BIOSC1275 GENOMICS

Instructor: Dr. Sarah Hainer
Pronouns: she | her
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Tophat join code: 893997
Class schedule: Tuesdays & Thursdays 1:00 - 2:15 pm in A214 Langley Hall
Office Location: A527 Langley Hall
Office Hours: Thursdays from 2:15-4pm in A527 Langley Hall

Office hours will be open door; therefore, multiple students can communicate with me at once. If you are unable to utilize these office hours, please contact me via email to schedule an appointment. If you require a private meeting, appointments outside of office hours are preferable.

PRE-REQUISITES

Completion of Genetics (BIOSC0350/0355 or BIOL0350/1315) with a grade of C or higher. It is expected that you have a good working knowledge of the material presented in one of these prerequisite courses, as no review of prior material will be provided.

COURSE DESCRIPTION: Why you should take this class

Recent years have seen an explosion in the number of organisms for which sequenced genomes are available. However, we are only beginning to understand how the information encoded in the million/billion DNA bases of eukaryotic genomes is organized and how that information is translated into function.

Throughout this course, we will start to answer central questions in the molecular biology and functional genomics fields, including:

- Given that only ~2% of the genome encodes for proteins, what is the function of the rest of the genome?
- What is the flow of information in the cell that controls gene function and activity?
- Which experimental approaches allow us to tackle these questions?
- How are advances in genomics helping to advance targeted medical care?

In addition, we will work together on developing the critical thinking and communication skills that are fundamental to become creative and productive professionals. Classes will integrate lectures, interactive discussions about these topics, and analysis of research papers.

OBJECTIVES: How this class will contribute to your development

This course will help you acquire a conceptual and experimental framework to comprehend central challenges in molecular biology and genomics and apply them in creative ways to solve original problems. By the end of this course you will be able to:

- Identify the principles underlying gene regulation in eukaryotes, the flow of information in the cell, and how it is encoded in the genome;
- Be proficient in genomics techniques, their applications, and their limitations;
- Integrate key concepts in molecular biology and functional genomics into solving problems;
- Critically analyze research articles, interpret data, and propose novel experiments;
- Investigate new topics independently and apply key concepts; and
- Clearly and effectively communicate ideas and results both orally and in writing.

CLASS FORMAT: How the class will be organized

Each class period will integrate lecture and discussion.
Background reading (according to the schedule below) will be required prior to the class, some of which will be evaluated through short quizzes. Classes will consist of lectures which will cover key topics (30-45 min), in-class discussions, and paper presentations/discussions.

INCLUSIVE AND EQUITABLE ENVIRONMENT

I am committed to fostering inclusivity in our pursuit of scientific knowledge and instruction. To this end, I encourage an environment of collaboration, open communication, and trust, which welcomes diversity and respects differences of opinion. It is these principles that allow us to discover new ways of thinking and behaving which lead to innovative ideas and academic success.

INSTRUCTOR COMMITMENT

I am invested in your success — specifically your ability to succeed in this course. I will provide an environment that is intellectually stimulating, emotionally supportive, safe, equitable, and free of harassment. Regardless of your personal backgrounds, you can count on me to:

- Teach and mentor you by providing as much information and discussion as possible about the course subject matter;
- Tailor my teaching to this specific class and its enrolled students;
- Help you envision, implement, and communicate research;
- Foster an environment in which people are able to give and receive respectful, constructive feedback.

We all thrive when our environment is happy, comfortable, and supportive. If you have any questions or concerns, my door is always open. Please also come speak with me if you are having issues with individuals within the class or otherwise. I can help guide you to the appropriate resources to deal with this within the Department and University.

