BIOSC 1945 Advanced Molecular Genetics

SPRING 2024

Faculty	Craig Kaplan 202A Life Sciences Annex **Preferred contact:** craig.kaplan@pitt.edu **Office phone (emergencies):**
Class Meeting	**Monday/Wednesday 3:00 pm - 4:15 pm 332 CATHEDRAL OF LEARNING** **Office Hours: In person Tuesdays 3:00 pm - 4:00 pm 102 Clapp Hall** **We will discuss a second scheduled time for Zoom office hours**
Course Objectives	Our class will be a series of modules, each focused on a particular cellular system and covering a biological vignette based on a paper from the primary literature. •Going deeper into the molecular biology of cells and the interfaces between molecular pathways for transcription, translation, RNA processing, DNA replication, and DNA damage. We will touch on paradigms for surveillance that introduce signaling concepts, and post-translational modification and control. •Experience with modern, cutting edge papers from the primary literature. •Understanding the scope and complexity of biological systems through current review articles. •Exposure and understanding of experimental techniques employed in our example papers.
Prerequisites	PREQ: BIOSC 1940; Minimum grade 'C'
Textbook	**Molecular Biology: Principles of Genome Function Third Edition**. *This is the same textbook utilized for BIOSC 1940. This textbook will serve as "backstop" for review/refresher of topics covered in 1940 as we go deeper. We will supplement the textbook with required readings from the primary literature.*

Learning Management System (LMS)	We are using Canvas as our LMS. Announcements will be posted to Canvas. Assignments/Problem Sets will be submitted to Canvas. Exams are in person and will be graded using Gradescope. Recorded lectures will be available on the Panopto page in Canvas. Any Zoom meetings (e.g. remote office hours, remote Exam review sessions) will be accessible on the Zoom link in Canvas.
Email Communication	All course announcements will be made on Canvas but it is possible that I may need to email students directly. **I would recommend that your notification settings for Canvas are such that you receive announcements as email as well**. You are expected to monitor your University-provided email account on a regular basis (good practice is at minimum twice a day). Failure to read University communications in a timely manner is not a valid excuse for understanding and complying with the content of electronic communications. While you may have University email forwarded to a non-University address of your choice, you do this at your own risk. Email forwarding may be managed at http://accounts.pitt.edu.
Grading	Grades will be determined through weighting of different forms of assessment, from Problem Sets to exams. **A+** 98.0-100% **A** 92.0-97.9% **A-** 90.0-91.9% **B+** 88.0-89.9% **B** 82.0-87.9% **B-** 80.0-81.9% **C+** 78.0-79.9% **C** 72.0-77.9% **C-** 70.0-71.9% **D+** 68.0-69.9% **D** 62.0-67.9% **D-** 60.0-61.9% **F** 59.9% and below

Grading weights	**Exams: 300 points total (100 apiece for two midterms and one final exam)** **Problem Sets: 100 points total (20 points per problem set)** **Paper Summary Sheets: 105 points total (15 points per summary sheet)** **Bonus points: Problem set assessments up to 25 points total (0, 2.5, or 5 points per problem set).** **Grade scale may be adjusted downwards (relaxed) but will not be adjusted upwards (more stringent)**
Academic integrity and student code of conduct	Cheating/plagiarism are violations of academic integrity. Students suspected of violating the University of Pittsburgh Code on Academic Integrity (https://www.as.pitt.edu/faculty/policies-and-procedures/academic-integrity-code) will be required to participate in the outlined procedural process as initiated by the instructor. A **minimum** sanction of a zero score for the assignment, exam or paper will be imposed. **Only explicitly discussed or stated in writing authorized materials may be used during homework or exams.** All other aids should be considered unauthorized unless explicitly authorized. Communication with any other student or individual that is not a TA/UTA/Professor of record for the course during an exam about the exam is not authorized. Course materials are not allowed to be distributed in any form, including but not limited to uploading or otherwise communicating material to any third party. You must submit for grading only material that is written exclusively in your own words and written or drawn by you, and not anything adapted from someone else's work. Violation of the Academic Integrity Code requires the instructor to submit an Academic Integrity Violation Report to the Dean's Office. Students agree that by taking this course all required papers may be subject to submission for textual similarity review to Turnitin.com for the detection of plagiarism. All submitted papers will be included as source documents in the Turnitin.com reference database solely for the purpose of detecting plagiarism of such papers. Use of Turnitin.com page service is subject to the Usage Policy and Privacy Pledge posted on the Turnitin.com site.

