BIOSC1275 GENOMICS

Instructor: Dr. Sarah Hainer
Pronouns: she/her/hers
Email: sarah.hainer@pitt.edu

Class location: Zoom (until January 27th) then 169 Crawford Hall
Class schedule: Tuesdays & Thursdays 2:30 - 3:45 pm
Office Location: A527 Langley Hall
Office Hours: Tuesdays & Thursdays 3:45 - 4:00 pm (for immediate questions after class) and Wednesdays 3:00 - 4:00 pm via Zoom. Additional meetings (to be held either virtual or in person) are available by appointment.

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.

UTA: Michelle Malizio
Pronouns: she/her/hers
Email: mrm239@pitt.edu

Office hours: Fridays 11:00 am - 12:00 pm via Zoom (once in person transition occurs, these will occur in a hybrid format). Additional meetings are available by appointment.

VIRTUAL TO IN-PERSON LEARNING NOTE DUE TO COVID-19
This course is designed to function fully in person beginning January 27. Requests for remote attendance will not be reviewed by myself or the department. If you believe you have a qualifying disability that prevents you from attending in-person instruction this semester, please contact Disability Resources and Services. If you are quarantined due to COVID-19, you may temporarily participate remotely by providing documentation. Under either of these circumstances, you may elect to preserve your privacy by not using video and by identifying yourself in Zoom using your initials or an alias that you have shared with me.

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

Until January 27, this will be a synchronous virtual class, held via Zoom.
All classes will be recorded and posted as quickly as possible for student viewing.

Please mute your microphone but feel free to leave your camera on (or off, as preferred).
During class, if you have a question, please unmute your microphone and ask. Alternatively, there is a chat box where you can type your questions (and I will try to respond as soon as possible, but certainly by the end of class). Finally, this can be joined either on a computer or on your cell phone.
On January 27th and beyond, classes are scheduled to be held in person, in Crawford 169.
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 (to be taken prior to class). Classes will consist of lectures which will cover key topics (30-45 min), in-class discussions, and paper 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 https://www.as.pitt.edu/e-mail-communication-statement-syllabi.

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.

CANVAS

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

LECTURE SLIDES

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

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 Canvas. 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 https://www.as.pitt.edu/faculty/policies-and-procedures/academic-integrity-code. 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 about which you should be aware:

- 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: https://www.diversity.pitt.edu/civil-rights-title-ix-compliance/make-report/information-responsible-employees.
- An important exception to the reporting requirement exists for academic work. 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, Pitt encourages you to reach out to these resources:
Title IX Office: 412-648-7860
SHARE @ the University Counseling Center: 412-648-7930 (8:30 am TO 5 pm Mon-Fri) 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: https://www.diversity.pitt.edu/civil-rights-title-ix-compliance/make-report

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 (50 points each, 25% total grade)**: Reading of assigned material prior to the classes will be evaluated by short quizzes, to be taken on Canvas. 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 Canvas for a specified amount of time ~24-48 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.**
- **Pre-class questions (100 points; 10% total grade)**: Questions to review previous lecture materials will be posted to Canvas. Due to the web format of this class, questions will be posted on Canvas (under Quizzes) ~24-48 hours prior to class and must be completed before class begins that day (even if the student is not in attendance). You are allowed to use your notes, but there is a time limit (scales with number of questions). 27 total pre-class question sets, each worth 4 points. The **introduction survey** counts as a pre-class question score. **Two missed pre-class questions (or your two lowest scores) will be dropped; no make-up pre-class questions will be offered as a result.**
- **Assignments (100 points each; 30% total grade)**: Assignments will be discussed before they are due. The first assignment (Assignment 1) involves examining and discussing genomic databases and their functionality. The second assignment (Assignment 2) will consist of designing a graphical abstract and highlights for a paper. The third assignment (Assignment 3) involves drawing out a technique. These assignments are due promptly on the date and time listed (prior to class on date listed). Assignments received after the described time on the date will receive reduced grades, scaled with the length of delay. Students will post assignments on Canvas for review and commenting by other students. Rubrics are included on Canvas for clarity in grading.
- **Review of Assignments (100 points; 10% of total grade)**: Each student must review 20 assignments by other students. Each student will review 10 classmates assignments for Assignment 1, 10 classmates assignments for Assignment 2, and 5 classmates assignments for Assignment 3. Students should provide a minimum of 2 comments (positive or critical) to students regarding their assignment, and this should be posted on Canvas. 4 points for each assignment reviewed, and points will only be given if 2 **thorough and thoughtful** comments are made. Review of classmate assignments are all due prior to class on the listed date.
- **Exams (125 points each; 25% total grade)**: Two exams (one midterm and one final) will integrate problem solving and evaluation of key concepts.

Assignments

1) A database related to functional genomics will be given to each student prior to the assignment. Gather and present information about this database. Students should make a single Powerpoint slide and record a ~2-3-minute presentation of themselves discussing the website (purpose for the website, using the website, etc). Assignment 1 is due 10 February 2021, uploaded to Canvas before class.