LETTERS OF RECOMMENDATION

If you have built a relationship with me through conversation within the classroom and office hours, you are welcome to request a letter of recommendation. I will only write a letter if I think it will be a strong letter. Therefore, if we have communicated minimally and/or if you are not doing well in this course, I will not be able to write a letter. If I am able to write you a letter, please make the request a minimum of three weeks prior to the letter due date. In addition, please send me the following documents along with your request via email:

- A link to the application/job/fellowship description
- Your CV/resume
- A university transcript
- The letter due date in bold in the body of the email
- Any specific awards/accomplishments that you would like me to highlight in the letter

EMAIL COMMUNICATION POLICY

Each student is issued a University email address (username@pitt.edu) upon admittance. This email address may be used by the University for official communication with students. Students are expected to read email sent to this account on a regular basis. Failure to read and react to University communications in a timely manner does not absolve the student from knowing and complying with the content of the communications. The University provides an email forwarding service that allows students to read their email via other service providers. Students that choose to forward their email from their pitt.edu address to another address do so at their own risk. If email is lost as a result of

forwarding, it does not absolve the student from responding to official communications sent to their University email address. The University's complete email communication policy can be viewed at www.bc.pitt.edu/policies/policy/09/09-10-01.html.

RECORDING POLICY

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

COURSEWEB

CourseWeb will be used to post course materials, including the syllabus, papers, lecture slides, and announcements.

LECTURE SLIDES

Slides will be posted on CourseWeb prior to each lecture. It is recommended that you take notes on these slides during lecture.

All handouts and CourseWeb postings by this instructor are the property of the University of Pittsburgh (unless otherwise stated) and are not for sale or dissemination outside of this class.

COURSE READINGS

There is no required textbook for this course. Readings for the course will include review articles and research papers that will be available on CourseWeb. Students should read these articles prior to the class for which they are assigned. To promote discussion, students should bring a printed copy or computer with digital copy of these texts to class.

MAKE-UP POLICY

Make-up exams will only be provided if a legitimate excuse is given for missing an exam; specific arrangements should be made with the Instructor prior to the scheduled exam. A doctor's note is required for a medical excuse. There will be no make-ups for quizzes (due to the lowest score dropped), assignments, or paper presentations.

ACADEMIC INTEGRITY

Students in this course are expected to comply with the University of Pittsburgh's Policy on Academic Integrity. Cheating/plagiarism will not be tolerated. Students suspected of violating the University of Pittsburgh Policy on Academic Integrity, noted below, will be required to participate in the outlined procedures as initiated by the Instructor. A minimum sanction of a zero score for the quiz, exam or assignment will be imposed. The full Academic Integrity policy is available http://www.provost.pitt.edu/info/aistudcode1.html. You may not use unauthorized materials during an exam or quiz, including notes, dictionaries, calculators, pagers, telephones, PDAs and any device that can connect to the internet. You must submit for grading only material that is written exclusively in your own words. Violation of the Academic Integrity Code requires the instructor to submit an Academic Integrity Violation Report to the Dean's Office.

SEXUAL MISCONDUCT, REQUIRED REPORTING, AND TITLE IX

The University is committed to combatting sexual misconduct. As a result, you should know that University faculty and staff members are required to report any instances of sexual misconduct, including harassment and sexual violence, to the University's Title IX office so that the victim may be provided appropriate resources and support options. What this means is that as your professor,

I am required to report any incidents of sexual misconduct that are directly reported to me, or of which I am somehow made aware.
There are two important exceptions to this requirement:

- A list of the designated University employees who, as counselors and medical professionals, do not have this reporting responsibility and can maintain confidentiality, can be found here: http://www.titleix.pitt.edu/report/confidentiality
- Disclosures about sexual misconduct that are shared as part of an academic project, classroom discussion or course assignment, are not required to be disclosed to the University's Title IX office.

If you are the victim of sexual misconduct, the University encourages you to reach out to:

- Title IX Office: 412-648-7860
- SHARE @ the University Counseling Center: 412-648-7930 (8:30am TO 5pm Monday-Friday) and 412-648-7856 (AFTER BUSINESS HOURS)

If you have a safety concern, please contact the University of Pittsburgh Police, 412-624-2121.
Other reporting information is available here: http://www.titleix.pitt.edu/report-0

DISABILITY INCLUSIVE RESOURCES

If you have a disability or impairment 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, 412-648-7890/412-383-7355, as early as possible in the term. Disability Resources and Services will verify your disability and determine accommodations for this course. Additional information can be viewed at www.studentaffairs.pitt.edu/drsabout.