Disability Resources and Services	If you have a disability for which you are or may be requesting an accommodation, you are encouraged to contact both your instructor and the Office of Disability Resources and Services, 140 William Pitt Union, 412-648-7890/412-624-3346 (Fax), as early as possible in the term drsrecep@pitt.edu . Disability Resources and Services will verify your disability and determine reasonable accommodations for this course. Note that DRS requires advanced notice (up to 7 business days) before a scheduled exam For more information, visit https://www.diversity.pitt.edu/disability-access/disability-resources-and-services
Attendance	Attendance is expected for all lectures and required for paper discussions. Excused absences are family emergency and illness (please provide reasonable documentation and advance communication where possible). Other illnesses are unexcused and that week's assignments may be docked in scoring to reflect any late submissions. I understand that there may be issues that are difficult to control, so please reach out to me in advance of a potential absences and I will consider options for a workaround.
Exam Regrades	Exam regrades will be handled through Gradescope. Submit a regrade request via feature inside Gradescope with rationale for why scoring was inaccurate or misapplied. Regrade requests are due within 1 week of Exam scores posting on Canvas. Look over your exams in a timely fashion.
G GRADE	(Language from Dan Wetzel) G grades are assigned to students who have been attending a course, have been making regular progress, and are prevented (by circumstances beyond their control) from completing the course after it is too late to withdraw. If you wish to petition for a G grade, you must submit a request for this grade and documentation of your reason(s) in writing to Dr. Kaplan at least one week prior to the last class.
Class Recording	Class recordings are not allowed without explicit permission of the instructor. Lectures will generally be recorded barring technical issues and posted to course Panopto page in Canvas.
Copyright	Course materials may be protected by copyright. United States copyright law, 17 USC section 101, et seq., in addition to University policy and procedures, prohibit unauthorized duplication or retransmission of course materials. See Library of Congress Copyright Office and the University Copyright Policy.

See next page for course schedule

Course Schedule BIOSC 1580 Spring 2023

Class	Day/Date		Class Goal	Assignment
Week 1	**Mo**	**1/8**	**Course introduction** **Molecular technique review, overview of central dogma molecular genetics, gene to gene product, levels of function, experimental design** **Module 1:** Host-pathogen arms races and the development of novel molecular systems	**Module 1 papers and review article readings.** *Textbook reference sections:* ***13.7*** *pp549-557* ***17.2 Experimental Approach*** *pp732-735*
Week 1	**We**	**1/10**	**Module 1 continued: Logic of host pathogen interactions, origins of CRISPR, pathogen sensing and restriction, pathogen anti-restriction systems**	
	Mo	*1/15*	*MLK DAY - NO CLASS*	
Week 2	***Tu***	***1/16***		***Paper Study/Summary Sheets due Module 1 Paper***
Week 2	**We**	**1/17**	**Discussion 1: Discovery of phage determinants that confer sensitivity to bacterial immune systems https://doi.org/10.1016/j.cell.2023.02.029**	
Week 2	**Fr**	**1/19**		***Problem Set 1 Due***
	Fr	*1/19*	*Spring Term Add/Drop period ends*	
Week 3	**Su**	**1/21**		***Problem Set 1 grading/assessment due***
Week 3	**Mo**	**1/22**	**Module 2: Protection of the genome** **Review of DNA damage sensing and different repair pathways, almost every repair pathway creates some danger if replication approaches or passes before repair is finished.** **Key assays for study of replication and repair in cells.**	**Module 2 Paper and Review article readings** **Technique papers:** Proximity Ligation Assay for Detecting Protein-Protein Interactions and Protein Modifications in Cells and Tissues in Situ https://pubmed.ncbi.nlm.nih.gov/33044803/ DNA Fiber Analysis: Mind the Gap! https://pubmed.ncbi.nlm.nih.gov/28645379/ *Textbook reference sections: 15.1-15.8 pp622-641 15.9 pp644-655, end of chapter summary pp658-660*

