2024 - Cancer genetics and genomics BIOS 25328

Instructors:

Lixing Yang
Hae Kyung Im
Teaching Assistant: Liz Gibbons

Schedule & location

Two weekly lectures (BSLC 324) MW 1:30-2:20 pm
One TA session per week (BSLC 324) F 1:30-2:20 pm

Prerequisites

- Basic computer literacy, coding, R (BIOS 20152 or equivalent)
- Introductory genetics (BIOS 20187)
- Introductory probability (covered by BIOS 20152)
- BIOS 20152 or equivalent

Course Description

Unprecedented technological progress over the last decade, especially high throughput sequencing technologies, has transformed the basic and translational research of cancer as well as other diseases. In this course, we will introduce the current state of the field, discuss how germline and somatic factors drive cancer initiation and progression, and demonstrate how to use omics data to advance our understanding of cancer. We will review recent literature in cancer genetics and genomics, learn about the standing questions in the field, and practice the analytical techniques to address these questions. Computational exercises will be an integral part of the course and provide you with a hand-on experience of state-of-the-art techniques.

Learning objectives

By the end of the course, students will be able to

- describe and perform a GWAS analysis with raw data, describe the statistics involved, and interpret the results.
- acquire basic coding and data analytic literacy

- present primary literature in the field of cancer genomics
- describe the difference between different types of genetic alterations in cancer and describe how they promote tumorigenesis
- Identify an appropriate approach for data analysis given a specific goal and dataset

Assessment of success

Student success will be assessed by their ability to resolve weekly problem sets, participate in class discussion, and the final presentation.

Problem Sets and graphic summary of papers (33%):

For the first half of the course, there will be computational and conceptual homework assignments to be turned in weekly. You may work with others to complete the problems but are expected to write up the material yourself and to master the material yourself. Solutions that look too similar may get points deducted.
For the second half of the course, each student will turn in a graphical summary of the assigned paper to be turned in before the discussion. These can be hand drawn and should be similar in spirit to the graphic summaries in cell papers (for example here)

Class Participation (33%): We will measure participation by the number of questions, comments, and responses to our polls through Canvas and google docs.

Final Presentation (34%): You will be expected to present a primary research paper (or set of papers) selected from the list below. You can suggest papers outside the list, but they need to be approved by the instructors. The presentation will be approximately 15 minutes in length. The presentation will be scored based on

- organization: overall structure, logic flow, etc.
- presentation quality: clear narrative, fluency, eye contact, etc.
- clarity: focused on the relevant concepts (don't get bogged down in details or technicalities)
- content: give enough details to understand the key ideas or hypotheses, relate to what we learned in class

Students will also score other students, an average of students scores will be averaged with the scores from the instructors and the TA.

We encourage you to **work in teams** and get help from others. However, you need to acknowledge that.

User of AI software. In this course, students are allowed to use AI tools (such as ChatGPT) on all assignments. Acknowledgement and citation required. Please see the APA guidelines for citing chatGPT here, the Chicago manual style here.

Honor statement

Students will add the following honor statement to every work they turn in:
"In submitting my work, I attest that it contains only my own independent work carried out according to the directions given to me by the instructor. I understand that academic integrity and honesty is a core principle of the University of Chicago and is expected at all times from its students."

Text and Materials

We will assign readings per lecture, listed in the schedule below.

Office Hours and Contact

Each instructor will be available for office hours

- Haky Im (haky@uchicago.edu) will hold office hours after her Monday lectures. You can also request a meeting by appointment. Office: Cummings 920 E. 58th St. Chicago, IL 60637, USA | 154-E (ring the bell at the entrance of the suite, if needed)
- Lixing Yang (lixingyang@uchicago.edu), Office hour: every Wed after class, or by appointment

TA:

- Liz Gibbons (gibbonsliz@uchicago.edu), Office hour: Thursday, 1:30 pm to 2:30 pm. Zoom: You can also email to schedule a meeting or ask questions.

A Note on Sexual Misconduct

Our school is committed to fostering a safe, productive learning environment. Title IX and our school policy prohibits discrimination on the basis of sex. Sexual misconduct — including harassment, domestic and dating violence, sexual assault, and stalking — is also prohibited at our school. Our school encourages anyone experiencing sexual misconduct to talk to someone about what happened, so they can get the support they need and our school can respond appropriately. If you wish to speak confidentially about an incident of sexual misconduct, want more information about filing a report, or have questions about school policies and procedures, please contact our Title IX Coordinator, which can be found on our school's website. Our school is legally obligated to investigate reports of sexual misconduct after a formal complaint is filed or signed by the Title IX Coordinator, but a request for confidentiality will be respected to the extent possible.

