**BISC 403 FALL 2017 ADVANCED MOLECULAR BIOLOGY Version 1**

Lectures: Tues-Thurs 12:30 – 1:50, ZHS163

Sections: Tues 4-5.50 VKC108 OR Weds 2-3:50 THH209

**Professors**:

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| Prof. Susan Forsburg, Office: RRI 104C Office hours: Thurs 2-3, and by appointment Tel/vox: (213) 740-7342, email: forsburg@usc.edu | Prof. John TowerOffice: RRI 219C Office hours: Tues 10-12 and by appointment.Tel/vox: (213) 740-5384email: jtower@usc.edu | TA: Meghan Petrieinfo to follow |

**Prerequisites:** BISC 320L (Molecular Biology) is a firm prerequisite for this course. BISC325 recommended.

**Overview:** Our 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 current research. A key part of this course develops skills reading primary research papers in discussion.

**Learning Objectives:**Develop the ability to think critically, analyze, synthesize, and use information to solve problems.

Understand and apply the scientific method, including forming hypotheses, designing experiments to test hypotheses, and collecting, analyzing, interpreting, and reporting data.

Develop the ability to evaluate primary scientific literature.

Acquire an appreciation for all levels of biological organization, including the molecular, cellular, organismal, and systems levels.

Understand the processes that underlie development, cellular differentiation, and reproduction.

Understand the synthesis, structure, and function of nucleic acids and proteins in prokaryotes and eukaryotes.

Understand the principles of inheritance from molecular mechanisms to population consequences.

Understand the flow of genetic information in populations and the relationship between genetics and evolutionary theory.

Understand the functioning of organisms, at the molecular, cellular, organ, and organismal levels.

**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). 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 instructor 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 sections will account for 20% of your grade.**

