

**NUCLEIC ACIDS, BIOSC 2150
SPRING TERM, 2013**

Instructors

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Office hours By appointment

Class meetings Lectures: Tuesdays 2:00-3:50 pm, 241 Crawford Hall
Note that class meetings are mandatory. Students are expected to attend and participate in all class meetings.

Course description

This course will focus on the molecular biology of DNA and RNA, and how biological information is stored, replicated, recombined, and processed. Topics to be discussed include: DNA Replication and its regulation; DNA Segregation; Homologous, Illegitimate and Site-specific Recombination; DNA Repair; RNA folding; perspectives on The RNA World; Aptamers and Riboswitches; Transfer RNA processing and quality control; Telomerase structure and function; Alternative pre-mRNA splicing regulation and evolution. This course will be taught at an advanced level with an emphasis on the primary literature. Prerequisites: undergraduate coursework in genetics and molecular biology.

Class meetings & format

Class meetings will primarily involve in-depth discussions of the reading assignments. Overviews of the topics to be discussed may involve mini lectures or workshops that integrate background material, including historical context, and Big Picture issues. For in-depth discussions of the papers, students should come prepared to present and critique different parts of the paper, including individual figures. To facilitate class discussions, instructors will post, in advance of the class meeting, 5 or 6 thought questions about the paper(s) to be discussed. It will be helpful to bring with you to class written responses to the posted questions.

Students will be expected to:

- Come to class well prepared to discuss the basic elements of each assigned paper, including the central question or hypothesis, the logic of the approaches used, the results found, conclusions and implications of the work, and questions remaining.
- Be prepared to apply their understanding of the papers discussed to new situations and challenges, such as to the construction and testing of a new (or alternate) hypothesis, or to the design of the next logical series of experiments, prediction of possible results, and discussion of possible pitfalls of the approaches.
- Be prepared to make a call as to the strengths and weaknesses of different elements of the paper.
- Take the initiative to do background reading as needed to understand terminology and concepts in the area of the subject matter to be discussed.

Reading assignments

This course will involve intensive reading. Reading assignments will be finalized one week in advance of the class meeting via postings on Courseweb. *Come to class prepared, and make this a regular habit.* Your advance preparation will enable you to contribute substantively to class discussions and workshop projects. Note that written quizzes and assignments will be also given weekly at the discretion of the instructor to test your understanding of the reading assignments.

- **Bring electronic or paper copies of the assigned papers with you to class.**

Courseweb

We will be using Courseweb to post the course materials and assignments. You will be responsible for all material posted on Courseweb, so accessing this site on a regular basis for updates, postings, and assignments will be helpful.

Grading

- 40% Instructor-specific assignments (10 points/class x 15 classes = 150 points)
- 40% News & Views Papers (two papers at 75 points each = 150 points)
- 20% Class participation (5 points/class x 15 classes = 75 points)

Final grades will be based on the following scale: percentages in the 90's = A range; 80's = B range; 70's = C range; 60's = D range; 50 or below = F.

News & Views Assignments will be due on Feb 19 (#1) and Apr 16 (#2)

- The News & Views paper should be 3 pages in length, single-spaced, **with one figure** similar to articles found in Science and Nature (see Courseweb for examples). The figure and references do not count in the 3-page limit.
- Focus: The paper should be carefully crafted to describe the **highlights and future perspectives** of one research paper closely related but not actually covered in class.

Academic Integrity

Students in this course will be expected to comply with the [University of Pittsburgh's Policy on Academic Integrity](#). Any student suspected of violating this obligation for any reason during the semester will be required to participate in the procedural process, initiated at the instructor level, as outlined in the University Guidelines on Academic Integrity. This may include, but is not limited to, the confiscation of the examination of any individual suspected of violating University Policy. Furthermore, no student may bring any unauthorized materials to an exam, including dictionaries and programmable calculators.

Disability Services

If you have a disability that requires special testing accommodations or other classroom modifications, you need to notify both the instructor and [Disability Resources and Services](#) no later than the second week of the term. You may be asked to provide documentation of your disability to determine the appropriateness of accommodations. To notify Disability Resources and Services, call (412) 648-7890 (Voice or TTD) to schedule an appointment. The Disability Resources and Services office is located in 140 William Pitt Union on the Oakland campus.