Accommodations

Student Disability Services (SDS) works to provide resources, support, and accommodations for all students with disabilities and works to remove physical and mitigate attitudinal barriers, which may prevent their full participation in the life of the university. SDS seeks to ensure that disability is included as a valued part of the institution's diversity and that accessibility is priority. More information here.

Course Schedule

The first 4 weeks will have one computational lab led by the TA. The following 4 weeks, the instructor and TA will lead paper discussions. In the last week, each student will present a research paper in class.

L	W	Subject	Who	Date
1	1	- Overview of sequencing technologies (DNA, RNA, etc)	Lixing	3/18

2	1	- Genetic architecture of common diseases and cancers - Hypothesis testing review	Haky	3/20
	1	- Intro to command line and R	TA	3/22
3	2	- GWAS of cancer risk, QC, UK Biobank -	Haky	3/25
4	2	- Multiple testing correction -	Haky	3/27
	2	- Computational lab - Multiple testing simulations	TA	3/29
5	3	- PCA & Population Structure -	Haky	4/1
6	3	- Pop Structure cont. Mixed Effects Model + LD score regression -	Haky	4/3
	3	- Computational lab - GWAS	TA	4/5
7	4	- Prediction of complex traits, polygenic risk scores -	Haky	4/8
8	4	- QTL analysis, functional annotations -	Haky	4/10
	4	- Computational lab - PRS	TA	4/12
9	5	- Post-GWAS analysis/Mendelian Randomization -	Haky	4/15
10	5	Lecture on point mutations	Lixing	4/17
	5	Paper discussion (mutation signature)	Lixing	4/19
11	6	Lecture on CNVs	Lixing	4/22
12	6	Paper discussion (aneuploidy)	Lixing	4/24
	6	Paper discussion (ecDNA)	TA	4/26
13	7	Lecture on SVs	Lixing	4/29
14	7	Paper discussion (chromothripsis)	Lixing	5/1
	7	Paper discussion (FGFR3-TACC3)	TA	5/3
15	8	Lecture on epigenetics	Lixing	5/6
16	8	Paper discussion (perturbing 3D structure)	Lixing	5/8
	8	Paper discussion (chromatin accessibility)	TA	5/10

16	9	Paper discussion (machine learning)	Lixing	5/13
17	9	student presentation		5/15
18	9	student presentation		5/17
	9	COLLEGE READING PERIOD		5/18-20
	10	COLLEGE READING PERIOD		5/20
19	10	Student presentations or Special topics in statistical genetics	students	5/22
	10	Lab		5/24
	finals	Memorial Day		5/27
	finals	Quarter ends / Convocation		6/1

Note: The papers listed here make up a tentative list, subject to change if more relevant papers are published during the course.

Examples of papers for final presentation

These are some examples of papers that could be used from the final presentation but the actual paper will be decided based on each student's interest and in agreement with the instructors.

Title	Year	URL	Rest of the citation
Genetic variation across and within individuals	2024	Link	Review of germline and somatic variations in humans
Genetic and molecular architecture of complex traits,	2024	Link	A good perspective paper with a survey of the of the state of the art in the field of human genetics and genomics and challenges by Tuuli L. et al.
GTEx flagship paper	2020	Link	
ENCODE flagship paper	2020	Link	