Week 3	**We**	**1/24**	**Module 2, continued** **Pathway decision tree, how are decisions made (what does the cell have, where is the cell in the cell cycle, what does the DNA look like)**	**Focus on Module 2 Review:** DNA double- strand break repair- pathway choice in somatic mammalian cells **https://doi.org/10.1038/s41580-019-0152-0** **Mini-vignette: Focus on** Figure 7 from: Fork Cleavage-Religation Cycle and Active Transcription Mediate Replication Restart after Fork Stalling at Co-transcriptional R-Loops **https://doi.org/10.1016/j.molcel.2019.10.026** *Textbook reference sections: 16.8 pp 699-709*
	Fr	*1/26*	*Extended Add/Drop period ends*	
Week 4	**Mo**	**1/29**	**Module 2, cont. Technologies to understand factors that regulate repair. Power of CRISPR and deep sequencing to do reverse genetics in mammalian cells.** **Understanding heat maps and display of complicated data. Example analysis, library preparation for deep sequencing.**	**Focus on Module 2 Preview: Illuminating the path to DNA repair https://doi.org/10.1016/j.cell.2021.10.005** **Focus on Mini-vignette from: Mapping the genetic landscape of DNA double- strand break repair https://doi.org/10.1016/j.cell.2021.10.002**
Week 4	**Tu**	**1/30**		***Paper Study/Summary Sheets due Module 2 Paper***
Week 4	**We**	**1/31**	**Discussion 2: Stepwise requirements for polymerases δ and θ in theta-mediated end joining https://doi.org/10.1038/s41586-023-06729-7**	
Week 4	**Fr**	**2/2**		***Problem Set 2 Due***
Week 5	**Su**	**2/4**		***Problem Set 2 grading/assessment due***
Week 5	**Mo**	**2/5**	**Module 3: Interpreting the genome through gene expression control** **Principles of gene expression. Gene-specific patterns of expression. Principles of cell identity establishment.**	**Module 3 Paper and Review article readings** *Textbook reference sections: 9.6-9.7 pp366-380, 18.3-18.4 pp785-797* **Focus on mini-vignette from:** Transcription factor stoichiometry, motif affinity and syntax regulate single-cell chromatin dynamics during fibroblast reprogramming to pluripotency **https://pubmed.ncbi.nlm.nih.gov/37873116/**

Week 5	**We**	**2/7**	**Module 3, continued. Genomic techniques for understanding chromatin and gene expression landscape**	
Week 6	**Su**	**2/11**	**Exam 1 Review Session ZOOM**	
Week 6	**Mo**	**2/12**	**Exam 1**	
Week 6	**We**	**2/14** ❤️ **or** 🚹**?**	**Variability in molecular processes** **Single cell and single molecule analyses. Data display.** **What can we learn from single cell studies? What are variables? Why is it difficult?**	
Week 7	**Su**	**2/18**		***Paper Study/Summary Sheets due Module 3 Paper***
Week 7	**Mo**	**2/19**	**Discussion 3: Suboptimization of developmental enhancers https://pubmed.ncbi.nlm.nih.gov/26472909/**	
Week 7	**We**	**2/21**	**Module 4: Transcription elongation in metazoans and interaction between transcription and genome stability** **Phases of transcription, transcription unit organization, promoter-proximal pausing and termination, surveillance, cycles of modification**	
Week 8	**Mo**	**2/26**	**Transcription and other processes (replication, repair, DNA damage)** **Looking ahead to Discussion 4**	
Week 8	**Tu**	**2/27**		***Paper Study/Summary Sheets due Module 4 Paper***
Week 8	**We**	**2/28**	**Discussion 4: R-loop-dependent promoter-proximal termination ensures genome stability https://pubmed.ncbi.nlm.nih.gov/37557913/**	
Week 8	**Fr**	**3/1**		***Problem set 3 due***
Week 9	**Su**	**3/3**		***Problem set 3 grading/assessment due***

