BISC 403 FALL 2023 ADVANCED MOLECULAR BIOLOGY
Lectures: Tues-Thurs 12:30 – 1:50 KAP163
Sections: Tues 4-5.50 GFS221 OR Weds 2-3:50 SOSB52
Professors:

Prof. Irene Chiolo Office: RRI 219A Office hours: Tue 9:30-11:30a email: chiolo@usc.edu	Prof. Oscar Aparicio Office: RRI 219B Office hours: TBD email: aparici@usc.edu	TA: Anik Mitra Office: TBD Office hours: TBD email: anikmitr@usc.edu

Prerequisites: BISC 320L (Molecular Biology) is a firm prerequisite for this course. BISC325 (Genetics) is 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 many levels of biological organization, including the molecular, cellular, and organismal.
Understand the DNA repair response in the context of nuclear architecture and dynamics.
Understand the DNA repair response in the context of chromatin and its crosstalk with transcription.
Understand the impact of DNA repair defects on genome stability of cells and organisms.

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 prepared to state the "take home message" of the paper, the background, the questions addressed by individual experiments, methods/results/conclusions of each figure, overall conclusions of the study, strengths and weaknesses. Did they prove their point? Students will be randomly called upon to **present** and points will be awarded for this presentation. **Discussion sections will account for 20% of your grade.**

Date	Lecturer	Topic
SECTION 1: DSB REPAIR		
Week 1: **22 August**	Chiolo	**DSB repair. Nuclear architecture. ChIP, site-specific DSB systems.**
24 August	Chiolo	Torres-Rosell J et al.. The Smc5-Smc6 complex and SUMO modification of Rad52 regulates recombinational repair at the ribosomal gene locus. Nat Cell Biol. 2007 Aug;9(8):923-31. doi: 10.1038/ncb1619.
Week 1 Background reading: Meaburn, K., Misteli, T. Chromosome territories. *Nature* **445**, 379–381 (2007). https://doi.org/10.1038/445379a Amaral N, Ryu T, Li X, Chiolo I. Nuclear Dynamics of Heterochromatin Repair. Trends Genet. 2017 Feb;33(2):86-100. doi: 10.1016/j.tig.2016.12.004. **Discussion paper:** Nagai S, et al. Functional targeting of DNA damage to a nuclear pore-associated SUMO-dependent ubiquitin ligase. Science. 2008 Oct 24;322(5901):597-602. doi: 10.1126/science.1162790.		
Week 2: **29 Aug**	Chiolo	**Nuclear dynamics. Focus tracking. MSD.**
31 Aug	Chiolo	Roukos V et. al. Spatial dynamics of chromosome translocations in living cells. Science. 2013 Aug 9;341(6146):660-4. doi: 10.1126/science.1237150.
Week 2 Background reading: Miné-Hattab J, Chiolo I. Complex Chromatin Motions for DNA Repair. Front Genet. 2020 Aug 27;11:800. doi: 10.3389/fgene.2020.00800. **Discussion paper:** Miné-Hattab J, Rothstein R. Increased chromosome mobility facilitates homology search during recombination. Nat Cell Biol. 2012 Apr 8;14(5):510-7. doi: 10.1038/ncb2472.		
Week 3: **5 Sept**	Chiolo	**Heterochromatin organization and repair. Focus clustering. Nuclear F-actin.**
7 Sept	Chiolo	Caridi CP, et al., Nuclear F-actin and myosins drive relocalization of heterochromatic breaks. Nature. 2018 Jul;559(7712):54-60. doi: 10.1038/s41586-018-0242-8.
Week 3 Background reading: Caridi CP et al.. Nuclear actin filaments in DNA repair dynamics. Nat Cell Biol. 2019 Sep;21(9):1068-1077. doi: 10.1038/s41556-019-0379-1. **Discussion paper:** Schrank BR et al. Nuclear ARP2/3 drives DNA break clustering for homology-directed repair. Nature. 2018 Jul;559(7712):61-66. doi: 10.1038/s41586-018-0237-5.		

Week 4: **12 Sept**	Chiolo	**Nuclear membrane functions in DSB repair. LINC complex. Microtubules.**

14 Sept	Chiolo	MIDTERM 1
Background reading Week 4 **Discussion paper:** Shokrollahi et al., DNA double-strand break-capturing nuclear envelope tubules drive DNA repair. bioRxiv 2023.05.07.539750; doi: https://doi.org/10.1101/2023.05.07.539750		
Week 5: **19 Sept**	Chiolo	**Phase separation of repair sites**
21 Sept	Chiolo	Spegg V. et al. Phase separation properties of RPA combine high-affinity ssDNA binding with dynamic condensate functions at telomeres. Nat Struct Mol Biol. 2023 Apr;30(4):451-462. doi: 10.1038/s41594-023-00932-w.
Background reading Week 5 Aguzzi A, Altmeyer M. Phase Separation: Linking Cellular Compartmentalization to Disease. Trends Cell Biol. 2016 Jul;26(7):547-558. doi: 10.1016/j.tcb.2016.03.004. **Discussion paper:** Altmeyer M, et al. Liquid demixing of intrinsically disordered proteins is seeded by poly(ADP-ribose). Nat Commun. 2015 Aug 19;6:8088. doi: 10.1038/ncomms9088.		
Week 6: **26 Sept**	Chiolo	**Transcription, ncRNAs**
28 Sept	Chiolo	Pessina F, et al. Functional transcription promoters at DNA double-strand breaks mediate RNA-driven phase separation of damage-response factors. Nat Cell Biol. 2019 Oct;21(10):1286-1299. doi: 10.1038/s41556-019-0392-4.
Background reading Week 6 d'Adda di Fagagna F. A direct role for small non-coding RNAs in DNA damage response. Trends Cell Biol. 2014 Mar;24(3):171-8. doi: 10.1016/j.tcb.2013.09.008 **Discussion paper:** Michelini F. et al.. Damage-induced lncRNAs control the DNA damage response through interaction with DDRNAs at individual double-strand breaks. Nat Cell Biol. 2017 Dec;19(12):1400-1411. doi: 10.1038/ncb3643.		
Week 7: **3 Oct**	Chiolo	**Loop extrusion. HiC**
5 Oct	MIDTERM 2	

Background reading Week 7

Rowley MJ, Corces VG. Organizational principles of 3D genome architecture. Nat Rev Genet. 2018 Dec;19(12):789-800. doi: 10.1038/s41576-018-0060-8.

Discussion paper:

Arnould C, et al. Loop extrusion as a mechanism for formation of DNA damage repair foci. Nature. 2021 Feb;590(7847):660-665. doi: 10.1038/s41586-021-03193-z

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. Aparicio's office for the required period.

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

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

2. **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.

3. 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.