

BISC 403 FALL 2022 ADVANCED MOLECULAR BIOLOGY

Lectures: Tues-Thurs 12:30 – 1:50 KAP 163

Sections: Tues 4-5.50 KAP 141 OR Weds 2-3:50 KAP 137 226

Professors:

Prof. Susan Forsburg, Office: RRI 104C Office hours: , and by appointment Tel/vox: (213) 740-7342, email: forsburg@usc.edu	Prof. John Tower Office: RRI 219C Office hours: Tues 10-12 and by appointment. Tel/vox: (213) 740-5384 email: jtower@usc.edu	TA: TBA Office TBA Office Hours TBA
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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 ageing.

Understand the synthesis, structure, and function of nucleic acids and regulation by epigenetics

Understand the principles of epigenetic 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.**

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: 23 August	Forsburg	Introduction to Chromosomes, histones, nucleosomes
25 August	Forsburg	2-Nucleosome assembly; Methods of analysis, Chaperones
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. Hammond 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: 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: 30 Aug	Forsburg	chromatin remodeling
1 Sept	Forsburg	histone modifications
Week 2 Background reading Tyagi M, Imam N, Verma K, Patel AK. Chromatin remodelers: We are the drivers!! Nucleus. 2016 Jul 3;7(4):388-404 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.bbagr.2014.03.001. Epub 2014 Mar 12.		
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: 6 Sept	Forsburg	binding motifs , Histone variants.
8 Sept	Forsburg	RNAi & CRISPR
Talbert PB1, Henikoff S1 Histone variants on the move: substrates for chromatin dynamics. Nat Rev Mol Cell Biol. 2017 Feb;18(2):115-126. 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. 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.		
Discussion paper: Long et al (2020), H2A.Z facilitates licensing and activation of early replication origins. Nature 577 :576.		
Week 4: 13 Sept	Forsburg	Case study: heterochromatin and silencing

15 Sept	Forsburg	MIDTERM 1
<p>Background reading Week 4 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.</p> <p>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.</p>		
Week 5: 20 Sept	Forsburg	Case study: Centromeres and chromosome segregation
22 Sept	Forsburg	Case Study: Genome organization
<p>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. Misteli, T. The Self-Organizing Genome: Principles of Genome Architecture and Function</p> <p>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. <u>Dev Cell</u>. 2016 Jun 6;37(5):413-27. doi: 10.1016/j.devcel.2016.05.006.</p>		
Week 6: 27 Sept	Forsburg	Case study: DNA methylation & Imprinting
29 Sept	Forsburg	Case Study: Epigenetics and cancer
<p>Background reading Week 6 Li E1, Zhang Y. DNA methylation in mammals. 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. 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</p> <p>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/</p>		
Week 7: 4 Oct	Forsburg	Case Study: Epigenetics and the environment
6 Oct	MIDTERM 2	

Background reading Week 7

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:

López-Rodríguez et al (2021) Multi- and Transgenerational Outcomes of an Exposure to a Mixture of Endocrine-Disrupting Chemicals (EDCs) on Puberty and Maternal Behavior in the Female Rat. Environmental Health Perspectives <https://doi.org/10.1289/EHP8795>

Week 8 11 Oct	Tower	Evolutionary theories of aging
SECTION 2: AGING		
13 Oct	FALL RECESS	
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 : 18 Oct	Tower	Mechanistic theories of aging
20 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: 25 Oct	Tower	Gene expression during aging
27 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: 1 Nov	Tower	Mitochondria
3 Nov	MIDTERM 3	
Week 11 Background reading: Tower, J. (2015) Programmed cell death in aging. Ageing Res Rev 23: 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: 8 Nov	Tower	Stem cells
10 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: 15 Nov	Tower	Cellular senescence, telomeres
17 Nov	Tower	Progerias
Week 13 Background reading: None		
Week 13 Discussion paper: Lynn et al (2015) Omega-3 and -6 fatty acids allocate somatic and germline lipids to ensure fitness during nutrient and oxidative stress in <i>Caenorhabditis elegans</i> . PNAS 112:15378-15383.		
Week 14: 22 Nov	Tower	Sirtuins, DR and IIS
24 Nov	THANKSGIVING	
Week 14 Background reading: None		
Week 14 Discussion paper: No discussion this week.		
Week 15: 29 Nov	Tower	Sleep and rhythms
1 Dec	Tower	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. (2015) Single Nucleotides in the mtDNA Sequence Modify Mitochondrial Molecular Function and Are Associated with Sex-Specific Effects on Fertility and Aging. Current Biology 25:2717-2722		
Final	Date and time in the course catalogue	

