@usc.edu">mastro@usc.edu</a>
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**Prerequisites:** BISC311 or BISC 320L (Molecular Biology) is a firm prerequisite for this course.

**Objective:** The course objective is to consider a few topics in Molecular Biology in depth. Topics are chosen by the faculty and generally represent active areas of their current research. The course also requires reading primary research papers for discussion.

**Format:** There is no required textbook for this course. You will receive digital copies of lecture handouts and reading materials. Resources and review articles will also be uploaded to Blackboard ([blackboard.usc.edu](http://blackboard.usc.edu)). Background reading in any general Genetics, Cell Biology, or Molecular Biology textbook may be helpful.

**Discussion Sessions: Participation is required for full points in the course.** Each week the professor will assign a relevant research paper related to that week's lectures. Students should be prepared to participate in a journal club about that paper, which will require reading the paper and any background **prior to discussion**.

Students should come to section with the discussion worksheet filled out, and prepared to state the "take home message" of the paper, describing particular strengths and weaknesses. Did they prove their point? Students will be randomly called upon to **present** background materials, or discuss any figure of the paper or method employed, and credit will be awarded for this presentation. Additional points will be awarded for active **participation** in discussion. **Discussion will account for 20% of your grade.**

Date	Lecturer	Topic
<b>SECTION 1: EPIGENETICS</b>		
<b>General reading: you should dip into these throughout the course</b>		
Khorasanizadeh S, (2004) The nucleosome: from genomic organization to Genomic regulation. Cell 116: 259.		
Margueron R, Reinberg D. Chromatin structure and the inheritance of epigenetic information. Nat Rev Genet. 2010 Apr;11(4):285-96..		
<b>Week 1: 26 August</b>	<b>Forsburg</b>	<b>Introduction to Chromosomes</b>
<b>28 August</b>	<b>Forsburg</b>	<b>Histones, nucleosomes, nucleosome assembly</b>
<b>Week 1 Additional reading:</b>		
Olins DE, Olins AL. Chromatin history: our view from the bridge. Nat Rev Mol Cell Biol. 2003 4:809-14.		
Alabert C, Groth A. Chromatin replication and epigenome maintenance. Nat Rev Mol Cell Biol. 2012 Feb 23;13(3):153-67		
<b>Discussion paper:</b> Randall and Kelly TJ The fate of parental nucleosomes during SV40 DNA replication.		

**Week 1 Additional reading:**

Olins DE, Olins AL. Chromatin history: our view from the bridge. *Nat Rev Mol Cell Biol.* 2003 4:809-14.  
 Alabert C, Groth A. Chromatin replication and epigenome maintenance. *Nat Rev Mol Cell Biol.* 2012 Feb 23;13(3):153-67

**Discussion paper:** Randall and Kelly TJ The fate of parental nucleosomes during SV40 DNA replication. *J Biol Chem.* 1992 Jul 15;267(20):14259-65.

**Week 2:**  
2 Sept

Forsburg

Chromatin remodeling I

4 Sept

Forsburg

Chromatin remodeling II; histone modifications I

**Week 2 Background reading**

Clapier CR, Cairns BR The biology of chromatin remodeling complexes. *Annu Rev Biochem.* 2009;78:273-304

De Koning L, Corpet A, Haber JE, Almouzni G. Histone chaperones: an escort network regulating histone traffic. *Nat Struct Mol Biol.* 2007 Nov 5;14(11):997-1007.

**Discussion paper:**

*Cell Stem Cell.* 2014 May 1;14(5):575-91. doi: 10.1016/j.stem.2014.02.013.

INO80 facilitates pluripotency gene activation in embryonic stem cell self-renewal, reprogramming, and blastocyst development.

Wang L1, Du Y2, Ward JM2, Shimbo T1, Lackford B1, Zheng X1, Miao YL3, Zhou B4, Han L5, Fargo DC2, Jothi R1, Williams CJ3, Wade PA6, Hu G7.

**Week 3:**  
9 Sept

Forsburg

Histone Modifications II; binding motifs

11 Sept

Forsburg

Histone variants.

**Week 3:**

Talbert PB, Henikoff S. Histone variants--ancient wrap artists of the epigenome. *Nat Rev Mol Cell Biol.* 2010 Apr;11(4):264-75. Epub 2010 Mar 3.

**Discussion paper:**

*Cell.* 2010 Jan 8;140(1):136-47. doi: 10.1016/j.cell.2009.11.006.

H2A.Z-containing nucleosomes mediate the thermosensory response in *Arabidopsis*.

Kumar SV1, Wigge PA.

