HEB1451: 23&Us
Syllabus (Half Course)
Research Seminar

Course Time: Tuesday and Thursday 10:30-11:45am
Course Location: MCZ541
Course Enrollment: Limit to 24 students

Course Instructor: Terence D. Capellini, Ph.D., M.Phil., M.A.
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Office Hours: M 11-12 or by appointment.
Office Hours Zoom Link: https://harvard.zoom.us/j/92692063674?pwd=MDlyd3c3U1FHNGg4d0lyRnIvSjRIdz09
Password: 210141

Course Website: https://canvas.harvard.edu/courses/114663

Prerequisite: LS1b (Genetics, Genomics, and Evolution), or equivalent genetics/genomics course approved by the instructor.

Course Description and Goals:
The charge to the scientific community upon the initial sequencing of the human genome in 2001, has been to make sense of what its 3 billion DNA bases do in the body. Recent advances in genetics, genomics, and developmental biology are indeed improving our understanding of human and non-human primate biological traits and in this regard connecting DNA bases to phenotypes and phenotypic variation. These disciplines, when incorporated into a multi-faceted context, can reveal the mechanistic basis of evolutionary adaptations and the functional connections between genotype and phenotype. This seminar is designed to investigate and critically evaluate foundational and novel research in humans, non-human primates and other organisms that employs the tools of these trades. In doing so, students are exposed to an integrative perspective upon which to explore classic and modern questions in functional biology. In the context of different course modules, students will be exposed to a series of guest lectures by world renown experts in the field of functional genomics and genetics

This course is divided into several different modules, each of which focuses on different genetic and genomic approaches to study organismic functional biology. These modules are:

-DNA, sequencing, and comparative genomics
-Human variation and functional genetics/genomics
-Comparative primate transcriptomics
-Gene regulation, epigenomics, and epigenetics

Course Content:
This is a partially "flipped" course. That means there will be approximately ***3 hours of live, in-class activities per week*** (1.5 hours on Tuesday and Thursday) devoted to discussions, in-depth instruction, special guest presentations, labs and team work on research projects. ***Lectures will be pre-recorded*** and (along with readings) should be ***viewed/read prior to each live class session***. Guest lectures will not be pre-recorded, but live and recorded on the dates listed. Nearly all of these guest lectures will be through Zoom, with links provided at a later date. They will then be uploaded to the course website and google drive. Lectures and readings will be posted a few weeks ahead of time to give you enough time to

watch the materials before class. See the course schedule (below) for more detailed information and topics.

Course Requirements:
(1) Attendance is mandatory. Each student is permitted to miss two class days, after which a letter grade (10% points off of final course grade) will be deducted for every additional class missed. For students missing more than two classes due to extenuating circumstances (illness, especially COVID-19, death in the immediate family, etc.), proper documentation is required (e.g., doctor's note, etc.).

(2) Since this a seminar course, it could at times involve considerable discussion and interrogation of current issues in genetics and genomics. Thus, active participation is required and will be used to assess student performance. I will make sure to use breakout sessions to help encourage discussion/collaboration and also gauge participation.

(3) There are two (2) quizzes that will count for 20% of the final grade (10% each). These will be distributed to the class prior to the day they are due. You are not permitted to work with another person on these two quizzes. These quizzes are geared towards evaluating your understanding of material covered in the lectures prior to the quiz date.
Quiz#1 will be sent to you via email on 2/14/23 right after class, and it will be due before class on 2/21/23.
Quiz#1 will cover materials from the first day of class up to the day the quiz is handed out.
Quiz#2 will be sent to you via email on 4/4/23 right after class, and it will be due before class on 4/11/23.
Quiz#2 will cover materials starting after Quiz#1 handout date to the day the quiz is handed out.

(4) There are two (2) short writing homework exercises assigned throughout the semester. Each assignment consists of a one-page, single-spaced abstract on one of the selected readings for the specific week (listed in red and with an asterisk on the course calendar). Details of these assignments are provided in the "HEB1451 Short Writing Assignments" document provided on the course website. Each assignment is due at the beginning of the class. These two assignments count for 10% of the final grade (5% each). These assignments are geared towards teaching concise scientific writing and serve to enhance class discussion. Each assignment is graded on how well the student demonstrates comprehension and synthesis of the selected papers, and on how they convey this understanding in a concise, intelligible manner. Points will also be deducted for improper citation, grammar, and spelling. Writing Assignment #1 will be due on 2/7/23, while Writing Assignment #2 will be due 2/28/23.