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| Date | Lecturer | Topic |
| **SECTION 1: EPIGENETICS**Allis CD, Jenuwein T. The molecular hallmarks of epigenetic control. Nat Rev Genet. 2016 Aug;17(8):487-500. doi: 10.1038/nrg.2016.59. Epub 2016 Jun 27. Review. |
| **Week 1:** **21 August** | **Forsburg** | **Introduction to Chromosomes** |
| **23 August** | **Forsburg** | **Histones, nucleosomes, nucleosome assembly; Methods of analysis** |
| **Week 1 Additional reading:** Cutter AR1, Hayes JJ2. A brief review of nucleosome structure. FEBS Lett. 2015 Oct 7;589:2914-22.Larson DR, Misteli T. The genome-seeing it clearly now. Science. 2017 Jul 28;357(6349):354-355. **Discussion paper:** Electron microscopic and biochemical evidence that chromatin structure is a repeating unit. Oudet P, Gross-Bellard M, Chambon P. Cell. 1975 Apr;4(4):281-300. |
| **Week 2:** **28 Aug** | **Forsburg** | **Chaperones; chromatin remodeling I** |
| **30 Aug** | **Forsburg** | **Chromatin remodeling II; histone modifications I** |
| **Week 2 Background reading**Tyagi M, Imam N, Verma K, Patel AK. Chromatin remodelers: We are the drivers!! Nucleus. 2016 Jul 3;7(4):388-404Hammond CM1, Strømme CB1, Huang H2, Patel DJ2, Groth A1 Histone chaperone networks shaping chromatin function. Nat Rev Mol Cell Biol. 2017 Mar;18(3):141-158. **Discussion paper:** Allfrey VG, Faulkner R, Mirsky AE. Acetylation and methylation of histones and their possible role in the regulation of RNA synthesis. Proc Natl Acad Sci U S A. 1964 May;51:786-94. |
| **Week 3:**4 Sept  | Forsburg | Histone Modifications II;  |
| 6 Sept | Forsburg | binding motifs , Histone variants. |
| **Week 3 Background reading:** Rothbart SB1, Strahl BD2. Interpreting the language of histone and DNA modifications. Biochim Biophys Acta. 2014 Aug;1839(8):627-43. doi: 10.1016/j.bbagrm.2014.03.001. Epub 2014 Mar 12.Talbert PB1, Henikoff S1 Histone variants on the move: substrates for chromatin dynamics. Nat Rev Mol Cell Biol. 2017 Feb;18(2):115-126. **Discussion paper:** Wojcik F1, Dann GP1,2, Beh LY1,3,4, Debelouchina GT1,5, Hofmann R1,6, Muir TW7Nat Commun. 2018 Apr 11;9(1):1394. doi: 10.1038/s41467-018-03895-5.Functional crosstalk between histone H2B ubiquitylation and H2A modifications and variants.. |
| **Week 4:** 11 Sept | Forsburg | RNAi & CRISPR |
| 13 Sept |  MIDTERM 1 |  |
| **Background reading Week 4**Castel SE, Martienssen RA. RNA interference in the nucleus: roles for small RNAs in transcription, epigenetics and beyond. Nat Rev Genet. 2013 Feb;14(2):100-12. doi: 10.1038/nrg3355. **Review**.van der Oost J1, Westra ER2, Jackson RN3, Wiedenheft B3 Nat Rev Microbiol. 2014 Jul;12(7):479-92. Unravelling the structural and mechanistic basis of CRISPR-Cas systems.**Discussion paper:** Gullerova M, Moazed D, Proudfoot NJ.Genes Dev. 2011 Mar 15;25(6):556-68. Autoregulation of convergent RNAi genes in fission yeast. |
| **Week 5:** 18 Sept | Forsburg | Case study: heterochromatin and silencing  |
| 20 Sept | Forsburg | Case study: Centromeres and chromosome segregation |
| **Background reading Week 5** McKinley K ad Cheeseman I. The molecular basis for centromere identity and function Nat Rev Mol Cell Biol. 2016 Jan;17(1):16-29.Allshire RC1, Madhani HD2,3. Ten principles of heterochromatin formation and function.Nat Rev Mol Cell Biol. 2018 Apr;19(4):229-244. doi: 10.1038/nrm.2017.119. Epub 2017 Dec 13.**Discussion paper:**  Ohzeki J1, Shono N1, Otake K1, Martins NM2, Kugou K1, Kimura H3, Nagase T4, Larionov V5, Earnshaw WC2, Masumoto H6. KAT7/HBO1/MYST2 Regulates CENP-A Chromatin Assembly by Antagonizing Suv39h1-Mediated Centromere Inactivation. Dev Cell. 2016 Jun 6;37(5):413-27. doi: 10.1016/j.devcel.2016.05.006. |
| **Week 6:** 25 Sept | Forsburg | Case study: DNA damage response  |
| 27 Sept | Forsburg | Case study: DNA methylation & Imprinting |
| **Background reading Week 6**J Mol Biol. 2015 Feb 13;427(3):626-36. doi: 10.1016/j.jmb.2014.05.025. Epub 2014 Jun 2.Reshaping chromatin after DNA damage: the choreography of histone proteins.Li E1, Zhang Y. DNA methylation in mammals.Cold Spring Harb Perspect Biol. 2014 May 1;6(5):a019133. doi: 10.1101/cshperspect.a019133.Jennifer Couzin-FrankelJan. 12, 2017 , A mysterious method of gene control sheds its secrets Science DOI: 10.1126/science.aal0613**Discussion paper:** Kirioukhova O1,2, Shah JN1, Larsen DS1, Tayyab M1, Mueller NE1, Govind G1,3, Baroux C4, Federer M4, Gheyselinck J4, Barrell PJ4,5, Ma H4,6,7, Sprunck S8, Huettel B9, Wallace H10, Grossniklaus U11, Johnston AJ12,13,14,15.Sci Rep. 2018 Jul 13;8(1):10626. doi: 10.1038/s41598-018-27863-7.Aberrant imprinting may underlie evolution of parthenogenesis. |
| **Week 7:**2 Oct | Forsburg | Case Study: Epigenetics and cancer |
| 4 Oct | Forsburg | Case Study: Epigenetics and the environment |
| **Background reading Week 7**Baylin SB, Jones PA. Epigenetic Determinants of Cancer. Cold Spring Harb Perspect Biol. 2016 Sep 1;8(9). pii: a019505. doi: 10.1101/cshperspect.a019505. Review.Feil R, Fraga MF. Epigenetics and the environment: emerging patterns and implications.Nat Rev Genet. 2012 Jan 4;13(2):97-109. doi: 10.1038/nrg3142. Review.**discussion paper:**The histone H3.3K27M mutation in pediatric glioma reprograms H3K27 methylation and gene expression.Chan KM, Fang D, Gan H, Hashizume R, Yu C, Schroeder M, Gupta N, Mueller S, James CD, Jenkins R, Sarkaria J, Zhang Z. Genes Dev. 2013 May 1;27(9):985-90. doi: 10.1101/gad.217778.113. Epub 2013 Apr 19.Background for this paper: http://www.asbmb.org/asbmbtoday/201506/Features/DIPG/ |