ASSESSMENTS: How will your learning progress be evaluated

The assessment of your progress will be evaluated in a variety of ways:

- **Quizzes (5% each; 25% total)**: Reading of assigned material prior to the classes will be evaluated by short quizzes. Six quizzes will be given as take-home assignments to be done INDEPENDENTLY, but with notes and papers, due on pre-defined dates. Each quiz will be posted on CourseWeb for a specified amount of time ~24 hours prior to the due date/time, and once opened you will have a defined amount of time to answer the questions (generally 1 hour). Therefore, I advise reading the paper prior to opening the quiz. The lowest quiz score will be dropped; no make-up quizzes will be offered as a result.
- **Attendance (2.5%)**: Attendance is required to enable participation in class discussion. Three classes can be missed for any reason with no penalization to this attendance grade. If more classes are missed, points will be deducted unless there is a sufficient reason (with supporting documentation, as necessary) for the absences. Please note that quizzes, assignments, and in-class presentations are still due on the specified dates, even if the class in which the material is due is missed. Attendance will be surveyed through Tophat.
- **Class participation (5%)**: Participation in discussions will be assessed. Tophat responses and active participation in class discussion will both be factored into this score.
- **Assignments (7.5% for Assignments 1&2, 10% Assignment 3; 25% total)**: Assignments will be discussed before they are due. Two assignments (Assignments 1&3) will consist of designing a graphical abstract and highlights for a paper. The third assignment (Assignment 2) will involve examining and discussing genomic databases and their functionality. Late assignments will not be accepted.

- **Paper presentation (12.5%)**: Each student group (5-6 individuals, six groups) will present a paper (~35 min presentation per group). Group presentations cannot be rescheduled. If you miss your presentation you will not get points for this assessment.
- **Exams (15% each, 30% total)**: Two exams (one midterm and one final) will integrate problem solving and evaluation of key concepts.

Assignments

1&3) You make work individually or with other members of the class on these assignments. Develop a graphical abstract and four ~85-character (spaces not included) highlights for a previously discussed paper (of the students/groups choosing) according to the guidelines provided by the journal *Cell* (Graphical abstract, highlights and summary). In addition, write a ~120-word abstract directed to a lay audience describing the paper. These assignments are due promptly at the time on the date listed. Assignments received after the described time on the date will receive reduced grades, scaled with the length of delay. You are permitted to discuss these assignments with classmates; however, work partners/groups should be noted on the top of the assignment and final documents should be **written in your own words**. Each student must submit their own assignment, not together with a group or partner.

2) Gather and present information (1 slide, 2 minutes per student) about one database related to functional genomics. A list of databases will be provided, and one student will be able to sign up for each database. Your PowerPoint slide must be emailed to Dr. Hainer by 9am on Thursday 20 February 2020, where a late assignment will not be accepted. Dr. Hainer will assemble the slides in order of email receipt for presentation in class.

SCHEDULE

This schedule is flexible. It may be modified throughout the semester. Quiz dates, exam dates, and assignment dates will NOT be altered.

Class	Topic	Prior activity	In-class activity
Tuesday 7 January 2020	How are eukaryotic genomes organized?	Survey	Introduction, Getting to know you activity, Lecture 1
Thursday 9 January 2020	How are eukaryotic genomes organized (continued)?	Read: Paper 1	Lecture 2
Tuesday 14 January 2020	Genome sequencing technologies	Read: Paper 2 & 3	Lecture 3
Thursday 16 January 2020	Genome sequencing technologies (continued)	Read: Papers 3 & 4 **Quiz 1 due via email to Dr. Hainer by 1pm [Quiz 1 will be on Paper 4]**	Lecture 4
Add/drop period ends 17 January 2020			