**Week 4:**  
16 Sept

Forsburg

RNAi

18 Sept

Forsburg

Case study: heterochromatin and silencing (\*this material on Midterm 2\*)

**Background reading Week 4**

RNA interference in the nucleus: roles for small RNAs in transcription, epigenetics and beyond.

Castel SE, Martienssen RA. *Nat Rev Genet.* 2013 Feb;14(2):100-12. doi: 10.1038/nrg3355. **Review.**

Beisel C, Paro R. Silencing chromatin: comparing modes and mechanisms. *Nat Rev Genet.* 2011

<b>Week 5:</b> 23 Sept	<b>MIDTERM 1</b>	
25 Sept	Forsburg	Case study: Centromeres and chromosome segregation
<p><b>Background reading Week 5</b> Verdaasdonk JS, Bloom K. Centromeres: unique chromatin structures that drive chromosome segregation Nat Rev Mol Cell Biol. 2011 May;12(5):320-32.</p> <p>Discussion paper: Nat Cell Biol. 2013 Sep;15(9):1056-66. doi: 10.1038/ncb2805. Epub 2013 Jul 21. A two-step mechanism for epigenetic specification of centromere identity and function. Fachinetti D1, Folco HD, Nechemia-Arbely Y, Valente LP, Nguyen K, Wong AJ, Zhu Q, Holland AJ, Desai A, Jansen LE, Cleveland DW.</p>		
<b>Week 6:</b> 30 Sept	Forsburg	Case study: DNA damage response
2 Oct	Forsburg	Case study: DNA methylation & Imprinting
<p><b>Background reading Week 6</b> Jones PA. Nat Rev Genet. 2012 Functions of DNA methylation: islands, start sites, gene bodies and beyond. Jones May 29;13(7):484-92. <b>Review.</b> Crosstalk between histone modifications during the DNA damage response. van Attikum H, Gasser SM. Trends Cell Biol. 2009 May;19(5):207-17. Epub 2009 Apr 1. Review.</p> <p><b>Discussion paper:</b> Cell. 2004 Nov 24;119(5):603-14. Methylation of histone H4 lysine 20 controls recruitment of Crb2 to sites of DNA damage. Sanders SL1, Portoso M, Mata J, Bähler J, Allshire RC, Kouzarides T.</p>		
<b>Week 7:</b> 7 Oct	Forsburg	Epigenetics and cancer
9 Oct	Forsburg	Epigenetics and the environment
<p><b>Background reading Week 7</b> Chi P, Allis CD, Wang GG. Covalent histone modifications--miswritten, misinterpreted and mis-erased in human cancers. Nat Rev Cancer. 2010 Jul;10(7):457-69.</p> <p>Epigenetics and the environment: emerging patterns and implications. Feil R, Fraga MF. Nat Rev Genet. 2012 Jan 4;13(2):97-109. doi: 10.1038/nrg3142. Review.</p> <p><b>discussion paper:</b> P. Dominguez-Salas et al., “Maternal nutrition at conception modulates DNA methylation of human metastable epialleles,” <i>Nature Communications</i>, doi: 10.1038/ncomms4746, 2014</p>		