2) 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). Notably, you should **MAKE** the figures (using Powerpoint, Illustrator, BioRender, or any other method) and **not copy premade figures or images from the paper (or other resource)**. 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 with independent graphics generated**. Each student must submit their own assignment, not together with a group or partner. Assignment 2 is due 1 March 2021, uploaded to Canvas before class.

3) **Draw a technique.** Draw out any genome-wide method we have discussed in class (ex: ATAC-seq, ChIP-seq, CUT&RUN, RNA-seq, etc). You should include a BRIEF (~20-150 word) legend to describe the figure. Notably, you should **MAKE** the figures (using PowerPoint, Illustrator, BioRender, or any other method) and **not copy premade figures or images from the paper (or other resource)**. 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 with independent graphics generated**. Each student must submit their own assignment, not together with a group or partner. Assignment 2 is due 5 April 2021, uploaded to Canvas before 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 11 January 2022	How are eukaryotic genomes organized?	Survey due 14 Jan 2022 (https://forms.gle/hmgWASjDn5aP4XYVA)	Introduction, Getting to know you, Lecture 1
Thursday 13 January 2022	How are eukaryotic genomes organized (continued)?	Read: Paper 1 (textbook Chapter 6) Pre-class questions due prior to class	Lecture 2
Tuesday 18 January 2022	Genome sequencing technologies	Read: Paper 2 Pre-class questions due prior to class	Lecture 3
Thursday 20 January 2022	Genome sequencing technologies (continued)	Read: Papers 3 Pre-class questions due prior to class **Quiz 1 [on paper 3], due prior to class**	Lecture 4

Add/drop period ends 21 January 2022			
Tuesday 25 January 2022	Recombination systems/genome editing	Read: Paper 4 Pre-class questions due prior to class	Lecture 5
Thursday 27 January 2022	Genome editing	Read: Paper 5 Pre-class questions due prior to class **Quiz 2 [on paper 5], due prior to class**	Lecture 6
Tuesday 1 February 2022	Genome-wide association studies (GWAS)	Read: Paper 6 Pre-class questions due prior to class	Lecture 7, Discuss assignment 1
Thursday 3 February 2022	GWAS (continued)	Read: Paper 7 Pre-class questions due prior to class **Quiz 3 [on paper 7], due prior to class**	Lecture 8
Tuesday 8 February 2022	Biological Data	Pre-class questions due prior to class	Lecture 9, Discuss assignment 1 (again)
Thursday 10 February 2022	Making figures	Pre-class questions due prior to class **Assignment 1 due prior to class**	Lecture 10, Discuss assignment 2
Tuesday 15 February 2022	How can we measure gene expression?	Read: Papers 8 & 9 Pre-class questions due prior to class	Lecture 11
Thursday 17 February 2022	How can we measure gene expression (single cells)?	Read: Papers 10 & 11 Pre-class questions due prior to class **Reviews of Assignment 1 due prior to class**	Lecture 12
Tuesday 22 February 2022	Single cell RNAseq (con't)	Pre-class questions due prior to class	Lecture 13 Discuss assignment 2
Thursday 24 February 2022	**Exam 1**		
Tuesday 1 March 2022	Nascent RNA-seq	Read: Paper 12 Pre-class questions due prior to class **Assignment 2 due prior to class**	Lecture 14
Thursday 3 March 2022	Comparative transcriptomics	Read: Paper 13 Pre-class questions due prior to class	Lecture 15

		Quiz 4 [on paper 13, due prior to class]	
Spring Break, no class 8 March or 10 March			
Tuesday 15 March 2022	How is gene expression regulated?	Read: Paper 14 Pre-class questions due prior to class **Reviews of Assignment 2 due prior to class**	Lecture 16
Thursday 17 March 2022	How is gene expression regulated (continued)?	Read: Paper 15 Pre-class questions due prior to class	Lecture 17
Tuesday 22 March 2022	Transcription factors	Read: Papers 16 & 17 Pre-class questions due prior to class	Lecture 18. Discuss assignment 3
Thursday 24 March 2022	Epigenomics	Read: Paper 18 Pre-class questions due prior to class	Lecture 19
Tuesday 29 March 2022	Epigenomics (continued)	Pre-class questions due prior to class	Lecture 20
Thursday 31 March 2022	Single cell Epigenomics	Read: Paper 19 & 20 Pre-class questions due prior to class **Quiz 5 [on paper 20, due prior to class]**	Lecture 21
Tuesday 5 April 2022	High-order Chromatin organization	Read: Paper 21 Pre-class questions due prior to class **Assignment 3 due prior to class**	Lecture 22
Thursday 7 April 2022	Metagenomics	Read: Paper 22 Pre-class questions due prior to class	Lecture 23
Tuesday 12 April 2022	Precision medicine	Read: Paper 23 Pre-class questions due prior to class **Reviews of Assignment 3 due prior to class**	Lecture 24
Thursday 14 April 2022	Bias in genomics	Read: Paper 24 Pre-class questions due prior to class **Quiz 6 [on Paper 24, due prior to class]**	Lecture 25
Tuesday 19 April 2022	Engineering a Genome	Read: Paper 25 Pre-class questions due prior to class	Lecture 26