Tuesday 21 January 2020	Recombination systems/genome editing	Read: Papers 5 & 6	Lecture 5
Thursday 23 January 2020	Genome editing	Read: Paper 7 **Quiz 2 due via email to Dr. Hainer by 1pm**	Lecture 6
Tuesday 28 January 2020	Guest Lecture: Dr. Miler Lee *Note: Dr. Hainer will not be present, but attendance will still be taken*	No reading. **Bring your laptop to class!**	Guest Lecture 1 **Bring your laptop to class!**
Thursday 30 January 2020	**No Class**	**Assignment 1 due via email to Dr. Hainer by 5pm**	
Tuesday 4 February 2020	Genome-wide association studies (GWAS)	Read: Papers 8 & 9	Lecture 7
Thursday 6 February 2020	Introduction to gene regulation and chromatin organization	Read: Papers 10 & 11	Lecture 8
Tuesday 11 February 2020	Chromatin organization	Read: Paper 12 **Quiz 3 due via email to Dr. Hainer by 1pm**	Lecture 9
Thursday 13 February 2020	How is gene expression regulated?	Read: Papers 13 & 14	Lecture 10 Selection of website for Assignment 2 will occur
Tuesday 18 February 2020	How is gene expression regulated (continued)?	Read: Paper 15 **Quiz 4 due via email to Dr. Hainer by 1pm**	Lecture 11 Selection of group presentation dates will occur
Thursday 20 February 2020	Assignment 2 discussion	**Assignment 2 due: email slide to Dr. Hainer by 9am!! Late assignments will not be accepted at all.**	Assignment 2 discussion - student led
Tuesday 25 February 2020	Catch up/Review Session		Selection of group presentation dates will occur
Thursday 27 February 2020	**Exam I**		**Exam 1**
Tuesday	Transcription factors	Read:	Lecture 12

3 March 2020		Paper 16	Student group presentation 1
Thursday 5 March 2020	Transcription factors	Read: Paper 17	Lecture 13 Student group presentation 2
Withdrawal ends 6 March 2020; Spring break			
Tuesday 17 March 2020	How can we measure gene expression?	Read: Paper 18	Lecture 14 Student group presentation 3
Thursday 19 March 2020	How can we measure gene expression (single cells)?	Read: Paper 19	Lecture 15 Student group presentation 4
Tuesday 24 March 2020	Applications of single cell technology	Read: Paper 20	Lecture 16 Student group presentation 5
Thursday 26 March 2020	Comparative transcriptomics	Read: Paper 21	Lecture 17 Student group presentation 6
Tuesday 31 March 2020	Epigenomics	Read: Paper 22 **Quiz 5 due via email to Dr. Hainer by 1pm**	Lecture 18
Thursday 2 April 2020	Guest Lecture: Dr. Kevin Kohl	Read: Papers 23 & 24 **Assignment 3 due via email to Dr. Hainer by 1pm**	Guest Lecture 2
Tuesday 7 April 2020	Guest Lecture: Dr. Vaughn Cooper	Read: Paper 25	Guest Lecture 3
Thursday 9 April 2020	Personalized medicine	Read: Papers 26 & 27 **Quiz 6 due via email to Dr. Hainer by 1pm [Quiz 6 is on Paper 27]**	Lecture 19
Tuesday 14 April 2020	Engineering a Genome	Read: Paper 28	Lecture 20
Thursday 16 April 2020	Catch up/Review Session		
Final: Saturday April 25, 8am-9:50am The final will be an online final that will be posted the week of finals week. It must be complete by 10am on Saturday April 25. Similar to quizzes, a timer will limit time spent once opened.			

ARTICLES

Read these articles prior to coming to class. All articles are posted on CourseWeb. To promote discussion, please bring a printed copy or computer with digital copy of the specified article to class.