(5) The is one group presentation (approximately mid-way through the course on 3/7/2023) where students working in pairs will present live in class on a recent functional genomics, genetics, or bioinformatics technology of interest or application of such technology to trait and/or disease studies. This will consist of a presentation for 10 minutes which will be handed in as well. Details of this assignment is provided in the "HEB1451 Technology Presentation Assignment" document provided on the course website.

(6) Each student is required to give a presentation on the bioinformatics research portion of their "Final Paper" highlighting the genomic and biological exploration of their work. The details of this assignment are provided in the "1451 Bioinformatics Presentation" document provided on the website. This presentation should be approximately 15 minutes in length and provide background, analysis, and conclusions. It constitutes 15% of the final grade. This presentation will be on 4/25/23.

(7) There is one final 15-20+ page paper due during Finals Period. The details of this assignment are provided in the "HEB1451 Final Paper Assignment" document provided on the website. This assignment focuses on a research project involving either the collection of genetics/genomics data from computational and/or experimental datasets, or an intensive topical review. The instructor must approve each student's topic by 3/2/23, listed in the course calendar below. Plus, there is a general paper outline due by 3/30/23, listed in the course calendar below. This paper constitutes 35% of the final course grade. The final paper is due by 5/11/2023 by 11:59pm.

Thus, the evaluation criteria for the final course grade are as follows:

- Class Participation 10%
- Two quizzes 20%
- Two 1-page Short Writing Assignments 10%
- One 10 minute Group Presentation 10%
- Final Bioinformatics Presentation 15%
- Final Paper Assignment 35%
- Attendance: 10% off final grade per missed class.

Grading Statement:
All assignments are graded on a sliding curve. Extra credit is not available for this course. Thus, it is imperative that the student stays on top of the reading and exercises, and that office hours are attended when necessary.

Grades will be assigned as follows:
A = 90-100%; B = 80-89%; C = 70-79%; D = 60-69%; F < 60%
(with minus and plus grades assigned at appropriate cutoffs).

Late Work:
Quizzes, writing assignments, and final project papers must be completed by the assigned time in order to receive credit. Extensions of time may be requested from the course faculty for quizzes and written work. Such requests need to be made ***prior*** to the deadline and are at the discretion of the instructor. *Please note:* for any joint research project work, requests should be made in collaboration with all team members where possible. Work submitted late without prior approval will be penalized -10% per day.

Required Readings:
There is not a textbook for this course, although at times some lecture materials may be drawn from "Introduction to Genomics" by Arthur Lesk, Second edition, 2012, Oxford University Press, Paperback, ISBN: 978-0-19-956435-4, "Bioinformatics and Functional Genomics" by Jonathan Pevsner, Third edition, 2015, Wiley Blackwell Press, ISBN: 978-1-118-58178-0 or required articles for each week. The required articles are listed in the calendar portion of this syllabus and pdfs for each article are downloadable from the course website. These articles serve as the basis for each "Short Writing Assignment" and therefore they should be downloaded at least the week before. One article will typically be assigned each week and specifically chosen as it relates to the work conducted by any of the guest lecturers. If there are issues with downloading these articles, it must be brought to the instructor's attention at least one week prior to the assignment due date. The textbook can be used to supplement classroom lectures and discussion, and provide a different context for learning select materials in the course. All readings should be completed before arriving to class on the day they are listed, as they will be the subject of lecture and discussion, and of course, the writing assignments due that day.

Virtual Classroom and Laboratory Etiquette:
At times our course will be conducted through Zoom. Help make this an intellectually friendly and productive environment by respecting others on the virtual online Zoom class. Along these lines:

(1) Please login and "arrive" on time and read all assigned materials before the start of each class.
(2) Before class begins turn off your cell phones and other computer related apps that may disrupt your or other student learning.
(3) Given the partial nature of this online course, it is important that during class session you do not text, instant message, or surf the web.
(4) Please, also mute yourself using the mute microphone function in Zoom and unmute or press the space bar (to unmute) to ask questions and make comments during in class discussion. You can also raise your hand in the participants tab in Zoom and we will acknowledge it.
(5) Please, never interrupt someone speaking in class, so please give some time (10 seconds or so) after someone finishes speaking to make a comment. This 10 second pause will help with delays due to connection issues. .

Disabilities:
Students needing academic adjustments or accommodations because of a documented disability must present their Faculty Letter from the Accessible Education Office and speak with the instructor by the end of the second week of the term. Failure to do so may result in the instructor's inability to respond in a timely manner.