Thursday 21 April 2022	Catch up/Review Session	Pre-class questions due prior to class	

ARTICLES

All articles are posted on Canvas. To promote discussion and understanding of lecture material, please read the articles prior 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) Accurate whole human genome sequencing using reversible terminator chemistry. Bentley DR, et al. Nature. 2008 Nov 6;456(7218):53-9
4) A guide to genome engineering with programmable nucleases. Kim H, Kim JS. Nat Rev Genet. 2014 May;15(5):321-34
    a. *Optional additional reading:* The next generation of CRISPR-Cas technologies and applications. Pickar-Oliver A, Gersbach CA. Nature Reviews. 2019 August;20
5) Prioritization of cancer therapeutic targets using CRISPR-Cas9 screens. Behan FM, et al. Nature. 2019 April; 568:511-16
6) Benefits and limitations of genome-wide association studies. Tam V, et al. Nature Reviews Genetics. 2019 August; 20:467-84
    a. *Optional: Human genome sequencing in health and disease. Gonzaga-Jauregui C, Lupski JR, Gibbs RA. Annu Rev Med. 2012;63:35-61*
7) Genome-wide association study identifies 30 loci associated with bipolar disorder. Bellivier F, et al. Nature Genetics. 2019 May; 51:793-803
8) Transcriptomic Technologies. Lowe R, et al. PLoS Computational Biology. 2017 May 18.
9) RNA sequencing: the teenage years. Stark R, Grzelak M, Hadfield J. Nature Reviews Genetiics. 2019 November; 20:631-656
10) Single cell transcriptomics comes of age. Aldridge S and Teichmann SA. Nature Communications. 2020; 11:4307
11) Beyond bulk: a review of single cell transcriptomics methodologies and applications. Kulkarni A, Anderson AG, Merullo DP, Konopka G. Current Opinion in Biotechnology. 2019; 58:129-136.
12) Nascent RNA analyses: tracking transcription and its regulation. Wissink, EM, et al. Nature Reviews Genetics. 2019 August 9; 20:705-723
13) Comparative transcriptomics in human and mouse. Breschi A, Gingeras TR, Guigo R. Nature Reviews Genetics. 2017 July; 18:425-40
14) Eukaryotic core promoters and the functional basis of transcription initiation. Haberle V and Stark A. Nature Reviews Molecular Biology. 2018 October; 19:621-637
15) Evaluating Enhancer Function and Transcription. Field A, Adelman K. Annual Review of Biochemistry. 2020 March; 15:25
    a. *Optional additional reading: Determinants of enhancer and promoter activities of regulatory elements. Andersson R, Sandelin A. Nature Reviews Genetics. 2019*
16) Transcription factor-DNA binding: beyond binding site motifs. Inukai S, Kock KH, Bulyk ML. Curr Opin Genet Dev. 2017 Apr;43:110-119

17) Genomic Methods in profiling DNA accessibility and factor localization. Klein DC, Hainer SJ. Chromosome Research. 2020.
18) From profiles to function in epigenomics. Stricker SH, Koferle A, Beck S. Nature Reviews Genetics 2017. 18:51-66
19) The epigenetic basis of cellular heterogeneity. Carter B and Zhao K. Nature Reviews Genetics 2020.
20) Profiling of pluripotency factors in single cells and early embryos. Hainer SJ, et al. Cell. 2019 May 16; 177:1-11
21) Organization and function of the 3D genome. Bonev B. Cavalli G. Nature Reviews Genetics. 2016 November; 17:661-78.
    a. *Optional: Understanding the 3D genome: Emerging impacts on human disease. Krumm A and Duan Z. Seminars in Cell & Dev Biol. 2019.*
22) Clinical metagenomics. Chiu CY and Miller SA. Nature Reviews Genetics. 2019 June; 20: 341-355
23) Genomics and Transcriptomics: The Powerful Technologies in Precision Medicine. Khodadadian A, et al. International Journal of General Medicine. 2020 13:627-640
24) Challenges and disparities in the application of personalized genomic medicine to populations with African ancestry. Kessler MD, et al. Nature Communications. 2016 October 11; 7:12521
    a. *Optional: Genomics is failing on diversity. Popejoy AB and Fullerton SM. Nature 2016 October 13; 538:161-164*
25) Synthetic Genomes. Zhang W, et al. Annual Review of Biochemistry. 2020 June; 89:77-101
    a. *Optional: Total synthesis of Escherichia coli with a recoded genome. Fredens J, et al. Nature. 2019 May 23; 569:514-518*