1) Lewin's Genes XI. Chapter 6: Genome sequences and gene numbers. Krebs J, Goldstein E, Kilpatrick S **This textbook may be useful for review of basic molecular biology*
2) Coming of age: ten years of next-generation sequencing technologies. Goodwin S, McPherson JD, McCombie WR. Nat Rev Genet. 2016 May 17;17(6):333-51
3) Human genome sequencing in health and disease. Gonzaga-Jauregui C, Lupski JR, Gibbs RA. Annu Rev Med. 2012;63:35-61
4) Accurate whole human genome sequencing using reversible terminator chemistry. Bentley DR, et al. Nature. 2008 Nov 6;456(7218):53-9
5) A guide to genome engineering with programmable nucleases. Kim H, Kim JS. Nat Rev Genet. 2014 May;15(5):321-34
6) The next generation of CRISPR-Cas technologies and applications. Pickar-Oliver A, Gersbach CA. Nature Reviews. 2019 August;20
7) Prioritization of cancer therapeutic targets using CRISPR-Cas9 screens. Behan FM, et al. Nature. 2019 April; 568:511-16
8) Benefits and limitations of genome-wide association studies. Tam V, et al. Nature Reviews Genetics. 2019 August; 20:467-84
9) Genome-wide association study identifies 30 loci associated with bipolar disorder. Bellivier F, et al. Nature Genetics. 2019 May; 51:793-803
10) Epigenome Regulation by Dynamic Nucleosome Unwrapping. Brahma S, Henikoff S. Trends in Biochemical Sciences. 2020 January; 45(1):13-26
11) Organization and function of the 3D genome. Bonev B. Cavalli G. Nature Reviews Genetics. 2016 November; 17:661-78.
12) Topological domains in mammalian genomes identified by analysis of chromatin interactions. Dixon JR, Selvaraj S, Yue F, Kim A, Li Y, Shen Y, Hu M, Liu JS, Ren B. Nature. 2012 Apr 11;485(7398):376-80
13) Histone exchange, chromatin structure, and the regulation of transcription. Venkatesh S, Workman JL. Nature Reviews Mol Cell Bio 2016 March; 16:178-189
14) Determinants of enhancer and promoter activities of regulatory elements. Andersson R, Sandelin A. Nature Reviews Genetics. 2019
15) An integrated encyclopedia of DNA elements in the human genome. ENCODE Project Consortium. Nature. 2012 Sep 6;489(7414):57-74
16) Genomic Methods in profiling DNA accessibility and factor localization. Klein DC, Hainer SJ. Chromosome Research. 2020.
17) Transcription factor-DNA binding: beyond binding site motifs. Inukai S, Kock KH, Bulyk ML. Curr Opin Genet Dev. 2017 Apr;43:110-119
18) Transcriptomic Technologies. Lowe R, et al. PLoS Computational Biology. 2017 May 18.
19) Defining cell types and states with single-cell genomics. Trapnell C. Genome Research. 2015 November; 25:1491-98
20) The single-cell transcriptional landscape of mammalian organogenesis. Cao J, et al. Nature. 2019 February 28; 566:496-501

21) Comparative transcriptomics in human and mouse. Breschi A, Gingeras TR, Guigo R. Nature Reviews Genetics. 2017 July; 18:425-40
22) Profiling of pluripotency factors in single cells and early embryos. Hainer SJ, et al. Cell. 2019 May 16; 177:1-11
23) The woodrat gut microbiota as an experimental system for understanding microbial metabolism of dietary toxins. Kohl KD, Dearing MD. Frontiers in Microbiology. 2016 July; 7:1165
24) Gut microbes of mammalian herbivores facilitate intake of plant toxins. Kohl KD, et al. Ecology Letters. 2014
25) Evolutionary pathways to antibiotic resistance are dependent upon environmental structure and bacterial lifestyle. Santos-Lopez A, et al. eLife. 2019; 8:e47612
26) The evidence framework for precision cancer medicine. Moscow JA, Fojo T, Schilsky RL. Nature Reviews Clinical Oncology. 2018 March; 15:183-192
27) A pan-cancer transcriptome analysis reveals pervasive regulation through alternative promoters. Demircioglu D, et al. Cell. 2019 September 5; 178:1465-77
28) Total synthesis of *Escherichia coli* with a recoded genome. Fredens J, et al. Nature. 2019 May 23; 569:514-518