Academic Integrity:
All Harvard University policies regarding ethics and honorable behavior apply to this course. As this is an online course, all mid-semester graded materials (quizzes, abstracts) must result from your sole effort. You may not work with anyone else on these assignments and use your class notes and readings to answer each question. On the other hand, for your final project, students will be encouraged to work with members of their team (if assigned) in both the analytical and writing portions of the project. For any /quiz/lab/writing project including the final project, any material or ideas obtained from other sources (e.g., information acquired from the web) must be supported by a legitimate source reference (i.e., from a peer reviewed article or book). Plagiarism will not be tolerated; that is, the student must not appropriate the writing of others and present it without citation to a refereed academic source. With that in mind, the student also cannot simply regurgitate ideas espoused by others, but must generate theses that are innovative, novel, and reflect the synthesis of ideas generated through learning from multiple sources. For more information on plagiarism follow the rules and guidelines found in the Student Handbook at http://handbook.fas.harvard.edu/icb/icb.do. If deemed necessary, student material can be checked for plagiarism on www.turnitin.com. Students violating these simple policies will receive a failing course grade and the issue will be forwarded to the Harvard College Honor Council for further inquiry.

Computer Resources:
During the course, there are training sessions involving the use of bioinformatics and genomic databases/ browsers. It will be helpful for each student to bring a laptop to class. For students desiring to perform their own genomic level analyses, access and server space will be provided. Each student will be instructed on setting up a UCSC session during the genome browser tutorial portion of this course.

If you would like to use Geneious for examining sequence data, please download a copy of Geneious by following these steps:
(1) The software is actually downloaded directly from Geneious (www.geneious.com)
(2) After installation is complete, select "use license server"
(3) Specify server name as: rclic1.rc.fas.harvard.edu
(4) Specify port: 27004
This software can be run from within the sciences, if using this from off
campus, a VPN connection would be necessary. Please let me know if you are having difficulty downloading this software.

Date	In class activity (Live)	Preparatory Lectures/Readings/ File Locations (in "Readings" and "Presentations")	Lecture	Assignments
1/24/23 Week 1	Genotype/Phenotype	Bradley & Lawler, 2011 Lesk, pages 42-47	TC1	None
1/26/23 Week 1	Introduction to Primates	No Readings	TC In-class	None
1/31/23 Week 2	Human Genome Project: DNA, Sequencing, Assembly, & Annotation	Lesk, pages 4-10; 80-90; 90-104	TC2	None
2/2/23 Week 2	Genome Browsers 1 Final Project Discussion **GO OVER SHORT WRITING ASSIGNMENT**	Pevsner, pages 49-59 Kent et al., 2002 (skim) Gonzalez et al.., 2020 (skim)	TC2supp. (ppt only)	None
2/7/23 Week 3	Human Variation, Population Genome Projects, and Their applications **GO OVER TECHNOLOGY PRESENTATIONS and ASSIGN GROUPS: 3 groups of three.**	Lesk, pages 52-58 Birney & Soranzo, 2015 *Simons Genome Diversity Project, 2016 *Estonian Genome Diversity Project, 2016	TC3	DUE: Short Writing Assignment #1
2/9/23 Week 3	**VIRTUAL CLASS: Guest Lecture**: Dr. Omer Gokcumen: Copy Number Variation	Saitou et al., 2021	OM3	None
2/14/23 Week 4	Comparative Genomics 1: Introduction	Pevsner, pages 937-940	TC4	Quiz#1 Handed Out (Due 2/21/23 before class)
2/16/23 Week 4	Genome Browsers 2 Final Project Discussion	No Readings	TC2supp. (ppt only)	None
2/21/23 Week 5	Comparative Genomics 2: Broad Phylogenetic Trends	Zoonomia Project, 2020	TC5A	Quiz#1 Due (before class)
2/23/23 Week 5	Comparative Genomics 3: Coding Mutations In Primates	Lesk, pages 143-146 Varki & Altheide, 2005	TC5B	None
2/28/23 Week 6	Comparative Genomics 4: Non-Coding Mutations in Primates CRISPR-Cas9 Editing	*McLean et al., 2011 *Prabhakar et al., Multiple.	TC6	DUE: Short Writing Assignment #2
3/2/23 Week 6	**VIRTUAL CLASS: Guest Lecture**: Dr. James Xue: Functional Assessment of Non-Coding Sequences	Griesemer, Xue, Reilly et al, 2021	JX6	Final Topic Approval Due
3/7/23 Week 7	Group Technology Presentations	No Readings	Students	Group Presentations
3/9/23 Week 7	Functional Genomics 1: Comparative Primate	Lesk, pages 265-287, 292 Pevsner, pages 433-436;	TC7	None