<b>Week 8</b> 14 Oct	<b>MIDTERM 2</b>	
16 Oct	Tower	Evolutionary theories of aging
<b>Week 8 Background reading:</b> Hughes, K. A., and R. M. Reynolds (2005) Evolutionary and Mechanistic Theories of Aging. <i>Annu. Rev. Entomol.</i> 50:421-45. Kenyon, C. J. (2010) The genetics of aging. <i>Nature</i> 464:504-512.		
<b>Week 8 Discussion paper:</b> Yoshida, K., T. Fujisawa, J. S. Hwang, K. Ikeo and T. Gojobori, 2006. Degeneration after sexual differentiation in hydra and its relevance to the evolution of aging. <i>Gene</i> 385, 64-70.		
<b>Week 9 :</b> 21 Oct	Tower	Mechanistic theories of aging
23 Oct	Tower	Mechanistic theories of aging
<b>Week 9 Background reading:</b> Kaeberlein, M. (2010) Lessons on longevity from budding yeast. <i>Nature</i> 464:513-519.		
<b>Week 9 Discussion paper:</b> Mair et al (2003) Demography of Dietary Restriction and Death in <i>Drosophila</i> . <i>Science</i> 301:1731		
<b>Week 10:</b> 28 Oct	Tower	Gene expression during aging
30 Oct	Tower	Oxidative stress and damage
<b>Week 10 Background reading:</b> Tower, J (2009) Hsps and aging. <i>Trends Endocrinol Metab</i> 20:216-22. <b>Week 10 Discussion paper:</b> Kenyon, C. J. et al (1993) A <i>C. elegans</i> mutant that lives twice as long as wild type. <i>Nature</i> 366:461-4.		
<b>Week 11:</b> 4 Nov	Tower	Mitochondria
6 Nov	<b>MIDTERM 3</b>	
<b>Week 11 Background reading:</b> Khrapko, K., Vijg, J. (2009) Mitochondrial DNA mutations and aging: devils in the details? <i>Trends Genetics</i> 25: 91-98.		
<b>Week 11 Discussion papers (2):</b> Vermulst et al (2008) DNA deletions and clonal mutations drive premature aging in mitochondrial mutator mice. <i>Nature Genetics</i> 40:392-4. Edgar D et al. Random point mutations with major effects on protein-coding genes are the driving force behind premature aging in mtDNA mutator mice. <i>Cell Metab.</i> 2009 Aug;10(2):131-8.		
<b>Week 12:</b> 11 Nov	Tower	Stem cells
13 Nov	Tower	Stem cells
<b>Week 12 Background reading:</b> Sahin, E., DePinho, R. A. (2010) Linking functional decline of telomeres, mitochondria and stem cells during aging. <i>Nature</i> 464:520-528.		
<b>Week 12 Discussion paper:</b> Conboy et al (2005) Rejuvenation of aged progenitor cells by exposure to a young systemic environment. <i>Nature</i> 433:760-764.		
<b>Week 13:</b> 18 Nov	Tower	Cellular senescence, telomeres
20 NOV	Tower	Progerias
<b>Week 13 Background reading:</b> Martin et al (2007) Genetic determinants of human health span and life span: progress and new opportunities. <i>PLOS Genetics</i> 3:e125.		

<b>Week 13 Background reading:</b> Martin et al (2007) Genetic determinants of human health span and life span: progress and new opportunities. PLOS Genetics 3:e125.		
<b>Week 13 Discussion paper:</b> Curran, S. P., et al (2009) A soma-to-germline transformation in long-lived <i>Caenorhabditis elegans</i> mutants. Nature 459:1079-1084.		
<b>Week 14:</b> 25 Nov	Tower	Sirtuins, DR and IIS
27 Nov	<b>THANKSGIVING</b>	
<b>Week 14 Background reading:</b> Tower, J. Arbeitman, M. 2009. The genetics of gender and life span. J Biol 8:38. Tower, J. 2006. Sex-specific regulation of aging and apoptosis. Mech Ageing Dev 127:705-18.		
<b>Week 14 Discussion paper: No discussion this week.</b>		
<b>Week 15:</b> 2 Dec	Tower	Sleep and rhythms
4 Dec		Replicators, Game theory, SAP
<b>Week 15 Background reading:</b>		
<b>Week 15 Discussion paper:</b> Camus et al., Mitochondria, Maternal Inheritance, and Male Aging, Current Biology (2012), <a href="http://dx.doi.org/10.1016/j.cub.2012.07.018">http:// dx.doi.org/10.1016/j.cub.2012.07.018</a>		

**Grading:** Midterm I 100 pts  
Midterm II 100 pts  
Midterm III 100 pts  
Final 100pts (non cumulative)  
Discussion participation: 100 pts  
TOTAL = 500 pts

Letter grades are determined by a curve based upon total points.

**Other Policies:**

1. Exam dates are firm. If a student misses an exam due to a true emergency (with an acceptable written excuse; written information concerning a death in the family must be provided), we MAY schedule a make-up exam, or at our discretion MAY permit the use of the average of other exams in determining the course grade. No one will be admitted to an exam after the first student has left the exam.
2. Regrading of exams will be done only by the professor who wrote the question. Regrading can only be done within one week of the day the exam is initially returned to the class.
3. **No special assignments for extra credit are given.**
4. Final exams will be kept in Dr. Forsburg's office for the required period.

**5. Academic integrity policies of the university will be strictly followed. Infractions can result in severe penalties. See SCampus for these policies.**

6. It may be necessary to make some adjustments in the syllabus during the semester.

7. Disability: Students requesting academic accommodations based on a disability are required to register with Disability Services and Programs (DSP) each semester. A letter of verification for approved accommodations can be obtained from DSP when adequate documentation is filed. Please be sure the letter is delivered to Dr. Tower or Dr. Forsburg as early in the semester as possible. DSP is open Mon-Fri, 8:30-5:00. The office is in Student Union 301 and their phone number is 740-0776.