Copyright Notice

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Statement on Classroom Recording

To ensure the free and open discussion of ideas, students may not record classroom lectures, discussion and/or activities without the advance written permission of the instructor, and any such recording properly approved in advance can be used solely for the student's own private use.

SCHEDULE OF CLASS MEETINGS & ASSIGNMENTS (Note that reading assignments will be finalized one week in advance of the class meeting)

	Dates	Lecture Topics & Instructor	Instructor	Reading Assignments Bkrd = background reading
Week 1	Jan 8	<i>Introduction to the course</i> DNA polymerases and Prokaryotic DNA Replication	Grabowski Schwacha	McHenry 2011
Week 2	Jan 15	DNA polymerase (continued) Eukaryotic Replication	Schwacha	Reyes-Lamothe 2010 Indiani 2009 Gai 2010 (Bkrd)
Week 3	Jan 22	Genome architecture: What's in there, what does it do, how is it organization, and did it get to be that way	Hatfull	Pedulla 2003
Week 4	Jan 29	Eukaryotic DNA replication (continued) Replication of Chromatin	Schwacha	Remus 2009 Yardimci 2010 Albert 2012 (Bkrd)
Week 5	Feb 5	Replication of Chromatin (continued) Chromosome cohesion and condensation	Schwacha	Smith 1989 Eaton 2010 Hirano 2006
Week 6	Feb 12	Chromosome cohesion and condensation (continued) Homologous recombination and Non-homologous end joining	Schwacha	Onn 2011 Uhlmann 2000 Symington 2011 (Bkrd)
Week 7	Feb 19	<i>News & Views Paper #1 due</i> Conservative site-specific recombination: changing partners and doing the twist, here, there, and everywhere	Hatfull	Grindley 2006
Week 8	Feb 26	Predicting RNA folds using energy minimization and chemical probing The RNA World: Perspectives on origins of catalysis	Grabowski	Weeks 2010 Deigan 2009 Cech 2009
Week 9	Mar 5	Aptamers and Riboswitches Part 1: Overview of biology & medical applications	Grabowski	Gold 2012 Breaker 2012
	Mar 10-17	SPRING BREAK		
Week 10	Mar 19	Aptamers and Riboswitches Part 2: Discovery of Fluoride Riboswitch	Grabowski	Baker 2011
Week 11	Mar 26	Transfer RNA processing, misfolding and turnover	Grabowski	Wilusz 2011
Week 12	Apr 2	Telomerase	Berman	Podlevsky 2012 Chen 2003 Zhang 2011
Week 13	Apr 9	Alternative pre-mRNA splicing: transcriptome-wide regulation	Grabowski	Wang 2012
Week 14	Apr 16	<i>News & Views Paper #2 due</i> Alternative pre-mRNA splicing: evolutionary dynamics	Grabowski	Merkin 2012
Week 15	Apr 23	Workshop on News & Views papers	Grabowski	N/A
FINAL		This course will not have a final exam.		

List of reading assignments by instructor (tentative)

Schwacha

- McHenry, C.S. 2011 Bacterial Replicases. *Current Opinions in Chemical Biology*, 15:587-594.
- Reyes-Lamothe, R., Sherratt, DJ, and MC Leake. 2010 Stoichiometry and Architecture of Active DNA replication Machinery in *Escherichia coli*. *Science* **328**:4989
- Indiani et. al. 2009 Translesion DNA polymerases remodel the replisome and alter the speed of the replicative helicase. *PNAS* 106: 6031-6038.
- Gai et. al. 2010 Origin DNA melting and unwinding in DNA replication. *Current Opinions in Structural Biology* 20:756-762.
- Remus D., Beuron, F., Tolun G., Griffith, J.D., Morris E.P., and Diffley J.F. 2009. Concerted loading of Mcm2-7 double hexamers around DNA during DNA replication origin licensing. *Cell* 139:719-730.
- Yardimci H., Loveland, A.B., Habuchi S., van Oijen, A.M. and Walter J.C. 2010 Uncoupling of Sister Replisomes during Eukaryotic DNA replication. *Mol. Cell* 40:834-840.
- Albert C., and Groth A. 2012 Chromatin replication and epigenome maintenance. *Nature Reviews Molecule Cell Biology* 13:153-167
- Smith S., Stillman B. 1989 Purification and Characterization of CAF-1, a human Cell factor required for Chromatin Assembly during DNA Replication in vitro. *Cell* 58:15-25.
- Eaton ML., Galani K., Kang S, Bell SP., MacAlpine DM. 2010. Conserved nucleosome positioning defines replication origins. *Genes Dev.* **24**:748-53.
- Hirano T. 2006 At the Heart of the Chromosome: SMC proteins in action. *Nat. Rev. Mol Cell Biol.* 7:311-322.
- Onn I., Koshland, D. 2011 In Vitro assembly of Physiological cohesin/DNA complexes. *PNAS* 108:12198-12205
- Uhlmann F., Wernic D., Poupard M-A., Koonin E.V., Nasmyth K, 2000 Cleavage of Cohesin by the CD Clan Protease Separin Triggers Anaphase in Yeast. *Cell* 103:375-386
- Symington LS., and Gautier J. 2011 Double-strand break end resection and repair pathway choice. *Annu Rev Genet* 45:247-271.