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| **Week 8**9 Oct | MIDTERM 2  |   |
| SECTION 2: AGING |
| 11 Oct | Tower | Evolutionary theories of aging |
| **Week 8 Background reading:** Hughes, K. A., and R. M. Reynolds (2005) Evolutionary and Mechanistic Theories of Aging. Annu. Rev. Entomol. 50:421-45.Tower, J. (2015) Mitochondrial maintenance failure in aging and role of sexual dimorphism. Archives Biochem Biophys 576:17-31**Week 8 Discussion paper:** 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. Gene 385, 64-70. |
| **Week 9 :** 16 Oct | Tower | Mechanistic theories of aging |
| 18 Oct | Tower | Mechanistic theories of aging |
| **Week 9 Background reading:** Kaeberlein, M. (2010) Lessons on longevity from budding yeast. Nature 464:513-519.**Week 9 Discussion paper:** Mair et al (2003) Demography of Dietary Restriction and Death in Drosophila. Science 301:1731 |
| **Week 10:** 23 Oct | Tower | Gene expression during aging |
| 25 Oct | Tower | Oxidative stress and damage |
| **Week 10 Background reading:** Tower, J (2009) Hsps and aging. Trends Endocrinol Metab 20:216-22.**Week 10 Discussion paper:** Kenyon, C. J. et al (1993) A C. elegans mutant that lives twice as long as wild type. Nature 366:461-4. |
| **Week 11:** 30 Oct | Tower | Mitochondria |
| 1 Nov | MIDTERM 3 |  |
| **Week 11 Background reading:** Tower, J. (2015) Programmed cell death in aging. Ageing Res Rev SepPtA: 90-100.**Week 11 Discussion paper:** Katajisto et al (2015) Asymmetric apportioning of aged mitochondria between daughter cells is required for stemness. Science 348:340-343. |
| **Week 12:** 6 Nov | Tower | Stem cells |
| 8 Nov | Tower | Stem cells |
| Week 12 Background reading: Sahin, E., DePinho, R. A. (2010) Linking functional decline of telomeres, mitochondria and stem cells during aging. Nature 464:520-528.**Week 12 Discussion paper:** Conboy et al (2005) Rejuvenation of aged progenitor cells by exposure to a young systemic environment. Nature 433:760-764. |
| **Week 13:** 13 Nov | Tower | Cellular senescence, telomeres |
| 15 Nov | Tower | Progerias |
| **Week 13 Background reading:** Martin et al (2007) Genetic determinants of human health span and life span: progress and new opportunities. PLOS Genetics 3:e125.**Week 13 Discussion paper:**  Curran, S. P., et al (2009) A soma-to-germline transformation in long-lived Caenorhabditis elegans mutants. Nature 459:1079-1084. |
| **Week 14:** 20 Nov | Tower | Sirtuins, DR and IIS |
| 22 Nov | THANKSGIVING  |  |
| **Week 14 Background reading: None****Week 14 Discussion paper: No discussion this week.** |
| **Week 15:** 27 Nov | Tower | Sleep and rhythms |
| 29 Nov |  | Replicators, Game theory, SAP |
| **Week 15 Background reading:** Tower, J. (2015) Mitochondrial maintenance failure in aging and role of sexual dimorphism. Archives Biochem Biophys 576:17-31**Week 15 Discussion paper:**  Camus et al., Mitochondria, Maternal Inheritance, and Male Aging, Current Biology (2012), http:// dx.doi.org/10.1016/j.cub.2012.07.018 |
| **Final** | Date and time in the course catalogue |  |

**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 based upon total points. We do not generally curve the course.

**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. We do not re-grade exams written in pencil.

**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.