Genome-Wide Association Study Identifies 32 Novel Breast Cancer Susceptibility Loci from Overall and Subtype-Specific Analyses	2020		Zhang, Haoyu, Thomas U. Ahearn, Julie Lecarpentier, Daniel Barnes, Jonathan Beesley, Guanghao Qi, Xia Jiang, et al.
A Transcriptome-Wide Association Study of High-Grade Serous Epithelial Ovarian Cancer Identifies New Susceptibility Genes and Splice Variants	2019		Gusev, Alexander, Kate Lawrenson, Xianzhi Lin, Paulo C. Lyra, Siddhartha Kar, Kevin C. Vavra, Felipe Segato, et al.
A Global Overview of Pleiotropy and Genetic Architecture in Complex Traits	2019		Watanabe, Kyoko, Sven Stringer, Oleksandr Frei, Maša Umićević Mirkov, Christiaan de Leeuw, Tinca J. C. Polderman, Sophie van der Sluis, Ole A. Andreassen, Benjamin M. Neale, and Danielle Posthuma.
Genome-Wide Association and Transcriptome Studies Identify Target Genes and Risk Loci for Breast Cancer	2019	Link	Ferreira, Manuel A., Eric R. Gamazon, Fares Al-Ejeh, Kristiina Aittomäki, Irene L. Andrulis, Hoda Anton-Culver, Adalgeir Arason, et al.
A Transcriptome-Wide Association Study Among 97,898 Women to Identify Candidate Susceptibility Genes for Epithelial Ovarian Cancer Risk	2018		Lu, Yingchang, Alicia Beeghly-Fadiel, Lang Wu, Xingyi Guo, Bingshan Li, Joellen M. Schildkraut, Hae Kyung Im, et al.
Delivering precision oncology to patients with cancer		Link	
Systematic review of Mendelian randomization studies on risk of cancer		Link	
Mutation strand asymmetry		Link	
Sequencing errors		Link	
Circular RNAs		Link	

Hypermutation		Link	
Oncogenic rearrangements in lung cancer		Link	

- GTEx flagship paper 2020 https://www.science.org/doi/10.1126/science.aaz1776
- ENCODE flagship paper 2020 https://www.nature.com/articles/s41586-020-2493-4
- Gusev, Alexander, Kate Lawrenson, Xianzhi Lin, Paulo C. Lyra, Siddhartha Kar, Kevin C. Vavra, Felipe Segato, et al. 2019. "**A Transcriptome-Wide Association Study of High-Grade Serous Epithelial Ovarian Cancer Identifies New Susceptibility Genes and Splice Variants.**" Nature Genetics 51 (5): 815–23.
- Lu, Yingchang, Alicia Beeghly-Fadiel, Lang Wu, Xingyi Guo, Bingshan Li, Joellen M. Schildkraut, Hae Kyung Im, et al. 2018. "**A Transcriptome-Wide Association Study Among 97,898 Women to Identify Candidate Susceptibility Genes for Epithelial Ovarian Cancer Risk**." Cancer Research 78 (18): 5419–30.
- Watanabe, Kyoko, Sven Stringer, Oleksandr Frei, Maša Umićević Mirkov, Christiaan de Leeuw, Tinca J. C. Polderman, Sophie van der Sluis, Ole A. Andreassen, Benjamin M. Neale, and Danielle Posthuma. 2019. "**A Global Overview of Pleiotropy and Genetic Architecture in Complex Traits.**" Nature Genetics 51 (9): 1339–48.
- Zhang, Haoyu, Thomas U. Ahearn, Julie Lecarpentier, Daniel Barnes, Jonathan Beesley, Guanghao Qi, Xia Jiang, et al. 2020. "**Genome-Wide Association Study Identifies 32 Novel Breast Cancer Susceptibility Loci from Overall and Subtype-Specific Analyses.**" *Nature Genetics* 52 (6): 572–81.
- Ferreira, Manuel A., Eric R. Gamazon, Fares Al-Ejeh, Kristiina Aittomäki, Irene L. Andrulis, Hoda Anton-Culver, Adalgeir Arason, et al. 2019. "**Genome-Wide Association and Transcriptome Studies Identify Target Genes and Risk Loci for Breast Cancer.**" *Nature Communications* 10 (1): 1741.
- Delivering precision oncology to patients with cancer https://www.nature.com/articles/s41591-022-01717-2
- Systematic review of Mendelian randomization studies on risk of cancer https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-022-02246-y

- Mutation strand asymmetry (www.ncbi.nlm.nih.gov/pmc/articles/PMC4753048/)
- Sequencing errors (http://science.sciencemag.org/content/355/6326/752)
- Circular RNAs (https://www.cell.com/cell/fulltext/S0092-8674(18)31635-0)
- Hypermutation (https://www.cell.com/cell/fulltext/S0092-8674(17)31142-X)
- Oncogenic rearrangements in lung cancer (https://www.cell.com/cell/fulltext/S0092-8674(19)30511-2)

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Spring 2024

Date	Event/Deadline
Monday, March 18	Spring Quarter Begins
Saturday, May 18 – Monday, May 20	College Reading Period
Monday, May 27	Memorial Day
Saturday, June 1	Convocation
Saturday, June 1	Spring Quarter Ends