Week 9	**Mo**	**3/4**	**Module 5: Co-transcriptional RNA processing in development and disease** **RNA processing and techniques to assess on genome-wide scale.** **Concepts: RNA processing is a necessary part of eukaryotic gene expression and a pathway for increased diversity and regulation but also pathology**	*Textbook reference sections: 10.1, 10.4-10.7, 10.9,10.11*
Week 9	**We**	**3/6**	**Phase separation, membrane-less compartments, intrinsically disordered proteins, RNA-protein interactions** **Looking ahead to Discussion 5**	
	Fr	*3/8*	*Spring deadline for submission of Monitored Withdrawal forms to Dean's Office*	
Week 9	**Fr**	**3/8**		***Problem Set 4 due***
	Su	**3/10**		***Problem Set 4 grading/assessment due***
	Mo	*3/11*	*Spring Recess* 🏝️	
	We	*3/13*	*Spring Recess* 🏖️	
Week 10	**Su**	**3/17**		***Paper Study/Summary Sheets due Module 5 Paper***
Week 10	**Mo**	**3/18**	**Discussion 5: TDP-43 represses cryptic exon inclusion in the FTD–ALS gene UNC13A https://pubmed.ncbi.nlm.nih.gov/35197626/**	
Week 10	**Tu**	**3/19**	**Exam 2 Review Session 208 Langley Hall – 7 p.m. to 8:30 p.m.**	
Week 10	**We**	**3/20**	**Exam 2**	
Week 11	**Mo**	**3/25**	**Module 6: Regulation through post-translational modification.** **Introduction to concepts in sensing and signaling**	*Textbook reference sections: 14.7-14.8 pp595-606 14.10-14.11 pp608-618*
Week 11	**We**	**3/27**	**Examples of regulation by modification (mostly phosphorylation and ubiquitinylation) from replication, transcription, translation, DNA damage repair**	

Week 12	⚠ **Sa**	**3/30**		***Paper Study/Summary Sheets due Module 6 Paper***
Week 13	**Mo**	**4/1** ⚠☣	**Discussion 6: Defining E3 ligase-substrate relationships through multiplex CRISPR screening https://pubmed.ncbi.nlm.nih.gov/37735597/**	
Week 13	**We**	**4/3**	**Module 7: Deeper Into Translation Genetic Code: more than redundancy** **Review of codons and how they are read out** **Origin and evolution of genetic code** **Regulation through decoding properties and tRNA pool identities. Regulation through translation speed/efficiency**	*Textbook reference sections: 11.1-11.3 pp434-444*
Week 14	**Mo**	**4/8**	**Translation review** **Complexities in translation** **How does translation sense different situations? Looking ahead to Discussion 7.**	*Textbook reference sections: Translation 11.4-11.11 pp445-474* *Surveillance/detection of problems in translation 11.12 pp475-484*
Week 14	**Tu**	**4/9**		***Paper Study/Summary Sheets due Module 7 Paper***
Week 14	**We**	**4/10**	**Discussion 7: RNF14-dependent atypical ubiquitylation promotes translation-coupled resolution of RNA-protein crosslinks https://pubmed.ncbi.nlm.nih.gov/37951216/**	
Week 14	**Fr**	**4/12**		***Problem Set 5 due***
Week 15	**Su**	**4/14**		***Problem Set 5 grading/assessment due***
Week 15	**Mo**	**4/15**	**TBD**	
Week 15	**We**	**4/17**	**Summary and Review for Final**	