	Transcriptomics	450-459; 460-465; 635-638. Khrameeva et al., 2020		
3/14/23 Week 8	Spring Break	No Readings	N/A	None
3/16/23 Week 8	Spring Break	No Readings	N/A	None
3/21/23 Week 9	**VIRTUAL CLASS:** Functional Genomics 2: Regulatory Control of Gene Expression	Gilbert 34-53	TC9	None
3/23/23 Week 9	**VIRTUAL CLASS: Guest Lecture**: Alexander Weitzel: Comparative Differential Gene Expression	Saxena et al., 2021	AW9	None
3/28/23 Week 10	**VIRTUAL CLASS: Guest Lecture:** Dr. Craig Lowe: Functional evolution of brain	Mangan et al. 2022	CL10	None
3/30/23 Week 10	Functional Genomics 3: Encode Project, Roadmap Epigenome Project, & eQTLs	Rivera and Ren, 2013	TC10	Final Project General Outline Due
4/4/23 Week 11	**VIRTUAL CLASS: Guest Lecture:** Dr. Alex Pollen: Cis-Regulation of Brain Development	Pollen et al., 2019	AP11	Quiz#2 handed out (due before class on 4/11/23)
4/6/23 Week 11	**Final Project Time**	No Readings	N/A	None
4/11/23 Week 12	**VIRTUAL CLASS: Guest Lecture:** Dr. Pushpanathan Muthuirulan: Uncoupling GWAS Variants	Muthuirulian et al. 2021	PM12	Quiz#2 Due (before class)
4/13/23 Week 12	**VIRTUAL CLASS: Guest Lecture:** Daniel Aldea, Regulatory Variants in Human Evolution	Aldea et al., 2021	DA12	None
4/18/23 Week 13	**VIRTUAL CLASS: Guest Lecture:** Dr. Michael Dannemann – Assessing the Regulatory Impacts of Neanderthal Variation	Dannemann et al., 2022	MD13	None
4/20/23 Week 13	**Final Project Time**	No Readings	N/A	None
4/25/23 Week 14	Student Bioinformatics Presentations	No Readings	Multiple Presentations	DUE: Student Bioinformatics Presentations

5/11/23	Final Paper Due	No Readings	N/A	Final Paper Due by 11:59pm

Resource Websites and Browsers:

Keeping track of genomes:
http://genomesonline.org/cgi-bin/GOLD/index.cgi

1000 genomes project website: http://www.1000genomes.org/

Blast: http://blast.ncbi.nlm.nih.gov/Blast.cgi

http://blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=blastn&BLAST_SPEC=TraceArchive&PAGE_TYPE=BlastSearch&PROG_DEFAULTS=on

CMS browser (selection): http://www.broadinstitute.org/mpg/cmsviewer/

ENCODE: https://genome.ucsc.edu/ENCODE/
http://www.genome.gov/10005107
http://www.encodeproject.org/ENCODE

Mouse ENCODE: http://www.mouseencode.org

Ensembl: http://www.ensembl.org/index.html

Epigenomics Roadmap: http://www.roadmapepigenomics.org/data

HGP website: http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml

HGDP Selection Browser: http://hgdp.uchicago.edu/cgi-bin/gbrowse/HGDP/

HAPMAP: http://hapmap.ncbi.nlm.nih.gov/

HaploReg: http://www.broadinstitute.org/mammals/haploreg/haploreg.php

Haplotter: http://haplotter.uchicago.edu/

UCSC Genome Browsers:
Main - https://genome.ucsc.edu/
Test - http://genome-test.cse.ucsc.edu/

UNIPROBE (TF predictions): http://the_brain.bwh.harvard.edu/uniprobe/

Vista Alignment: http://genome.lbl.gov/vista/index.shtml

Vista Enhancer Browser: http://enhancer.lbl.gov/

Additional software resources from lab/company pages:
http://pritchardlab.stanford.edu/software.html
http://kingsley.stanford.edu/Lab_Protocols.html
http://bejerano.stanford.edu/resources.html
http://web.mit.edu/manoli/
http://bustamantelab.stanford.edu/software.html
http://giladlab.uchicago.edu/Data.html
http://132.239.197.19/bli/mouse/hi-c/index.html
http://www.sanger.ac.uk/resources/software/genevar/
http://www.hsph.harvard.edu/liming-liang/software/eqtl/
http://www.ncbi.nlm.nih.gov/pubmed/22693428