Hatfull

- *Cell*. 2003 Apr 18;113(2):171-82. Origins of highly mosaic mycobacteriophage genomes. Pedulla ML, Ford ME, Houtz JM, Karthikeyan T, Wadsworth C, Lewis JA, Jacobs-Sera D, Falbo J, Gross J, Pannunzio NR, Brucker W, Kumar V, Kandasamy J, Keenan L, Bardarov S, Kriakov J, Lawrence JG, Jacobs WR Jr, Hendrix RW, Hatfull GF.
- *Annu Rev Biochem.* 2006;75:567-605. Mechanisms of site-specific recombination. Grindley ND, Whiteson KL, Rice PA.

Grabowski

- *Cell*. 2009:599-602. Crawling out of the RNA world. Cech TR.
- *Curr Opin Struct Biol.* 2010:295-304. Advances in RNA structure analysis by chemical probing. Weeks KM.
- *Proc Natl Acad Sci U S A.* 2009:97-102. Accurate SHAPE-directed RNA structure determination. Deigan KE, Li TW, Mathews DH, Weeks KM.
- *Cold Spring Harb Perspect Biol.* 2012. Aptamers and the RNA world, past and present. Gold L, Janjic N, Jarvis T, Schneider D, Walker JJ, Wilcox SK, Zichi D.
- *Cold Spring Harb Perspect Biol.* 2012 Feb 1;4(2). Riboswitches and the RNA world. Breaker RR.
- *Science.* 2012 Jan 13;335(6065):233-5. Epub 2011 Dec 22. Widespread genetic switches and toxicity resistance proteins for fluoride. Baker JL, Sudarsan N, Weinberg Z, Roth A, Stockbridge RB, Breaker RR.
- *Science.* 2011 Nov 11;334(6057):817-21. tRNAs marked with CCACCA are targeted for degradation. Wilusz JE, Whipple JM, Phizicky EM, Sharp PA.
- *Mol Cell.* 2010 Mar 12;37(5):597-606. Box H/ACA small ribonucleoproteins. Kiss T, Fayet-Lebaron E, Jády BE.
- *Cell.* 2012 Aug 17;150(4):710-24. doi: 10.1016/j.cell.2012.06.041. Transcriptome-wide regulation of pre-mRNA splicing and mRNA localization by muscleblind proteins. Wang ET, Cody NA, Jog S, Biancolella M, Wang TT, Treacy DJ, Luo S, Schroth GP, Housman DE, Reddy S, Lécuyer E, Burge CB.
- *Science.* 2012 Dec 21;338(6114):1593-9. doi: 10.1126/science.1228186. Evolutionary dynamics of gene and isoform regulation in Mammalian tissues. Merkin J, Russell C, Chen P, Burge CB.

Berman

- Podlevsky JD, Chen JJ. (2012). It all comes together at the ends: telomerase structure, function, and biogenesis. *Mutat Res.* **730**, 3-11.
- Chen JL, Greider CW. (2003). Determinants in mammalian telomerase RNA that mediate enzyme processivity and cross-species incompatibility. *EMBO J.* **22**, 304-14.
- Zhang Q, Kim NK, Feigon J. (2011). Architecture of human telomerase RNA. *Proc Natl Acad Sci U S A.* **108**, 20325-32.