Grading: Midterm I 100 pts
Midterm II 100 pts
Midterm III 100 pts
Final 100 pts (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. It may be necessary to make some adjustments in the syllabus during the semester.

6. Please advise the faculty ASAP of any known conflicts, any DSP provisions, or other relevant information.

7. Academic Conduct:

Plagiarism – presenting someone else's ideas as your own, either verbatim or recast in your own words – is a serious academic offense with serious consequences. Other forms of academic dishonesty are equally unacceptable (cheating on exams, changing answers before requesting regrade, etc.). We have zero tolerance for academic misconduct. Please familiarize yourself with the discussion of plagiarism in SCampus in Part B, Section 11, "Behavior Violating University Standards" policy.usc.edu/scampus-part-b. See additional information in SCampus and university policies on scientific misconduct, policy.usc.edu/scientific-misconduct.

8. Students are expected to comply with all aspects of USC's COVID-19 policy. Failure to do so may result in removal from the class and referral to Student Judicial Affairs and Community Standards.

9. Support Systems:

Student Health Counseling Services - (213) 740-7711 – 24/7 on call

engemannshc.usc.edu/counseling

Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.

National Suicide Prevention Lifeline - 1 (800) 273-8255 – 24/7 on call

suicidepreventionlifeline.org

Free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week.

Relationship and Sexual Violence Prevention Services (RSVP) - (213) 740-4900 – 24/7 on call

engemannshc.usc.edu/rsvp

Free and confidential therapy services, workshops, and training for situations related to gender-based harm.

Office of Equity and Diversity (OED) | Title IX - (213) 740-5086

equity.usc.edu, titleix.usc.edu

Information about how to get help or help a survivor of harassment or discrimination, rights of protected classes, reporting options, and additional resources for students, faculty, staff, visitors, and applicants. The university prohibits discrimination or harassment based on the following protected characteristics: race, color, national origin, ancestry, religion, sex, gender, gender identity, gender expression, sexual orientation, age, physical disability, medical condition, mental disability, marital status, pregnancy, veteran status, genetic

information, and any other characteristic which may be specified in applicable laws and governmental regulations.

Bias Assessment Response and Support - (213) 740-2421

studentaffairs.usc.edu/bias-assessment-response-support

Avenue to report incidents of bias, hate crimes, and microaggressions for appropriate investigation and response.

The Office of Disability Services and Programs - (213) 740-0776

dsp.usc.edu

Support and accommodations for students with disabilities. Services include assistance in providing readers/notetakers/interpreters, special accommodations for test taking needs, assistance with architectural barriers, assistive technology, and support for individual needs.

USC Support and Advocacy - (213) 821-4710

studentaffairs.usc.edu/ssa

Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.

Diversity at USC - (213) 740-2101

diversity.usc.edu

Information on events, programs and training, the Provost's Diversity and Inclusion Council, Diversity Liaisons for each academic school, chronology, participation, and various resources for students.

USC Emergency - UPC: (213) 740-4321, HSC: (323) 442-1000 – 24/7 on call

dps.usc.edu, emergency.usc.edu

Emergency assistance and avenue to report a crime. Latest updates regarding safety, including ways in which instruction will be continued if an officially declared emergency makes travel to campus infeasible.

USC Department of Public Safety - UPC: (213) 740-6000, HSC: (323) 442-120 – 24/7 on call

dps.usc.edu

Non-emergency assistance or information.